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The three campuses of the Mayo Graduate School provide an advanced clinical and research training environment for conducting an integrated, multidisciplinary, predoctoral training program based in the study of cell and molecular biology of breast cancer. Thirty-two full-time faculty members currently participate in Mayo's didactic tumor biology training curriculum which supports the training of postdoctoral trainees in NCI sponsored postdoctoral training programs at Mayo. This strong multidisciplinary tumor biology curriculum provides the foundation for the didactic component of a specialized predoctoral training program in breast cancer. The development of this new training program has been facilitated through the development of two new graduate courses in the cell and molecular biology of breast cancer, as well as through the initiation of a new journal club and an intramural research workshop for trainees in this training program. The research training component of this new predoctoral track is laboratory-based and is fostered by Mayo's highly competitive and interdisciplinary research environment and by the heightened interest in breast cancer research stimulated through the recent development of the Mayo Women's Cancer Program within the Mayo Cancer Center.

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Victor J. Marchi 7/29/96

PI - Signature Date

Biology of Breast Cancer: A Predoctoral Training Program

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Annual Report DAMD17-94-J-4116

This revised annual report is submitted in response to the critique of our earlier submission dated September 1996, for **DAMD17-94-J-4116**, entitled the "Biology of Breast Cancer Predoctoral Training Program". In this revised report we present documentation for the successful establishment of the Biology of Breast Cancer Predoctoral Training Program at the Mayo Clinic through the body of the report, below, and a series of detailed tables and appendix materials that follow the text, as well as a supporting letter from Dr. Franklyn Prendergast, Director of the Mayo Cancer Center (Appendix exhibit A). Presently there are seven predoctoral trainees participating in this program, including two from underrepresented minorities. In addition, one trainee recently has completed the program and received the Ph.D. degree (see Table I). Herein we address the issues raised in the earlier critque, and detail progress on the six specific tasks that were proposed in the original application:

- **Task 1:** Organize Biology of Breast Cancer Predoctoral Training Program faculty and curriculum.
- **Task 2:** Establish new courses in specialized aspects of tumor biology, emphasizing the cell and molecular biology of breast cancer.
- **Task 3:** Establish appropriate mechanisms for student recruitment into this new training program.
- **Task 4:** Implement the new Biology of Breast Cancer Predoctoral Training Program curriculum.
- **Task 5:** Assess student progress.
- **Task 6:** Assess Biology of Breast Cancer Predoctoral Training Program effectiveness and formalize assessment in a written report.

PROGRAM PROGRESS

Task 1, "Organize Biology of Breast Cancer Predoctoral Training Program Faculty and Curriculum," is addressed in the following section:

The Biology of Breast Cancer Predoctoral Training Program is a multidisciplinary predoctoral training program in the biology of cancer. The focus of the Biology of Breast Cancer Predoctoral Training Program is to provide an educational environment that stimulates excellence in scientific thought and training while simultaneously providing exposure to all of the major fields of study relevant to tumor biology. Our goal is to provide students in the Biology of Breast Cancer Predoctoral Training Program with a solid and uniquely multidisciplinary knowledge base in the current study of cancer. A second goal of this program is to stimulate new working alliances between students and staff participating in breast cancer related research, education, and clinical endeavors within the Mayo Cancer Center. Research and training in the Biology of Breast Cancer Predoctoral Training Program is broadly focused on gene regulation, cell cycle control, cancer genetics, oncogene and tumor suppressor action, tumor immunology, signal transduction, antitumor pharmacology, and the application of this information to biology of breast, ovarian and uterine cancers. Students participate in laboratory-based research, as well as in a formal tumor biology curriculum that integrates current concepts in cell growth control with the natural history of human tumors.

Qualifications of the Program Directors

Dr. Nita J. Maihle, Associate Professor in Tumor Biology and Associate Director for Basic Research in the Mayo Cancer Center is Director of the Biology of Breast Cancer Predoctoral Training Program. Dr. Maihle has participated in the recent re-organization of the tumor biology curriculum and is a well qualified tumor biologist with extensive experience in the training of pre- and postdoctoral fellows. She has an ongoing and productive breast cancer-related research program, and is the Principal Investigator of two NCI-funded RO1 grants. As Associate Director for Basic Research in the Mayo Cancer Center, Dr. Maihle plays a key role in facilitating the coordination, implementation, and funding of a substantial portion of the basic research in cancer biology at the Mayo Clinic. Dr. Maihle is also in her final year as a charter member of the NIH Cell Biology and

Physiology Study Section (Subcommittee 2) which has its primary responsibility in the review of RO1, R29, R23 and RCDA applications. Thus, Dr. Maihle brings significant administrative experience and a broad persepctive to this predoctoral training program. She devotes 10% of her effort to the administration of this training program. Her primary responsibilities are to: 1) oversee recruitment and selection of Ph.D. candidates, 2) to monitor the overall direction of the program and to ensure the equitable selection of trainees, 3) to monitor and ensure the progress of all trainees through periodic review with both trainees and their mentors, 4) to coordinate all courses, journal clubs, research seminars, and other activities of the Biology of Breast Cancer Predoctoral Training Program, 5) to provide trainees with advice on potential problems or conflicts, and 6) to prepare progress reports for institutional and DAMD review, and to participate in the institutional assessment of the success of this training program. In addition, Dr. Maihle serves as the principal liaison to the Mayo Cancer Center, to coordinate and fully integrate the activities of the Biology of Breast Cancer Predoctoral Training Program with those of the Mayo Cancer Center. Dr, Maihle also is responsible for coordinating several of the course offerings in the Biology of Breast Cancer Predoctoral Training Program, including the "Origins of Human Cancer", "Growth Factors, Oncogenes and Tumor Supressors", and "Current Topics in Tumor Biology" (with Dr. Salisbury).

Dr. Jeffrey L. Salisbury, Professor of Biochemistry and Molecular Biology and Education Coordinator of the Mayo Biology of Breast Cancer Predoctoral Training Program, is a member of the Mayo Cancer Center's Advisory Committee. As Co-Director of the Biology of Breast Cancer Predoctoral Training Program, Dr. Salisbury devotes 10% of his effort to administration of the Biology of Breast Cancer Predoctoral Training Program and participation in its activities. Dr. Salisbury was appointed to the Mayo Graduate School staff in 1989. Prior to his appointment at Mayo he was an Associate Professor of Neuroscience, Anatomy, and Oncology in the School of Medicine at Case Western Reserve University (Cleveland OH), and prior to that he was an Assistant Professor of Anatomy and Structural Biology at Albert Einstein College of Medicine (Bronx, NY.) Dr. Salisbury is a well-qualified Molecular/Cell Biologist with extensive experience in the training of pre- and postdoctoral students. He has served on the National Education Committee of the American Society for Cell Biology (two consecutive 3 year terms), and is currently a member of the Mayo Graduate School Education Committee. He conducts an established, cancer-related research program with long-standing emphasis on centrosome dynamics during the cell cycle, and more recently on hypertrophic centrosomes in breast tumor cells. Dr. Salisbury brings a broad perspective on graduate training to the Biology of Breast Cancer Predoctoral Training Program. His primary responsibilities include oversight of student recruitment, student progress, and coordination within the Biology of Breast Cancer Predoctoral Training Program curriculum. He works closely with Dr. Maihle in these efforts. In addition, Dr. Salisbury is responsible for coordinating several of the course offerings in the Biology of Breast Cancer Predoctoral Training Program, including "Principles of Cell and Tissue Design", the "Cell Biology of Cancer", and "Current Topics in Tumor Biology" (with Dr. Maihle).

Program Faculty

Qualifications of the Program Faculty

The Biology of Breast Cancer Predoctoral Training Program faculty consists of a training faculty of 13 full and 4 associate members and an affiliated teaching and resource faculty of approximately 25 additional members drawn from seven different departments (see Table II for a list of Full and Associate Members, and exhibit B: Peterson's Guide listing of all program faculty). While individual faculty are associated with traditional discipline-based departments (such as Biochemistry, Molecular Biology, Experimental Pathology, Pharmacology, etc.) the administrative structure of the Biology of Breast Cancer Predoctoral Training Program is that of an interdisciplinary programmatic unit. This programmatic structure reflects the interdisciplinary nature of the major research and academic efforts of the associated faculty.

Stringent criteria for participation of faculty as full or associate members in this training program have been established to ensure both a research training focus in the area of cancer biology, as well as academic excellence. Criteria used to identify full faculty members in the Biology of Breast Cancer Predoctoral Training Program include:

- Members of the training faculty with "**Full**" status will have an established track record of accomplishment in biomedical research as demonstrated by significant publications of high scientific merit, excellence, and innovation. These investigators also have consistent records of extramural funding in support of their research programs (see Table III: Research Support).
- The collective interests of this training faculty are quite broad, but show direct cancer relevance. These interests include: cell signalling, cancer genetics, gene regulation, tumor immunology, oncogene and tumor suppressor action, cell cycle regulation, tumor virology, gene therapy, hormone responsiveness, and molecular cytology. All training faculty must be members of the NCI-designated Mayo Cancer Center.
- In addition to having an established track record of scientific excellence, the minimum requirement for all investigators to be included as full members of this training program is that they must have mentored at least one Ph.D. candidate, serving in the capacity as thesis advisor, and that student must have left his/her laboratory to continue biomedical research training in a postdoctoral fellowship position with unequivocal training potential in a high quality academic environment.
- In addition to the criteria outlined above for full members of this training program, four of the Biology of Breast Cancer Predoctoral Training Program Faculty are designated as "**Associate**" status, based on their more limited research and/or training experience (see Table II). In each case, however, these individuals have already distinguished themselves through their research contributions and their interpersonal skills as faculty members with outstanding mentorship potential. Therefore, only a few select faculty have been chosen for this category. Biology of Breast Cancer Predoctoral Training Program Associate membership status requires that the program member has demonstrated clear potential to successfully mentor Ph.D. candidates in the Biology of Breast Cancer Predoctoral Training Program through excellence in their scientific publications, their cancer research focus, and active participation in Biology of Breast Cancer Predoctoral Training Program educational activities. Associate members have teaching and examining privileges in the Biology of Breast Cancer Predoctoral Training Program curriculum, and may co-advise (with a full faculty member) Ph.D. candidates in their laboratory.
- Finally, an "**affiliated**" faculty of approximately 25 members, drawn from both clinical and basic science departments also contribute to the Biology of Breast Cancer Predoctoral Training Program through participation in a variety of relevant educational activities and as clinical instructors. These affiliated faculty may serve as advisory members of qualifying exam and thesis committees, however, they may not serve as research mentors for students who matriculate into the Biology of Breast Cancer Predoctoral Training Program (see Appendix exhibit B for a complete listing of affiliated members).

Administrative Structure

The Biology of Breast Cancer Predoctoral Training Program is administrated overall through the Mayo Graduate School, and is closely allied with the Mayo Cancer Center. Day-to-day program administration operates largely through the Director (Maihle) and Co-director (Salisbury), and the Tumor Biology Education Committee (Drs. Salisbury, Maihle, Jelinek, Tindall, and Federspiel, and a trainee, Mr. J. Baines). The Tumor Biology Education Committee meets regularly (every two months) to discuss student recruitment, student progress, and coordination within the Biology of Breast Cancer Predoctoral Training Program curriculum. In addition, the Directors of the three cancer-related training grants (Drs. Salisbury, Maihle, Getz, and David) and the Director of the Mayo Cancer Center (Dr. Prendergast) meet regularly (every 6-8 weeks) to discuss ongoing programs and activities related to cancer research and education. The entire Tumor Biology Training faculty interact frequently through courses, journal clubs, and research workshops, and meets twice a year to discuss administration and ongoing activities of the Biology of Breast Cancer Predoctoral Training Program.

Task 2, "Establish new courses in specialized aspects of tumor biology, emphasizing the cell and molecular biology of Breast cancer and Task 4, "Implement the new Biology of Breast Cancer Predoctoral Training Program curriculum," are addressed in the following section:

Biology of Breast Cancer Predoctoral Training Program Curriculum

We have established and implemented a broadly based curriculum in Tumor Biology at the Mayo Clinic. The Biology of Breast Cancer Predoctoral Training Program curriculum includes didactic course work, journal clubs, research seminars and clinical activities. Students who matriculate into the Biology of Breast Cancer Predoctoral Training Program must meet the general course requirements of the Mayo Graduate School in which a minimum of 13 credits are required from the Graduate School Core Curriculum. Students must also complete at least 20 credits from the didactic Tumor Biology required and elective course curriculum. The Mayo Graduate School core curriculum courses are selected from at least two areas with a minimum of three credits from each area. A student's program of core courses is individually developed in consultation with his/her advisor. Credits derived from seminars and journal clubs are not permitted as core course requirements. Tumor Biology students generally select core courses from the following list of core offerings:

Mayo Graduate School Core Course Offerings (credits)

Principles of Cell & Tissue Design (3)
General Biochemistry (series of 3 x 3 credit courses; total 9)
Introduction to Molecular Biology (3)
Molecular Biology Theory and Application (3)
General Pharmacology (series of 3 x 3 credit courses; total 9)
Basic Graduate Immunology (3)
Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research (1)
(This course is required for all Mayo graduate students and postdoctoral fellows.)

The academic curriculum of the Biology of Breast Cancer Predoctoral Training Program also includes track requirements(*) and elective courses, as outlined below:

Tumor Biology Track Course Offerings (Credits)

*Tumor Biology I: Introduction to Tumor Biology (3)
*Tumor Biology II: Origins of Human Cancer (3)
*Tumor Biology III: Growth Factors, Oncogenes, and Tumor Suppressors (3)
*§Current Topics in Tumor Biology (1) (see listing, Appendix exhibit C)
*Research Seminars in Tumor Biology (1)
*Cell Biology of Cancer (3)
*The Business of Science and the Science of Business (1)
Biology of Pancreatic Cancer (1)
*Biology of Breast Cancer (1)
¶Biology of Gastrointestinal Tumors (1)
¶Biology of Haematopoietic Cancers (1)
¶Biology of Prostate Cancer
Gene Therapy and Cancer (1)
Cytogenetics (2)
Cytology Laboratory
Introduction to Statistical Models (1)
Introduction to Clinical Epidemiology (1)
Design of Clinical Studies (1)
AACR Course in Histopathology of Cancer (1)
Laboratory Rotations in Tumor Biology (3 required rotations, 2 credits each = 6 total)

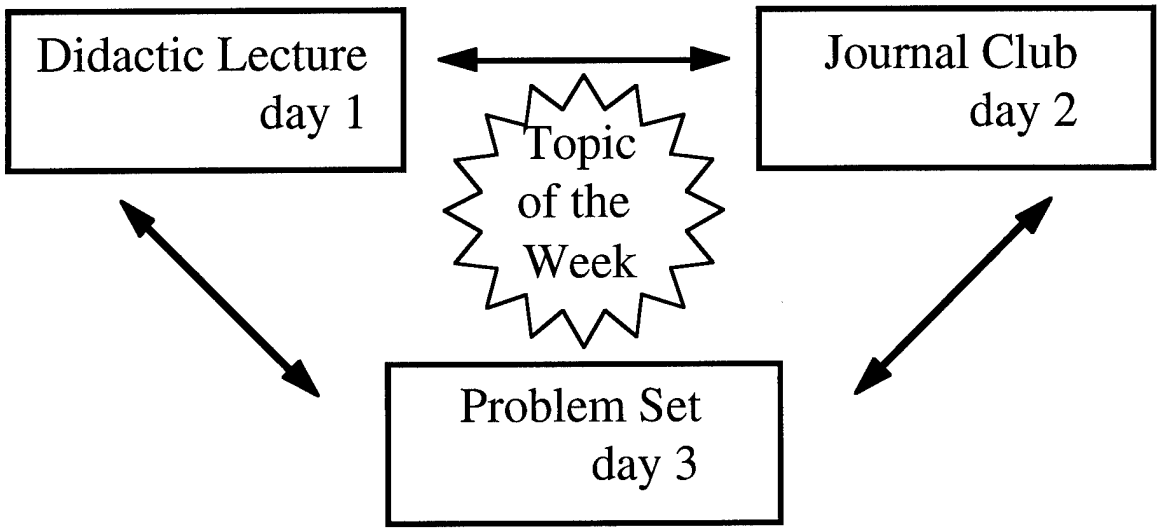
Research in Tumor Biology (Thesis Research (0))

* Course outlines for required courses are included in the Appendix exhibit C).
§ Students must register in this journal club one quarter each year, but they are expected to attend all quarters.
¶ New courses to be added to the curriculum in 1997-1998 academic years.

Additional advanced elective courses may be chosen in any area from the Mayo Graduate School Bulletin (see Appendix exhibit D) to fulfill the overall degree requirement of 42 credits. In addition, all students in the Biology of Breast Cancer Predoctoral Training Program are required to take formal classes in Radiation Safety, Animal Care and Use, and also participate in an NIH Grant Writing Workshop. These required courses are organized by various divisions and departments within the Mayo Clinic, and, therefore, are not offered for Graduate School credit (not administrated by the Mayo Graduate School).

Innovative Strategies for Teaching

The required Biology of Breast Cancer Predoctoral Training Program track courses (designated with an asterisk * above) establish a solid foundation in the first-year students' understanding of the biology of cancer and share several distinguishing and innovative strategies for teaching which enhance learning and student/faculty participation. For example, Tumor Biology I, II, III, and the Cell Biology of Cancer are given as a series during the first four consecutive quarters following matriculation. Individually, these courses meet three times per week with an overview and historical review of a selected topic(s) for the current week presented in a didactic lecture format during the first class session. This is followed by a student presentation of a current or historically relevant research paper(s) in the area of the week's topic during the second class session using the journal club format. Finally, a round table problem set discussion focuses on questions and problems relevant to the week's topic during the third class session. The research paper presentation and round table problem set discussions enhance the effectiveness of these courses through the direct involvement of students in learning, information processing, and application of information to problems within the framework of the week's topic(s). These sessions allow students to organize and categorize information into meaningful units and to 'discover' novel relationships and extract and assimilate important points in an interactive and participatory manner. In this way, students are accountable for the assimilation of new information on an ongoing basis, they are intellectually challenged, and they are required to apply newly gained knowledge to relevant problem-solving exercises. A 'snap shot' example of the lecture materials, journal club papers, and problem set for one unit from the introductory course Tumor Biology I is provided in the Appendix (exhibit D).



Instruction in the Responsible Conduct of Research

All graduate students and postdoctoral fellows are required to formally register for and participate in a one credit hour series of presentations and discussions on the responsible conduct of research, scientific integrity, and ethical principles in research (ETHIC 5000: Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research). This course meets one hour per week during the summer quarter (10-12 sessions) and is taught by faculty of the Mayo Graduate and Medical Schools, including Tumor Biology Faculty. A course outline for the most recent year is presented in the Appendix (exhibit C). Specific topics covered in this course include:

- Perspective on Ethical Conduct of Biomedical Research
- Scientific Fraud and its Consequences
- Authorship
- Data Storage and Ownership
- Emerging Issues in Electronic Data Acquisition, Storage and Publishing
- Collection and Interpretation of Data
- Conflict of Interest
- Use of Animals in Research
- The Thermodynamics of Money
- Use of Humans in Research
- Recombinant DNA Research

In addition, a second one credit hour Tumor Biology course (TBio. 5300: Business of Science and Science of Business, see Appendix exhibit C) addresses selected ethical issues in biomedical research. This course is required for all Tumor Biology Trainees. Of special interest in regard to ethical issues covered this past year in TBio. 5300 was a unit on Integrity and Misconduct in Research and a case study on industry funding of drug development and inappropriate pricing of essential drugs (i.e., the Mortel/Levamisole controversy).

Both of these courses include 10-12 weekly didactic lectures followed by round table discussions of the the relevant topic of the day. Class sessions are well attended by faculty, and senior graduate students and fellows, in addition to the graduate students and postdoctoral fellows who are formally registered for the course.

Continuing Education

Senior students who have already completed the formal course requirements, and postdoctoral fellows who are supported by other cancer-related training grants register for graduate credit and attend the journal club sessions which are integral to the required Biology of Breast Cancer Predoctoral Training Program courses. In this way, these trainees contribute to the critical mass of the class, they also enhance the multidisciplinary nature of the discussions, and through this mechanism these trainees revisit current topics in cancer biology during their advanced training years. In this manner, advanced trainees have the opportunity to reinforce key concepts as well as to remain current with regard to advances in the rapidly developing areas of cancer biology. Likewise, the Biology of Breast Cancer Predoctoral Training Program faculty and their key laboratory personnel actively participate in these regular weekly journal club sessions. Interactions among training faculty and stimulating scientific discussions are further encouraged through a monthly Tumor Biology Tea (tea, coffee, pop, and cookies) immediately following selected journal club sessions.

Integration of the Clinical Perspective

The Biology of Breast Cancer Predoctoral Training Program is designed to give the trainee a broad and well-rounded understanding of cancer from both the basic science and clinical perspectives. Integration of the clinical activities of the Mayo Cancer Center (see support letter from Dr. Franklyn Prendegast, Director of the Mayo Cancer Center, Appendix exhibit A) into the training program of Tumor Biology trainees is achieved in at least six different ways.

- First, clinical fellows and residents from a broad spectrum of cancer relevant programs (e.g., oncology hematology/oncology, orthopedic research, gynecologic oncology, pediatric oncology, etc.) formally enroll and participate in Biology of Breast Cancer Predoctoral Training Program courses and journal clubs (for example during this past academic quarter three clinical fellows were formally enrolled in Tumor Biology I, and a total of six fellows and residents regularly attended and actively participated throughout the academic quarter). Active participation by clinical residents and fellows adds considerably to the multidiscplinary perspective of the student body, and to class discussions.
- Second, clinical staff present didactic lectures in their areas of specialty in Biology of Breast Cancer Predoctoral Training Program courses (see selected course outlines in Appendix exhibit C). For example in the Biology of Pancreatic Cancer course, individual lectures were given by clinical staff practicing in Surgery, Medical Oncology, and Surgical Pathology. Likewise, in the Tumor Biology I course, clinical staff presented lectures in epidemiology, chemical carcinogenesis, and tumor pathology.
- Third, Biology of Breast Cancer Predoctoral Training Program trainees are required to attend Mayo Cancer Center Research Workshops ("Works in Progress," see 1996 program; Appendix, exhibit E), Mayo Cancer Center Grant Rounds (see 1996 Program, Appendix, exhibit E), and Oncology Society and Hematology Society lectures, and receive course credit for participating in these activities (TBio 5101: "Research Seminars in Tumor Biology").
- The Biology of Breast Cancer Predoctoral Training Program curriculum also is integrated with clinical practice wherever possible through special course related activities. For example, during a week this past quarter where tumor pathology and the use of clinical specimens in cancer research were the Tumor Biology I course topics, class members were taken as small groups on tours of the Surgical Pathology Suite. During these tours students observed the gross dissection of surgical specimens(including breast carcinomas), rapid freezing and cryomicrotomy, microscopic examination (via video monitors) and diagnosis by staff pathologists, and report to the OR surgeons. All surgical procedures in which cancer is suspect are subject to immediate pathological examination in this manner, while the patient is still undergoing surgery. Some samples are turned around from the OR to the Pathology Suite for diagnosis and results are communicated back to the OR in under four minutes. Needless to say, the activities in this unit are dynamic and intense, and each student group was able to observe these activities over a two-hour period, with ongoing commentary from pathology residents and staff pathologists who were performing the procedures. Similary, all Biology of Breast Cancer Predoctoral Training Program trainees are required to attend clinical rounds (at least once) with a Mayo staff member (any division or department) during their training. Direct exposure to clinical activities such as these are tremendously useful for students to understand, based on first-hand observation, the intensity, dedication, and skill involved in the clinical care and treatment of breast cancer patients. These activities also promote the involvement of our clinical faculty in Biology of Breast Cancer Predoctoral Training Program activities.
- During their senior year in the Biology of Breast Cancer Predoctoral Training Program, trainees participate in the first year Mayo Medical School curriculum by proctoring a problem set during the two weeks when cancer biology is introduced to the medical students. This activity gives Tumor Biology trainees an opportunity to interact with medical students and to gain practical experience at the instructor level.
- Finally, all Tumor Biology trainees have one or more clinical staff advisors participate as members of their Thesis Advisory Committee. Sometimes this involvement is fairly technical, e.g., participation by a Mayo Cancer Center biostatistician in study design and analysis. In other instances, however, clinical advisors may be directly involved in helping the trainee define a clinically relevant question in their system, and/or assist them with tumor specimen acquisition or data analysis. For example, as one component of Mr. Roger's

thesis, he is examining the differential expression of the calmodulin-like protein (CLP) in various histologic subtypes of human breast cancer.

Additional Academic Activities

Seminars by Students, Faculty and Invited Speakers: Extensive institutional resources support invitation of nationally and internationally recognized scientists and clinicians to Mayo. Approximately 350-400 speakers come to the Mayo Clinic campus each year. Trainees are, therefore, exposed to diverse biomedical research opportunities, and institutionally/departmentally-based research seminars throughout the year (see an example of a weekly Mayo Staff Bulletin and related Mayo Cancer Center seminars; Appendix exhibits E). In addition, students attend monthly Mayo supported dinner/research seminars given by the Research, Laboratory Medicine, Oncology, Hematology and Genetics Societies of the Mayo Clinic. These events are especially suited to interactions between students, postdoctoral fellows, and faculty in an informal yet scholarly atmosphere dedicated to scientific discussion. During each of their research years, Biology of Breast Cancer Program Trainees also present research seminars and research posters in the Mayo Cancer Center Research Retreat.

Attendance at National Research Meetings: All students are supported to attend at least one national scientific meeting each year even if they are not presenting an abstract. If they are presenting their work, attendance at additional meetings is encouraged and supported by the Mayo Foundation. Mentors take an active role in introducing their students to the professional identity and 'networking' critical to success in a biomedical research career through this mechanism. In recent years Biology of Breast Cancer trainees have attended and/or presented at the following national meetings: AACR, ASCB, FASEB, Annual Oncogene Meetings, Annual Human Cancer Meeting, Cold Spring Harbor Cancer Genetics Meetings, Salk Tyrosine Phosphorylation Meetings, and various Gordon Conferences and Keystone Meetings.

Research Training

Selection of Thesis Laboratory, Mentor, and Thesis Committee: Biology of Breast Cancer trainees typically matriculate in August and are required to complete three laboratory-based (minimum 8 weeks each) rotations during their first year. All of the full and associate faculty may serve as potential mentors for these research rotations. Selection of the thesis mentor follows completion of successful laboratory-based rotations by mutual consent of the student and mentor with the sanction of the Tumor Biology Education Committee and Mayo Graduate School Education Committee. The selection of a research laboratory coincides with the qualifying examination which consists of a written thesis proposal and its defense before a thesis committee consisting of a minimum of 4 tumor biology faculty (including the thesis advisor), a clinician, and an extramural committee member from outside the institution. Typically the clinical and extramural committee members' research specialties are related to the general area of the student's thesis topic. Following successful completion of the qualifying exam, research progress is assessed through regular Thesis Advisory Committee meetings (minimum of one Thesis Advisory Committee meeting per year). While Thesis Advisory Committee members are available for advice, technical assistance, and consultation throughout the year, these meetings provide a formal opportunity for input by the Thesis Advisory Committee on progress and experimental aspects of the thesis project. The chair of the Thesis Advisory Committee formally reports the outcome of each committee meeting in writing to the Tumor Biology Education Committee and to the Mayo Graduate School. In addition, students present their research progress in quarterly research workshops (one oral presentation per year) and in a yearly, institution wide, Mayo Graduate School Research Symposium (poster format). In addition, all Biology of Breast Cancer Predoctoral Training Program participate in the Annual Mayo Cancer Center Research Retreat (poster format).

Thesis Research: The Biology of Breast Cancer Predoctoral Training Program places strong emphasis on thesis research. All full training program faculty members have demonstrated records of research training at both the predoctoral and postdoctoral levels. The specific details of an individual student's research training plan are developed following the selection of a thesis advisor and a thesis research laboratory in

consultation with the Thesis Advisory Committee. The thesis research project must be hypothesis driven and experimental in nature and must, in addition, have a direct application to the biology of cancer.

Ph.D. Thesis: The thesis is the most important document that the Tumor Biology Ph.D. candidate prepares during the course of graduate study, and is a record of the scientific accomplishments that justify the awarding of the degree. The thesis is archival. Consequently, the Mayo Graduate School has developed standards for its format and style that are followed closely. The thesis examination consists of a formal thesis research seminar open to all members of the Mayo community followed by a meeting with the Thesis Examining Committee during which the scientific merit and accomplishments of the candidate are evaluated. Successful completion of a research thesis typically also results in two or more research manuscripts submitted for publication in peer-reviewed journals of high scientific standards.

Task 3, "Establish appropriate mechanisms for student recruitment into this new training program" is presented below:

Trainee Candidates

The curriculum and thesis research is a predoctoral training program leading to the Ph.D. degree in Biomedical Sciences. Each year, 3 to 5 students are accepted into the program for an appointment term of 4 to 5 years. The program strives for a steady state level of 12 to 16 students. Students recruited for matriculation into the Biology of Breast Cancer Predoctoral Training Program will be selected on the basis of outstanding academic credentials, a stated desire to study and conduct research in the area of breast cancer biology or related disciplines, and an assessment of individual potential by the training faculty. Many of the applicants to the Mayo Graduate School have had research experience within the Mayo system through undergraduate research internships (see below). Typically, candidates for admission to Mayo's graduate programs apply directly to the Graduate School where their academic credentials, letters of recommendation, and personal statements are placed on record. Application materials are selected for consideration by individual program educational committees based on the candidate's stated interests. For consideration for admission to the Biology of Breast Cancer Predoctoral Training Program, the applicant should:

- Hold a bachelor's degree from an accredited college or university with a minimum 3.25 grade point average on a 4.0 scale.
- Have received scores on the verbal, analytical, and quantitative aptitude tests of the Graduate Record Examination indicating a strong academic ability (i.e. above the 75th percentile), with subject tests in biology and biochemistry being highly recommended.
- Have a minimum scientific undergraduate course background (with evidence of superior performance) including: one year of physics, two years of chemistry, one year of biochemistry, and two years of upper level biology.
- Supply supporting documents including: official transcripts, official copies of GRE or MCAT scores, and three letters of recommendation.
- Applicants will be invited to visit the institution during the selection process to meet the faculty and to be introduced to the Biology of Breast Cancer Predoctoral Training Program, the Mayo Cancer Center, and the Mayo Graduate School.
- M.D./Ph.D. candidates considered for admission to the Mayo Medical/Graduate Schools will be introduced to the Biology of Breast Cancer Predoctoral Training Program and representative faculty during their interview and recruitment visits. Where interests overlap and evaluated potential are judged to be exceptional, these students will be targeted for recruitment into the Biology of Breast Cancer Predoctoral Training Program.

Applications are solicited through national mailings directed to appropriate undergraduate departments, through the Mayo home page (http://www.mayo.edu), advertisements in mainstream national scientific journals (e.g. *Nature*, *Science*), as well as journals targeted to the recruitment of minority applicants

(e.g. *Winds of Change, Black Issues in Higher Education*), the *Peterson's Guide* (cf. Appendix exhibit B), and through the Mayo Graduate School Degree Program Booklet (Appendix exhibit G).

Biology of Breast Cancer Predoctoral Training Program Minority Representation

The Biology of Breast Cancer Predoctoral Training Program has placed special emphasis on recruitment and training of underrepresented minorities. Currently the predoctoral class consists of a total of 7 students, 2 of whom are underrepresented minorities (28%, including one Native American, and one Hispanic student). In addition, two of the seventeen training faculty, including the Director of the Mayo Cancer Center, are members of underrepresented minority groups.

Minority Student Recruitment Strategy

Our success in recruiting and training minority applicants is based in large part on a concerted effort by Mayo to move aggressively forward in this area. In 1991 Mayo created an Office of Minority Student Affairs and focused significant human and financial resources on recruiting and supporting minority students. Dr. Richard McGee was recruited as Associate Dean for Student Affairs and he established the Office of Minority Student Affairs as a resource to support recruitment activities of the various departments and programs within the Mayo Graduate School. This office coordinates minority recruitment activities.

Our overall strategy for minority student recruitment is a broad-based effort aimed at both identifying potential minority applicants early in their academic career, and establishing long-term relationships with minority undergraduate schools and minority students in non-minority schools. Mayo faculty representatives (including Dr. McGee and co-PI on this application, Dr. Maihle) attend almost all national meetings which attract minority science students, including:

- MARC/MBRS national meetings
- The Society for the Advancement of Chicano and Native Americans in Science (SACNAS)
- The American Indian Science and Engineering Society (AISES)
- The Association of Minority Health Professions School (AMHPS)

Additionally, a number of individual schools with high minority enrollment are visited each year by Tumor Biology faculty. An extensive mailing list has been created with which information is sent each year to several hundred schools with high minority populations and advisors of minority students at non-minority schools.

Minority Undergraduate Summer Research Programs

Special emphasis is placed on identifying and recruiting students from underrepresented minority groups through the Mayo Minority Scholar Program (MMSP) and the Summer Undergraduate Research Fellowship (SURF) program. These research programs recruit and support students from around the U.S. for a 10-12 week summer laboratory-based research experience. Interest in this program has grown tremendously; for the summer of 1996, nearly 1000 students applied, including 300 underrepresented minorities. Sixty fellowships were awarded including 27 to minority students. Through these mechanisms Mayo staff often know and culture individual minority students for several years prior to their matriculation into a graduate program or the Medical School. Thereby Tumor Biology staff members are able to establish a relationship with individual minority applicants well in advance of their matriculation and they are able to assist in the transition to Mayo and Rochester.

Task 5 "Assess student progress", and Task 6, "Assess Biology of Breast Cancer Predoctoral Training Program effectiveness and formalize assessment in a written report," are addressed together, below:

Student progress is monitored on an ongoing basis by their performance in individual courses, journal clubs, qualifying exams and Thesis Advisory committee meetings. The overall mechanism for evaluation effectiveness of this new training program are detailed below.

The Biology of Breast Cancer Predoctoral Training Program is scheduled for an extramural program evaluation during early 1998 (see original application) in anticipation of a 1998-1999 campus-wide review of the institution's educational programs, and its accreditation by the North Central Association of Colleges and Schools. For this review, we will solicit an External Review Committee (4 members) to evaluate the success of the Biology of Breast Cancer Predoctoral Training Program and to make suggestions for its improvement and continued progress. Members of the External Review Committee will be selected based on their demonstrated expertise in breast cancer research and their experience in graduate education. Two individuals have already been contacted regarding their willingness to serve in this capacity (i.e., Dr. Mary Claire King, Dr. Mina Bissell), and two other potential reviewers have recently been contacted, but have not yet confirmed their willingness to participate. The External Review Committee will report directly to the Mayo Graduate School Education Committee. Following the initial External Review Committee report, this committee will be asked to meet at three to four year intervals to monitor the continued progress of our training program. Proposed short-term and long-term criteria to be used to evaluate the success of this training program will include assessment of both past trainee success, and ongoing program activities including the curriculum. These criteria are outlined separately below.

Trainee Evaluation

Trainee evaluation will take place at five levels and will be assessed by comparison of established and objective data relating recruitment credentials, program completion, academic performance, placement, and ultimately career achievement.

- The ability to recruit outstanding Ph.D. candidates into the Biology of Breast Cancer Predoctoral Training Program.
- Retention of these individuals and their successful completion of the program.
- Academic performance of trainees, including coursework evaluation, and consideration of reports from the trainee's Qualifying Exam and Thesis Advisory Committees.
- Success of trainees in gaining competitive postdoctoral fellowships and extramural funding in future years.
- Ultimately, the appointment of these trainees to independent research positions with evidence of ongoing research activities relevant to breast cancer will be assessed.

Curriculum and Program Evaluation

Curriculum and Program evaluation will include the eight areas listed below, as well as additional areas defined by the External Review Committee.

- Course content and appropriateness to the biology of breast cancer.
- Thoroughness of didactic and formal training in the biology of breast cancer.
- Effectiveness of teaching and examining methods and procedures.
- Vitality and effectiveness of student/faculty interactions in the academic components of the program.
- Evidence of faculty mentorship and establishment of intramural and extramural professional networks.
- Scope and role of individual faculty participation in the Biology of Breast Cancer Predoctoral Training Program.

- Integration of the clinical perspective and understanding of physician and patient concerns in the diagnosis and treatment of breast cancer.
- Overall effectiveness of the Director, Co-director, Education Committee, and of the Graduate School in administrating the Biology of Breast Cancer Predoctoral Training Program.

In preparation for the External Review Committee's evaluations, we will conduct an internal review by addressing the same criteria through the Mayo Graduate School Education Committee.

APPENDIX MATERIALS

LIST OF TABLES AND EXHIBITS

Table I. Current Tumor Biology Predoctoral Trainees

Name	Undergraduate School	GPA	GRE	Qualifying Exam
Jonathan Baines*	University of Arizona, Tucson	3.39/4.0	(MCAT 64)	to be taken
Nohelia Canales*	Mount St Mary's, Los Angeles	3.34/4.0	1690	to be taken
Greg Eley	University of Georgia	3.01/4.0	2070	to be taken
Julie Johnson	University of Wisconsin, Madison	3.38/4.0	1880	to be taken
Steve Ritland	University of Wisconsin, Eau Clair	3.54/4.0	2010	passed 12/96
Michael Rogers	Brigham Young Univ., Provo	3.66/4.0	2390	passed 06/96
Sheri Holmen	Western Michigan Univ., Kalamazoo	3.94/4.0	1700	passed 10/96
Magaret Adelsman	Mayo Clinic Graduate School			Graduated with Ph.D. 6/96

* Members of underrepresented minority groups.

TABLE II. Tumor Biology Program Training Faculty

Senior Members

Name	Departmental Affiliation	Role	% Effort
Abraham, Robert T., Ph.D.	Immunology	Training Program Faculty Member	5
Getz, Michael J., Ph.D.	Molecular Biology	Training Program Faculty Member	5
Jelinek, Diane F., Ph.D.	Immunology	Training Program Faculty Member	5
Leibson, Paul J., M.D., Ph.D.	Immunology	Training Program Faculty Member	5
Leof, Edward B., Ph.D.	Thoracic Diseases Research	Training Program Faculty Member	5
Maher, L. James III, Ph.D.	Biochemistry	Training Program Faculty Member	5
Maihle, Nita J., Ph.D.	Molecular Biology	Co-Director and Faculty Member	10
Prendergast, Franklyn G., M.D., Ph.D.	Pharmacology	Training Program Faculty Member	5
Salisbury, Jeffrey L., Ph.D.	Molecular Biology	Director and Faculty Member	10
Smith, David I., Ph.D.	Experimental Pathology	Training Program Faculty Member	5
Spelsberg, Thomas C., Ph.D.	Biochemistry	Training Program Faculty Member	5
Tindall, Donald J., Ph.D.	Molecular Biology	Training Program Faculty Member	5
Toft, David O., Ph.D.	Biochemistry	Training Program Faculty Member	5

Junior Members

Federspiel, Mark J., Ph.D.	Molecular Medicine	Associate Faculty Member	5
James, C. David, Ph.D.	Experimental Pathology	Associate Faculty Member	5
Jenkins, Robert B., M.D., Ph.D.	Experimental Pathology	Associate Faculty Member	5
Lloyd, Ricardo V., M.D.	Experimental Pathology	Associate Faculty Member	5

TABLE III. Other Support

ABRAHAM, R. T.

ACTIVE

R01 AI 36076-2 (Paya) 08/01/94 - 07/31/97
NIH/NIAID $132,883
HIV and NF-κB Interactions in Monocytes

ACS #19-2 (Abraham) 01/01/95 - 12/31/97
ACS $106,000
Effects of Rapamycin on IL-2 Signaling Pathways

U01 AI 34577-3 (Gleich) 08/01/93 - 07/31/97
NIH/NIAID $337,172
Mechanisms of Eosinophil-Associated Inflammation. Project Leader - Project 3: Mechanisms of Platelet Activation by Major Basic Protein

R01 GM 47286-5 (Abraham) 05/01/96 - 04/30/00
NIH/NIGMS $125,000
Signal Transduction from the T-Cell Antigen Receptor

Leukemia #1-4 (Abraham) 07/01/92 - 06/30/97
LSA $40,000
Interleukin 2 Signal Transduction and T-cell Growth Regulation

R01 CA 47752-7 (Leibson) 03/01/93 - 12/31/97
NIH/NCI $133,906
Mechanisms of Natural Killer Cell Activation

U01 CA 52995-7 (Powis) 08/01/96 - 07/31/01
NIH/NCI $88,374
Cancer Drugs Active Against Signal Transduction Targets

PENDING

None

FEDERSPIEL, M. J.

ACTIVE

FED 96-35204-3787-1 (Federspiel) 10/15/96 - 10/31/98
United States Department of Agriculture $96,148
Expression of Soluble Receptor and Envelope Proteins As an Antiviral Strategy

FEDERSPIEL, M. J. (CONTINUED)

MAYO-1 (Federspiel) 06/01/96 - 05/31/97
Fraternal Order of Eagles $35,000
Development of a Nude Mouse Experimental Model That Employs ALV-Based Retroviral Vectors to Study Breast Carcinoma Tumorigenesis

PENDING

FNDT-1 (Federspiel) 01/01/97 - 12/31/99
Susan G. Komen Breast Cancer Foundation $34,564
The Antitumor Effects of IL-6 and Soluble IL-6 Receptor on Breast Cancer Tumorigenesis

DAMD-1 (Federspiel) 01/01/97 - 09/30/99
Department of Defense $100,729
The Antitumor Effects of IL-6 and Soluble IL-6 Receptor on Breast Carcinoma Tumorigenesis

FNDT-1 (Federspiel) 01/01/97 - 12/31/00
PEW Scholars Award $50,000
The Antitumor Effects of Human IL-6 and Human Soluble IL-6 Receptor on Human Breast Carcinoma Tumorigenesis

R01 AI 41626-1 (Federspiel) 07/01/97 - 06/30/01
NIH/NIAID $215,447
Manipulating Viral Genes to Inhibit Viral Replication

GETZ, M. J.

ACTIVE

9 R01 HL 54281-13 (Getz) 08/01/95 - 07/31/99
NIH/NHLBI $186,458
Regulation of Cell Proliferation

2 T32 CA 09441-14 (Getz) 06/01/93 - 03/31/98
NIH/NCI $281,950
Multidisciplinary Basic Research Training in Cancer

R21 CA 65800-2 (Getz) 10/01/96 - 09/30/97
NIH/NCI $30,000 (Getz Component)
03M
Role of CAF, A Coactivator of Fos, in Breast Cancer

Breast Cancer Research Foundation (Getz) 05/01/96 - 04/30/97
Stromal Interactions in Human Breast Cancer $50,000

GETZ, M. J. (CONTINUED)

PENDING

R01 CA 73644-01 (Getz) 04/01/97 - 03/31/02
NIH/NCI $164,218
Stromal Interactions in Invasive Human Breast Cancer

USAMRMC DAMD-1 (Getz) 10/01/97 - 09/30/00
Stromal Interactions in Invasive Human Breast Cancer $203,088

JAMES, C. D.

ACTIVE

CA 55728 (James) 08/01/95 - 07/31/00
NIH/NCI $121,893
Genetic Alterations in CNS Tumor Development

PENDING

None

JELINEK, D. F.

ACTIVE

1 P01 CA 62242 (Jelinek, Project III) 09/30/94 - 07/31/97
NIH/NCI $24,444 (Project III)
Studies on Monoclonal Gammopathies--Molecular and Biological Role of CD40 in Myeloma

R01 CA 62228-01 A2 (Jelinek) 04/01/95 - 03/31/98
NIH/NCI $117,882
Molecular and Biological Role of CD40 in Myeloma

R01 CA 69655 (Maihle) 07/01/96 - 06/30/00
NIH $144,134
IL-6 and sIL-6R Growth Inhibition of Breast Carcinoma Cells

PENDING

None

JENKINS, R. B.

ACTIVE

DAMD17-94-J-4216-2 (Hartmann) 09/01/94 - 08/31/98
Department of Defense $153,100
Outcome After Prophylactic Mastectomy in Individuals at High Risk for Breast Cancer: A Combined Clinical-Biological Study

P30 CA 15083-22 (Jenkins) 03/01/93 - 02/28/97
NIH/NCI $1,542,474
Cancer Center Support Grant - Cytogenetics Core

U01 CA 50905-7 (Jenkins) 01/13/95 - 11/30/98
NIH/NCI $234,882
An Investigation of the Molecular Pathology of Gliomas

PENDING

DAMD-1 (Spelsberg) 10/01/97 - 09/30/00
Department of Defense $66,985
Role of Novel Estrogen/TGF-B Inducible Gene in Breast Cancer

DAMD-1 (Bhatia) 10/01/97 - 09/30/01
Department of Defense $45,627
Isolation and Cloning of the Genes Associated With Breast Cancer

LEIBSON, P. J.

ACTIVE

R01 CA 47752-07 (Leibson) 03/01/92 - 12/31/97
NIH/NCI $133,906
Mechanisms of Natural Killer Cell Activation

R01 GM 47286-05 (Abraham) 05/01/96 - 04/30/00
NIH/NIGMS $125,000
Signal Transduction From the T Cell Antigen Receptor

PENDING

None

LEOF, E. B.

ACTIVE

1 R01 GM 54200-01 (Leof) NIH/NIGMS TGFβ Receptors and Cell Proliferation	05/01/96 - 04/30/99 $138,250
1 R01 HL 55934-02 (Limper) NIH/NHLBI Control of the Pneumocystis carinii Cell Cycle	09/30/95 - 08/31/99 $156,066

PENDING

1 R01 GM/CA 55816-01 (Leof) NIH/NIGMS/NCI TGFβ Receptor Dynamics	04/01/97 - 03/31/02 $173,316
NRA-96-OLMSA-03 (Jessup) NASA Use of NASA Bioreactor to Study Cell Cycle Regulation	07/01/97 - 06/30/01 $149,402

LLOYD, R. V.

ACTIVE

R01 CA 42951-10 (Lloyd) NIH/NCI Studies of Normal and Neoplastic Human Pituitary Tissue	07/01/95 - 06/30/98 $138,793
R01 CA 37238-12A1 (Lloyd) NIH/NCI Regulation of Pituitary Hyperplasia and Neoplasia	07/01/95 - 04/30/00 $135,692

PENDING

None

MAHER, L. J.

ACTIVE

5 R29 GM 47814 (Maher) NIH Control of DNA Transcription by RNA Ligands	05/01/93 - 04/30/98 $69,722

MAHER, L. J. (CONTINUED)

5 R01 GM 54411-02 (Maher)	09/01/95 - 08/31/99
NIH	$88,703
Electrostatic Forces in DNA Bending by Proteins	
Siebens Molecular Medicine Award (Maher)	04/01/96 - 03/31/97
Identification of Potential RNA Decoys for NF-κB	$30,000

PENDING

None

MAIHLE, N. J.

ACTIVE

1 R01 CA 69655 (Maihle)	07/01/96 - 06/30/01
NIH/NCI	$144,134
IL-6 and sIL-6R Growth Inhibition of Breast Cancer Cells	
1 R01 CA 57534 (Maihle)	08/01/92 - 05/31/97
NIH/NCI	$145,079
Truncated *c-erbB* Receptors in Women With Ovarian Cancers	
1 R21 CA 65800 (Ingle)	09/30/94 - 09/29/98
NIH/NCI	$152,095
Development of Breast Cancer Research Program at Mayo	
DAMD 17-94-J-4116 (Maihle)	09/01/94 - 08/31/98
USAMRDC	$92,446
Biology of Breast Cancer Research Program at Mayo	
P30 CA 15083-23 (Prendergast)	03/01//96 - 02/28/97
NIH/NCI	$1,556,683
Cancer Center Support	
U10 CA 25224 (O'Connell)	04/10/96 - 12/31/00
NIH/NCI	$1,228,461
North Central Cancer Treatment Group	
U10 CA 37404 (Loprinzi)	08/01/96 - 05/31/01
NIH/NCI	$605,822
Community Clinical Oncology Program	

MAIHLE, N. J. (CONTINUED)

PENDING

1 R01 CA 51197 (Maihle) — 04/01/97 - 03/31/02
NIH/NCI — $166,292
Tissue-Specific Oncogenesis Mediated by *c-erbB*

U.S. Army Medical Research Command (Maihle) — 10/01/97 - 09/30/00
Analysis of sErbB1 Levels in Breast Cancer Patients Pre- and Post-Chemotherapy — $99,570

PRENDERGAST, F. G.

ACTIVE

R01 GM 34847-12 (Prendergast) — 09/01/96 - 08/31/97
NIH — $210,481
Structure-Luminescence Correlations in Proteins

P30 CA 15083-23 (Prendergast) — 03/01/96 - 02/28/97
NIH/NCI — $1,556,683
Cancer Center Support

PENDING

None

SALISBURY, J. L.

ACTIVE

DAMD17-94-J-4116-2 (Maihle) — 09/01/94 - 08/31/98
Department of Defense — $92,446
Biology of Breast Cancer: A Predoctoral Training Program, AIBS #0281

R21 CA 65800 (Ingle) — 09/30/94 - 09/29/98
NIH/NCI — $261,414
Development of Breast Cancer Research Program at Mayo

Fraternal Order of Eagles (Salisbury) — 06/01/96 - 05/31/97
Centrosome Hypertrophy in Human Breast Tumors — $35,000

Susan G. Komen Breast Cancer Foundation (Salisbury) — 01/01/97 - 12/31/99
Abnormal Centrosomes in Human Breast Cancer As a Marker for Tumor Aggressiveness — $30,000

SALISBURY, J. L. (CONTINUED)

PENDING

None

SMITH, D. I.

ACTIVE

5 R01 CA 48031-09 (Smith) 08/01/96 - 07/31/01
NIH/NCI $201,613
Chromosome Breakpoints in Renal and Small Cell Lung Cancer

PENDING

None

SPELSBERG, T.C.

ACTIVE

P01 HD 09140-20 (Toft) 04/01/96 - 03/31/01
NIH/NICHD $119,130
Mode of Action of Reproductive Hormones. Project 1: Chromatin Acceptor Sites for Progesterone

PO1 AG 04875-11 (Riggs) 07/01/94 - 06/30/99
NIH/NIA $247,155
Physiology of Bone Metabolism in an Aging Population. Project 3: Sex steroids, growth factors, and bone cell function.

RO1 AR 41418-4 (Turner) 12/04/94 - 12/03/98
NIH/NIAMS $128,005
Regulation of Bone Balance by Estrogen and Antiestrogens

RO1 HL 54281-12 (Getz) 04/01/95 - 03/31/99
NIH/NHLBI $186,458
Regulation of Cell Proliferation

RO1 AR-43627-1 A1 (Spelsberg) 07/01/96 - 06/30/01
NIH/NIAMS $177,222
A Novel TGF-β Inducible Early Gene (TIEG) in Human Osteoblasts

PENDING

None

TINDALL, D. J.

ACTIVE

1 R01 DK 47592-02 (Tindall) — 09/30/93 - 08/31/97
NIH — $115,329
Androgenic Regulation of Prostate Growth

1 R01 CA 70892 (Young) — 04/01/96 - 03/31/01
NIH — $151,491
Novel Markers for Prostate Cancer

PENDING

None

TOFT, D. O.

ACTIVE

P50 HD 09140-21 (Toft) — 04/01/96 - 03/31/01
NIH — $148,810
Mode of Action of Reproductive Hormones. Project 2: Isolation and Characterization of Progesterone Receptors

R01 DK 46249-03 (Toft) — 12/01/93 - 11/30/98
NIH — $156,584
Hsp90 Association With Steroid Receptors and Other Proteins

T32 HD 07108-18 (Toft) — 07/01/92 -06/30/97
NIH — $88,800
Reproductive Biology Training

PENDING

None

Mayo Foundation

Rochester, Minnesota 55905 Telephone 507 284-2511

Mayo Clinic Mayo Medical School
Mayo Graduate School of Medicine

Franklyn G. Prendergast, M.D., Ph.D.
Department of Pharmacology

January 7, 1997
fax:(507)284-9349
e-mail<prendergast@mayo.edu>

Jeffrey L Salisbury, Ph.D.
Department of Biochemistry and
Molecular Biology
Mayo Clinic
200 First Street, SW
Rochester, MN 55905

Dear Jeff,

This is to affirm the unequivocal support of the Mayo Cancer Center for the Tumor Biology Training Program. I have long hoped to see such interdisciplinary training here at Mayo and believe strongly in the invaluable role the graduates of such a program will play in future biomedical research in general, cancer research in particular. Accordingly, the Tumor Biology Training Program in the future will be even more integral a component of the overall Education Program of the Mayo Cancer Center and may well form the cornerstone of our ongoing efforts to build more formal research training for hematology/oncology residents and fellows. From my own experience reviewing many predoctoral training grants elsewhere, I am fully aware that they do not and cannot be expected to meet all of the costs for the entire program. The reviewers of this submittal will want to know that the Mayo Cancer Center already supports this initiative but more importantly, I will set in place mechanisms to assure continuation of that supplementary financial support in the coming years from Mayo Cancer Center's Mayo-provided discretionary funds.

The academic contributions of the fledgling Mayo Tumor Biology Program are already evident here, the *possibilities* are even more exciting. Perhaps the most gratifying aspect is the cross functional expertise being developed with non-MD personnel gaining an intimate understanding of subjects usually reserved for medical students and residents and MD PhD students enjoying the best of the medical and biological research worlds have to offer. This is terrific. Good luck and be assured that you have our unreserved, tangible support.

Yours sincerely,

Franklyn G. Prendergast, M.D.,Ph.D.
Edmond and Marion Guggenheim
Professor of Biochemistry and Molecular Biology
Director, Mayo Cancer Center

FGP:jmk

mayo

MAYO GRADUATE SCHOOL

Tumor Biology Program

Program of Study

The Tumor Biology Program of the Mayo Graduate School offers multidisciplinary training in the cell and molecular biology of cancer that leads to the Ph.D. and M.D./Ph.D. degrees in biomedical sciences. The focus of this program is to provide an educational environment that encourages excellence in scientific thought and training, while simultaneously providing exposure to all of the major fields of study relevant to tumor biology. Research and training in the Tumor Biology Program is particularly focused on gene regulation, cell-cycle control, oncogene and tumor suppressor action, tumor immunology, signal transduction, antitumor pharmacology, and the biology of breast, ovarian, uterine, lung, GI, and prostate cancers. Successful applicants participate in laboratory-based research, as well as in a formal tumor biology curriculum that integrates current concepts in cell growth control with those of human carcinogenesis.

Research Facilities

Faculty members of the Tumor Biology Program are housed in a new twenty-story research building and in several research laboratories in adjoining buildings on the Mayo Foundation campus in Rochester, Minnesota. Outstanding facilities for education and research include state-of-the-art video teleconference classrooms, well-equipped individual research laboratories, and research core facilities for nucleic acid and peptide synthesis and sequencing, NMR and mass spectroscopy, flow cytometry, and confocal light and electron microscopy. All research laboratories and faculty and student offices are networked through the institutional computer resource facility, which provides up-to-date computing, a worldwide database, and other information services.

Financial Aid

Candidates accepted into the Tumor Biology Program are supported by a Tumor Biology Training Grant, institutional funds, and individual predoctoral fellowships. An annual stipend of $15,000 is currently provided for all students accepted into the program. Health care services of the Mayo Clinic and a group hospitalization insurance plan are also available at very favorable rates.

Cost of Study

In addition to the yearly stipend, all costs, except those for books, are provided by the program. Students pay no tuition or ancillary fees.

Living and Housing Costs

Living costs in Rochester are comparable to those in cities of similar size within the Upper Midwest and are generally lower than those in urban areas of the East and West coasts. A single student can live comfortably on the stipend provided.

Student Group

While small by university standards (135 graduate students, including 24 M.D./Ph.D. students), the Mayo Graduate School offers a unique setting for clinical and basic research and education in the biomedical sciences. The Tumor Biology Program is geared to train a small number of highly motivated students who intend to pursue research careers in the general area of cancer biology and who hold the promise of becoming future leaders in this important field.

Student Outcomes

Approximately two thirds of students enrolled in Mayo Ph.D. programs graduate with a Ph.D. degree, students take just under five years to complete the Ph.D. program at Mayo, and 100 percent of Mayo Ph.D. graduates have gone on to postdoctoral fellowships.

Location

The city of Rochester combines the best of two worlds—the warmth and friendliness of a small town with the bustling commerce, entertainment, and conveniences of a metropolis. Lectures, symphony concerts, art exhibits, and a civic theater contribute to a cosmopolitan atmosphere, unusual for a city of Rochester's size. Sports and recreational centers are conveniently located, including facilities for year-round ice skating, swimming, and tennis, as well as facilities for golf, soccer, and baseball.

The Graduate School

The Mayo Graduate School is a division of Mayo Foundation, which includes Mayo Clinic, Mayo Graduate School of Medicine, Mayo Medical School, Mayo School of Health-Related Sciences, and affiliated hospitals. Mayo Foundation is accredited by the Commission on Institutions of Higher Education of the North Central Association of Colleges and Schools.

Applying

Admission to the Tumor Biology Program is competitive. Applicants are required to submit official transcripts from each college or university attended, three letters of recommendation, a summary of scientific interests and career goals, and scores from a recent GRE General Test. Qualified applicants are encouraged to schedule a personal interview. Applications to the M.D./Ph.D. program are initiated via the AMCAS system and must be submitted by November 15. The Ph.D. portion of the M.D./Ph.D. application should be submitted by December 31. Applications for the Ph.D. program should be submitted by December 31. Mayo Foundation is an affirmative action and equal opportunity educator and employer.

Correspondence and Information

Tumor Biology Program
Mayo Graduate School
200 First Street, SW
Rochester, Minnesota 55905
Telephone: 507-284-4356
E-mail: phd.training@mayo.edu

THE FACULTY AND THEIR RESEARCH

Robert T. Abraham, Associate Professor; Ph.D., Pittsburgh, 1981. Signal transduction; cell-cycle regulation; leukemogenesis.
Matthew M. Ames, Professor; Ph.D.; California, San Francisco, 1976. Development and characterization of novel antitumor agents.
Amy G. Andrews, Assistant Professor; D.V.M., Michigan State, 1987. Animal models in cancer studies.
James A. Bonner, Assistant Professor; M.D., Wayne State, 1985. Radiobiology.
David E. Clapham, Professor; Ph.D., 1979, M.D., 1981, Emory. Receptors, G proteins, and ion channels; patch clamp, imaging, and molecular biology techniques.
Chella S. David, Professor; Ph.D., Iowa State, 1966. Immunogenetic aspects of immune response, with emphasis on the major histocompatibility complex class II Ia genes and T-cell receptor gene.
Gordon W. Dewald, Professor; Ph.D., North Dakota, 1972. Cytogenetics and molecular cytogenetics of congenital disorders and hematologic malignancies.
Charles Erlichman, Professor; M.D., Toronto (Canada), 1974. Pharmacology of drugs used in cancer therapy.
Mark J. Federspiel, Assistant Professor; Ph.D., Michigan State, 1987. Retroviral vectors; targeted viral inactivation; molecular medicine.
Lorraine A. Fitzpatrick, Professor; M.D., Chicago, 1980. Bone disease; calcification; vascular biology.
*Sandra J. Gendler, Associate Professor; Ph.D., USC, 1984. Tumor cell biology; mucins in cancer and cystic fibrosis.
Michael J. Getz, Professor; Ph.D., Texas at Houston, 1972. Molecular biology of peptide growth factors; biology of tissue factor in tumorigenesis.
Joseph P. Grande, Assistant Professor; Ph.D., 1983, M.D., 1985, Chicago. Extracellular matrix and breast cancer; tumor pathology.
Lynn C. Hartmann, Associate Professor; M.D., Northwestern, 1983. Mechanisms of carcinogenesis in epithelial ovarian cancer; drug/hormone resistance; familial cancers.
James N. Ingle, Professor; M.D., Johns Hopkins, 1971. Clinical trials, hormonal therapy, and prognostic/predictive factors in breast cancer.
Diane F. Jelinek, Assistant Professor; Ph.D., Texas Southwestern Medical Center at Dallas, 1985. Cytokine-mediated signaling in human malignant plasma cells and breast carcinoma cells.
Robert B. Jenkins, Associate Professor; Ph.D., 1981, M.D., 1983, Chicago. Genetics of brain, prostate, and women's cancer.
Scott H. Kaufmann, Associate Professor; M.D./Ph.D., Johns Hopkins, 1981. Pharmacology of topoisomerase-directed antineoplastic agents; apoptosis; resistance to anticancer drugs.
Paul J. Leibson, Associate Professor; Ph.D., 1979, M.D., 1981, Chicago. Tumor immunology; lymphocyte activation; antiviral immunity.
Vanda A. Lennon, Professor; M.B.B.S., Sydney (Australia), 1966; Ph.D., Melbourne (Australia), 1973. Immunobiology of autoimmunity and cancer; ionic channel protein antigens in carcinomas of lung, ovary, and breast.
Edward B. Leof, Associate Professor; Ph.D., North Carolina, 1982. Regulation of cellular proliferation; genetics of pneumocystis carinii.
John A. Lust, Assistant Professor; M.D./Ph.D., Boston University, 1983. Role of IL-6 and IL-6R in pathogenesis of multiple myeloma; detection of minimal residual disease in myeloma transplant patients by PCR.
L. James Maher, Associate Professor; Ph.D., Wisconsin, 1988. Nucleic acid biochemistry; triple helix DNA.
Nita J. Maihle, Associate Professor; Ph.D., Yeshiva (Einstein), 1983. Molecular basis of cancer; human breast, ovarian, and prostate carcinomas; gliomas.
David J. McKean, Professor; Ph.D., Johns Hopkins, 1972. Signaling and gene transcription events in T helper lymphocytes; MHC class II protein transport.
Mark A. McNiven, Associate Professor; Ph.D., Maryland, 1987. Cytoskeletal dynamics in mammalian cells; molecular basis of cellular migration during metastasis; vesicle-based transport in epithelial cells.
L. Joseph Melton III, Professor; M.D., LSU, 1969. Chronic disease epidemiology.
Heidi Nelson, Associate Professor; M.D., Washington (Seattle), 1981. Colon and rectal cancers.
Judith R. O'Fallon, Professor; Ph.D., North Carolina, 1973. Cancer clinical trials design, conduct, and analysis.
Dennis J. O'Kane, Assistant Professor; Ph.D., SUNY at Stony Brook, 1979. Telomerase activity as a diagnostic marker for cancer; translational research on new tumor markers.
David H. Persing, Associate Professor; M.D./Ph.D., California, San Francisco, 1988. Precore promoter mutations in hepatic tumors; HLA association with chronic papillomavirus infections; association of chronic infection with lymphoproliferation.
Mark R. Pittelkow, Associate Professor; M.D., Mayo, 1979. EGF-related growth factor/receptor function: epidermal keratinocyte and melanocyte regulation of growth and differentiation.
Karl C. Podratz, Professor; M.D./Ph.D., St. Louis, 1974. Molecular prognostic determinants in gynecologic malignancies.
Franklyn G. Prendergast, Professor; M.B.B.S., West Indies, 1968; Ph.D., Minnesota, 1977. Fluorescence spectroscopy; protein structure and dynamics; biochemistry and bioluminescence.
Corey Raffel, Associate Professor; M.D./Ph.D., California, San Diego, 1980. Pediatric neuro-oncology; gene therapy and cancer.
Jeffrey L. Salisbury, Professor; Ph.D., Ohio State, 1978. Cell-cycle control; centrosomes; mitotic spindle poles; breast cancer.
Thomas C. Spelsberg, Professor; Ph.D., West Virginia, 1967. Steroid action on early (*c-myc*) gene transcription; steroids and TGF-β action on bone cell functions; early gene expression.
Emanuel E. Strehler, Associate Professor; Ph.D., ETH Zurich (Switzerland), 1981. Intracellular Ca^{2+} homeostasis and signalling; molecular mechanisms of disease.
Stephen N. Thibodeau, Associate Professor; Ph.D., Washington (Seattle), 1979. Cancer genetics.
Donald J. Tindall, Professor; Ph.D., North Carolina, 1973. Mechanism of androgen action in prostate cancer.
David O. Toft, Professor; Ph.D., Illinois, 1967. Mechanisms of action of steroid receptors and heat shock proteins.
Raul Urrutia, Assistant Professor; M.D., Cordoba (Argentina), 1987. Cell differentiation.
Richard M. Weinshilboum, Professor; M.D., Kansas, 1967. Molecular pharmacogenetics of drug metabolism, including antineoplastic agents.
Peter J. Wettstein, Professor; Ph.D., North Carolina at Chapel Hill, 1977. Role of minor histocompatibility antigens in allograft rejection.
Anthony J. Windebank, Professor; B.M.B.Ch., Oxford, 1974. Molecular mechanisms of neurotoxic cell injury; growth factors and regeneration.
Lester E. Wold, Professor; M.D., Chicago, 1977. Immunocytochemistry; bone tumors and tumor-like conditions; breast diseases.
Charles Y.-F. Young, Assistant Professor; Ph.D., Brigham Young, 1984. Calpain inhibitor–induced apoptosis in human prostate adenocarcinoma cells.

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*Scottsdale campus.

Appendix Exhibit C

Tumor Biology I: Introduction for Tumor Biology
(TBio 5000 and 5150, Fall Quarter, 1996)
Tuesdays, Wednesdays, Thursdays, 2:30 - 3:30 p.m.
UPDATED 10/10/96

Week 1 (Dr. N. Maihle)

Tuesday, October 1, 1996

A. What are the properties of cancer/transformed cells?

a) the life of a transformed cell
b) *in vitro* properties of transformed cells.
c) *in vivo* properties of transformed cells.

Wednesday, October 2, 1996

B. Tumor Biology Journal Club

Boveri's "On the Origin of Malignant Tumors" (1927)

Thursday, October 3, 1996

C. Introduction to Journal Club and Problem Set Formats

Week 2 (Dr. N. Maihle)

Tuesday, October 8, 1996

A. Methods Used to Study Cancer Cells *In Vitro*

a) establishment of tumor cells/cell lines in culture
b) immortalization
c) senescence/apoptosis
d) analysis of heterologous sequences by cell fusion and transfection methods

1) focus formation
2) soft agar colony formation

Wednesday, October 9, 1996

B. Tumor Biology Journal Club

Temin's soft agar colony assay, 1970
Transforming *vs.* immortalizing sequences (Land [1983] and Ruley ([1983])

Thursday, October 10, 1996

C. Student Discussion Problem Set

Week 3 (Dr. M. Pittelkow)

Tuesday, October 15, 1996

A. Methods Used to Study Cancer Cells *In Vivo*

a) Animal models of chemical carcinogenesis
b) Naturally occurring animal models of genetic predisposition to cancer

Wednesday, October 16, 1996

B. Moertel Lecture (Dr. Donald Coffey, Johns Hopkins University Medical Center)

Thursday, October 17, 1996

C. Student Discussion Problem Set

Week 4 (Dr. M. Federspiel)

Tuesday, October 22, 1996
A. Methods Used to Study Cancer Cells *In Vivo* (continued)

a) Animal models of DNA and RNA tumor virology

Wednesday, October 23, 1996
B. Tumor Biology Journal Club

Rous' Sarcoma Virus (1911)/Temin's Protovirus Hypothesis

Thursday, October 24, 1996
C. Student Discussion Problem Set

Week 5 (Dr. N. Maihle)

Tuesday, October 29, 1996
A. Methods Used to Study Cancer Cells *In Vivo* (continued)

a) Nude mice/SCID mice/xenografts

Wednesday, October 30, 1996
B. Tumor Biology Journal Club

Thursday, October 31, 1996
C. Student Discussion Problem Set

Week 6 (Dr. C. David)

Tuesday, November 5, 1996
A. Methods Used to Study Cancer Cells *In Vivo* (continued)

a) Genetically Engineered Models of Mouse Carcinogenesis

1) transgenics
2) knockouts

Wednesday, November 6, 1996
B. Tumor Biology Journal Club

Thursday, November 7, 1996
C. Student Discussion Problem Set

Week 7 (Dr. J. Maher)

Tuesday, November 12, 1996
A. Antisense and Antigene Agents Targeted to Cancer-related Genes

Wednesday, November 13, 1996
B. Tumor Biology Journal Club

Thursday, November 14, 1996
C. Introduction to Analysis of Human Tumors (Dr. J. Grande)

Week 8 (TBio Staff and Guest Lecturer)

Tuesday, November 19, 1996
A. Introduction to Analysis of Human Tumors (Dr. A. Thor, Visiting Faculty Member, Northwestern University Medical School): Pitfalls and Perks in the Analysis of Human Tumors

Wednesday, November 20, 1996
B. Tumor Biology Journal Club

Thursday, November 21, 1996
C. Tour of Surgical Pathology Suite (Dr. J. Grande)

Week 9 (Dr. H. Long)

Tuesday, November 26, 1996
A. IRB Policies and Protocols Relevant to Studies on Human Tumors

Wednesday, November 27, and Thursday, November 28, 1996
Thanksgiving Holiday/No Class

Week 10 (TBio Staff)

Tuesday, December 3, 1996
A. Cytogenetic Analysis of Human Tumors (Dr. R. Jenkins)

Wednesday, December 4, 1996
B. Infomatics, Data Management, and the Analysis of Human Tumors (Dr. C. Chute)

Thursday, December 5, 1996
C. In Situ Hybridization and Immunohistochemical Techniques in the Analysis of Human Tumors (Dr. R. Lloyd)

Week 11 (INDEPENDENT STUDY)

December 10-12, 1996

Week 12 (FINAL EXAM)

Due on Monday, December 16 by 5 p.m. (deliver to 1401 Guggenheim, Ms. Sharon Jones; **no late exams accepted**).

Tumor Biology: Origins of Human Cancer
TBIO 8250
2:30 - 3:30 p.m., Tuesdays and Thursday, 1093 Guggenheim
[50% participation/50% term paper]

January 7	Origins of Human Cancer: An Overview (Maihle)
January 8	Tumor Biology Journal Club
January 9	Problem Set (Maihle)
January 14	Origins of Human Cancer: Etiology and Genetics (Smith)
January 15	Tumor Biology Journal Club
January 16	Problem Set (Smith and Maihle)
January 21	Origins of Human Cancer: Progression and Metastasis (Gendler)
January 22	Tumor Biology and Journal Club
January 23	Problem Set (Gendler and Maihle)
January 28	Origins of Human Cancer: Epidemiology and Prevention (Yang)
January 29	Tumor Biology Journal Club
January 30	Tumor Immunology: An Overview (Malcolm Mitchell)
February 4	Problem Set (Epidemiology and Prevention; Yang and Maihle)
February 5	Tumor Biology Journal Club (Tumor Immunology; Jelinek)
February 6	Problem Set (Tumor Immunology; Jelinek)
February 11	Paraneoplastic Syndromes (Lennon)
February 12	Tumor Biology Journal Club
February 13	Problem Set (Lennon and Jelinek)
[February 18-20 No Class]	
February 25	Introduction to Clinical Research (O'Fallon)
February 26	Tumor Biology Journal Club
February 27	Problem Set (O'Fallon and Maihle)
March 4	Introduction to Chemotherapy (Ames)
March 5	Tumor Biology Journal Club
March 6	Problem Set (Ames and Maihle)

March 11	Tumor Imaging: An Overview (Robb)
March 12	Experimental Tumor Imaging (Ehman)
March 13	Problem Set (Maihle)
March 18	Introduction to Surgical Oncology (Nelson)
March 19	Tumor Biology Journal Club
[March 20	No Class]
March 25	Introduction to Radiation Therapy (Bonner)
March 26	Tumor Biology Journal Club
March 27	Experimental Gene Therapy (Raffel)/TERM PAPERS DUE

Tumor Biology: Origins of Human Cancer
TBIO 8250

2:30 - 3:30 p.m. , Tuesdays and Thursday, 1093 Guggenheim
Dr. Nita Maihle and Tumor Biology Staff

Course Objectives: Students will be introduced to advanced principles of human cancer biology, including cancer etiology, progression, epidemiology and prevention, immune surveillance, paraneoplastic syndromes, advanced diagnostics and imaging, chemotherapy, radiation therapy, and principles of surgical oncology, as well as experimental therapeutics.

Recommended Text: Tannock, I. F. and Hill, R. P., *The Basic Science of Oncology*, 1992, McGraw Hill, NY, NY.

Evaluation: (S/N); 50% class participation (Active learning is a requirement in this course, and is best demonstrated through participation in class discussions, especially through journal club and problem set discussions).

50% term paper* (due Thursday, March 27, 1997, by 4:30 p.m., turn into Ms. Sharon Jones, Guggenheim 1401).

*Term paper topics must be selected from the following list, and only one student may select a given topic. (Other topics will be considered by permission of the instructor). The purpose of this paper is to review the major principles of tumor biology introduced in this course in the context of a given human malignancy (see list, below). Papers should be typewritten, no more than 20 double-spaced pages (exclusive of tables/figures), and must address each of the major aspects of the spectrum of tumor biology (from epidemiology/prevention through current and experimental therapies) relevant to the tumor type of interest. All papers should include a brief introductory outline, appropriate subheadings, and complete references (including references for tables/figures). In addition, a concise description of forefront areas of research for a given tumor type, and a proposal of key experiments that could significantly advance this field should be included.

B cell lymphomas
basal cell carcinomas
bladder carcinoma
breast carcinomas
cervical carcinomas
chondrosarcomas
choriocarcinomas
colon carcinomas
endometrial carcinomas
Ewing's sarcoma
gliomas
(including astrocytomas and glioblastomas)
hemangiosarcomas
hepatocellular carcinoma
Kaposi's sarcoma
lung carcinomas
medulloblastomas
melanomas
mesothieliomas
multiple myeloma
nasaopharyngeal carcinoma
osteosarcoma
ovarian carcinomas
pancreatic carcinomas
prostate carcinomas
renal carcinoma
rhabomyosarcoma
T cell lymphomas
teratomas
testicular carcinoma
testicular carcinoma
thyroid carcinomas

TBIO III
Spring Quarter, 1997
(50% participation/50% term paper)

April	1-3	(No class, Spring Break)
	8	Introduction to Cell Growth Control (Salisbury)
	9	Tumor Biology Journal Club
	10	Problem Set
		(AACR Meeting 4/12 - 16)
	15	Tumor Virology - DNA (Maihle)
	16	Tumor Biology Journal Club
	17	Problem Set
	22	Tumor Virology - RNA (Maihle)
	23	Tumor Biology Journal Club
	24	Problem Set
	29	Infectious Disease and Cancer Etiology (Persing)
	30	Tumor Biology Journal Club
May	1	Problem Set
May	6	Growth Factors/Receptors (Maihle)
	7	Tumor Biology Journal Club
	8	Problem Set
	13	Cytokines/Receptors (Jelinek)
	14	Tumor Biology Journal Club
	15	Problem Set
	20	Intracellular Mediators - Kinases (Maihle)
	21	Tumor Biology Journal Club
	22	Problem Set
	27	Intracellular Mediators - G Proteins (Abraham)
	28	Tumor Biology Journal Club
	29	Problem Set
June	3	Transcriptional Regulation by Growth Factors (Tindall)
	4	Tumor Biology Journal Club
	5	Problem Set
	10	Tumor Suppressors (Smith)
	11	Tumor Biology Journal Club
	12	Problem Set
	17	Tumor Suppressors (Thibodeau)
	18	Tumor Biology Journal Club
	19	Problem Set

-New Course-

"PRINCIPLES IN PANCREATIC CANCER"

Tumor Biology Track (TBio 5200)

- This educational activity is aimed at integrating basic concepts on development, cellular and molecular biology of the pancreas together with current information on the etiology, diagnosis, and treatment of pancreatic cancer.

- The faculty include members from diverse medical disciplines including cell and molecular biology, pathology, clinical gastroenterology, oncology, and surgery.

LECTURES

Guggenheim 1093-G
Friday, 3- 4 p.m.

October 25	**Pancreatic Cancer: What is the Problem?** Dr. Eugene P. DiMagno, Gastroenterology Research Unit, SMH
November 1	**Development, Cell Biology, and Histology of the Pancreas** Dr. Raul Urrutia, Gastroenterology Research Unit, SMH
November 8	**Histopathology of Pancreatic Cancer** Dr. Lawrence J. Burgart, Surgical Pathology
November 15	**Experimental Models of Pancreatic Cancer** Dr. Raul Urrutia, Gastroenterology Research Unit, SMH
November 22	**Cellular and Molecular Mechanisms of Pancreatic Cancer** Dr. Raul Urrutia, Gastroenterology Research Unit, SMH
December 6	**Current and Future Non-Surgical Treatments of Pancreatic Cancer** Dr. Richard M. Goldberg, Medical Oncology.
December 13	**Surgical Treatment of Pancreatic Cancer** Dr. Michael Sarr, Gastroenterology Research Unit/Surgery, SMH

For More Information Contact
Dr. Raul Urrutia (4-7500)

BIOLOGY OF BREAST CANCER
SPRING QUARTER, 1997

Guggenheim 1093
Fridays
1:30 p.m. - 2:30 p.m.

APRIL	4	No Class (Spring Break)	
	11	Breast Cancer: The Magnitude of the Problem	James Ingle, M.D.
	18	Development, Cell Biology and Histology of the Breast	Jeffrey Salisbury, Ph.D.
	25	Histopathology of the Breast	Lester Wold, M.D.
May	2	Experimental Models of Breast Cancer	Sandra Gendler, Ph.D.
	9	Oncogenes, Growth Factors, and Breast Cancer	Nita Maihle, Ph.D.
	16	Tumor Suppressors and Breast Cancer	(TBA)
	23	Breast Cancer Diagnosis and Imaging	Ruth Johnson, M.D.
	30	Surgical Treatment of Breast Cancer	John Donohue, M.D.
June	6	Radiation Therapy for Breast Cancer	Ivy Petersen, M.D.
	13	Breast Cancer Chemotherapy	James Ingle, M.D.
	20	Experimental Therapies for Breast Cancer	Nita Maihle, Ph.D.
	27	Final Examination Due (by 5:00 p.m.)	

Appendix Exhibit C

Business of Science, Science of Business
TBio 5300
K. E. Bennet, M.B.A. and N. J. Maihle, Ph.D.
Mayo Graduate School
Summer Quarter, 1996

1) Introduction (August 2) [KEB/NJM]

- Orientation and Objectives

2) Administrative Structures in Support of Research (August 5) [KEB]

- Not-for-Profit
- For Profit

3) Overview of Research Accounting (Auust 7) [KEB]

- Research Budgets
- Direct versus Indirect costs

4) Sources of Financial Support for Research (August 9) [NJM]

- Intramural Support

- Extramural Support

    - Federal
    - Private

5) Sources of Financial Support for Research (August 12) [KEB]

- Corporate

    - Strategic Alliance, Joint Development
    - Licensing/Venture Capital

6) Introduction to Intellectual Property (August 14) [KEB]

Definition of Intellectual Property

Protection of Intellectual Property

- Patents
- Trade Secrets

Ownership of Intellectual Property

CONTINUATION PAGE: STAY WITHIN MARGINS INDICATED

7) Introduction of Cases (August 16) [KEB]

8) Commercialization of Research Discoveries (August 21) [KEB]

- Licensing
- Market Value of Invention

9) Independent Study on Cases (August 19)

10) Laws and Policies Governing Conduct of Research (August 23)

Institutional [NJM]
State, Federal and International [KEB]

11) Case Presentations "Levamisole" (August 26) [KEB/NJM]

12) Case Presentations - "University of Florida" (August 28) [KEB/NJM]

13) Course Wrap-Up (August 30) [KEB/NJM]

Appendix Exhibit C

Lecture Series Faculty

Course Director: Anthony J. Windebank, M.D.
Professor of Neurology
Dean, Mayo Graduate School

Kevin Bennet
Office of Strategic Alliances

Lorraine Fitzpatrick, M.D.
Professor of Medicine

Ray A. Ghanbari, Ph.D.
Director, Research Computing Facility

J. Michael Homan
Assistant Professor of Medical Informatics

Claudia T. Kappen, Ph.D.
Assistant Professor of Biochemistry/Molecular Biology

James J. Lipsky, M.D.
Professor of Pharmacology and Medicine

Richard McGee, Ph.D.
Associate Professor of Pharmacology

Kathleen A. Meyerle, J.D.
Legal Counsel

John C. Mitchell, III, M.D.
Associate Professor of Medicine

Corey Raffel, M.D., Ph.D.
Associate Professor of Neurosurgery

Robert A. Rizza, M.D.
Professor of Medicine

Daniel J. Schaid, Ph.D.
Associate Professor of Biostatistics

7/17/96

The Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research

SUMMER, 1996

4:30 to 5:30 p.m.

Sponsored by:

Mayo Graduate School
and
General Clinical Research Center

Appendix Exhibit C

The Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research

Quality in research is predicated upon both sound scientific principles and unimpeachable integrity. Training in ethics and scientific integrity occurs informally through mentoring, role modeling, and unwritten codes of scientific conduct in the professional milieu.

Past concern over misconduct in biomedical research caused the Department of Health and Human Services to establish the Office of Research Integrity. Mayo Foundation has developed its "Policy on Ethics in Research," a copy of which you all should have. This lecture series is designed to bring to your attention a number of issues, alert you to the available literature, and open the avenues of discussion to strengthen professional standards and set the tone for future generations of researchers.

July 10, 1996 — **Room 1-507, Baldwin Building**

Introduction - Perspective on Ethical Conduct in Biomedical Research

Richard McGee, Ph.D.
Anthony J. Windebank, M.D.

July 17, 1996 — **Room 1-507, Baldwin Building**

Scientific Fraud and its Consequences

Kathleen Meyerle, J.D.
Anthony J. Windebank, M.D.

July 24, 1996 — **Room 1-507, Baldwin Building**

Authorship

Robert A. Rizza, M.D.

July 31, 1996 — **Room 1-507, Baldwin Building**

Data Storage and Ownership

Claudia T. Kappen, Ph.D.

August 7, 1996 — **Room 1-507, Baldwin Building**

Emerging Issues in Electronic Data Acquisition, Storage and Publishing

Ray A. Ghanbari, Ph.D.
J. Michael Homan

August 14, 1996 — **Room 1-507, Baldwin Building**

Collection and Interpretation of Data

Daniel J. Schaid, Ph.D.

August 21, 1996 — **Room 1-507, Baldwin Building**

Conflict of Interest

James J. Lipsky, M.D.

August 28, 1996 — **Room 1-507, Baldwin Building**

Use of Animals in Research

Lorraine Fitzpatrick, M.D.

September 4, 1996 — **Room 1-507, Baldwin Building**

The Thermodynamics of Money

Kevin E. Bennet

September 11, 1996 — **Room 1-507, Baldwin Building**

Use of Humans in Research

John C. Mitchell III, M.D.

September 18, 1996 — **Judd Hall, Mayo Building**

Recombinant DNA Research

Corey Raffel, M.D., Ph.D.

I. History of Using Animal Models in Biomedical Research/Tumor Biology

A. Introduction

Statical ESSAYS:
CONTAINING
HÆMASTATICS;
Or, An Account of some
Hydraulic and *Hydroſtatical*
EXPERIMENTS
MADE ON THE
Blood *and* Blood-Veſſels *of* ANIMALS.
ALSO
An ACCOUNT of ſome EXPERIMENTS on STONES in the *Kidneys* and *Bladder*; with an ENQUIRY into the NATURE of thoſe *animalous* CONCRETIONS.
To which is added,
An *APPENDIX*,
CONTAINING
OBSERVATIONS and EXPERIMENTS relating to ſeveral SUBJECTS in *The Firſt Volume*. The greateſt Part of which were read at ſeveral *Meetings* before the ROYAL SOCIETY.
With an *INDEX* to both VOLUMES.
VOL. II.
Deſideratur Philoſophia Naturalis vera & activa, cui Medicinæ Scientia inædificetur. Fran. de Verul. Inſtaur. Magna.
By *STEPHEN HALES*, D. D. F. R. S. Rector of *Faringdon*, *Hampſhire*, and Miniſter of *Teddington*, *Middleſex*.
The SECOND EDITION, Corrected.
LONDON:
Printed for W. INNYS and R. MANBY, at the Weſt End of St. *Paul's*; and T. WOODWARD, at the *Half Moon* between the Temple-Gates, *Fleet-ſtreet*. M.DCC.XL.

Fig. 2. Title page from "Statical Essays" (Hales, 1740).

Aristotle (384 - 322 B.C.):
comparitive dissections

Claude Bernard (1813 - 1878):
experimental physiology

Louis Pasteur (1827 - 1895):
microbiology

Bernard (1865):
". . . it is proper to choose certain animals which offer favorable anatomical arrangements or special susceptibility to certain influences. For each kind of investigator we shall be careful to point out the proper choice of animals. This is so important that the solution of a physiological or pathological problem often depends solely on the appropriate choice of the animal for the experiment so as to make the result clear and searching."

Castle, Little & others (early 1900's):
studied mice to demonstrate the genetic basis of cancer

Laboratory Animal Medicine: Historical Perspectives
(ed. J. Fox, B. Cohen & F. Loew, Academic Press)

B. Criticism of the Use of Animals in Science

1840's - Society for the Prevention of Cruelty to Animals (SPCA) - England

1860's - American SPCA (New York, Philadelphia, Boston)

II. Animal Welfare Concerns and Policies (3)

National Institutes of Health and Public Health Service Principles for Use of Animals

The personnel

1. Experiments involving live, vertebrate animals and the procurement of tissues from living animals for research must be performed by, or under the immediate supervision of, a qualified biological, behavioral, or medical scientist
2. Housing care, and feeding of all experimental animals must be supervised by a properly qualified veterinarian or other scientist competent in such matters

The research

3. The research should be such as to yield fruitful results for the good of society and not random or unnecessary in nature
4. The experiment should be based on knowledge of the disease or problem under study and so designed that the anticipated results will justify its performance
5. Statistical analysis, mathematical models, or *in vitro* biological systems should be used when appropriate to complement animal experiments and to reduce numbers of animals used
6. The experiment should be conducted so as to avoid all unnecessary suffering and injury to the animals
7. The scientist in charge of the experiment must be prepared to ternimate it whenever he/she believes that its continuation may result in nunnecessary injury or suffering to the animals
8. If the experiment or procedure is likely to cause greater discomfort than that attending anesthetization, the animals must first be rendered incapable of perceiving pain and be maintained in that condition until the experiment or procedure is ended. The only exception to this guideline should be in those cases where the anesthetization would defeat the purpose of the experiment and data cannot be obtained by any other humane procedure. Such procedures must be carefully supervised by the principal investigator or another qualified senior scientist
9. Postexperimental care of animals must be such as to minimize discomfort and the consequences of any disability resulting fro the experiment, in accordnce with acceptable practices n veterinary medicine
10. If it is necessary to kill an experimental animal, this must be accomplished in a humane manner, i.e., in such a way as to ensure immediate death in accordance with procedures approved by an institutional committee. *No animal shall be discarded until death is certain*

The facilities

11. Standards for the construction and use of housing, service, and surgical facilities should meet those described in the publication, "Guide for the Care and Use of Laboratory Animals," DHEW No. (NIH) 78-23, or a s otherwise required by the United States Department of Agriculture regulations established under the terms of the Laboratory Animal Welfare Act (P.L. 89-544) as amended 1970 and 1976 (P.L. 92-579 and P.L. 94-279)

Transportation

12. Transportation of animals must be in accord with applicable standards and regulations; especially those inteded to reduce discomfort, stress to the animals, or spead of disease. All animals being received for use as experimental subjects and having arrived at the terminal of a common carrier, must be promptly picked up and delivered, uncrated, and placed in acceptable permanent facilities

III. Overview of Animal Models Used in Tumor Biology

Xiphophons (fish)	*hamsters
chickens	*rats
cats	*guinea pigs
dogs	
woodchucks	*mice
cows	
monkeys	*Rodentia (mammals)

(DNA, viruses, cells, tissues)

IV. Introduction to Mice as an Experimental Model in Tumor Biology

house mouse: mice have lived in close association with people since the dawn of civilization

12 MOUSE GENETICS (ed. Silver, 1995; Oxford Univ. Press)

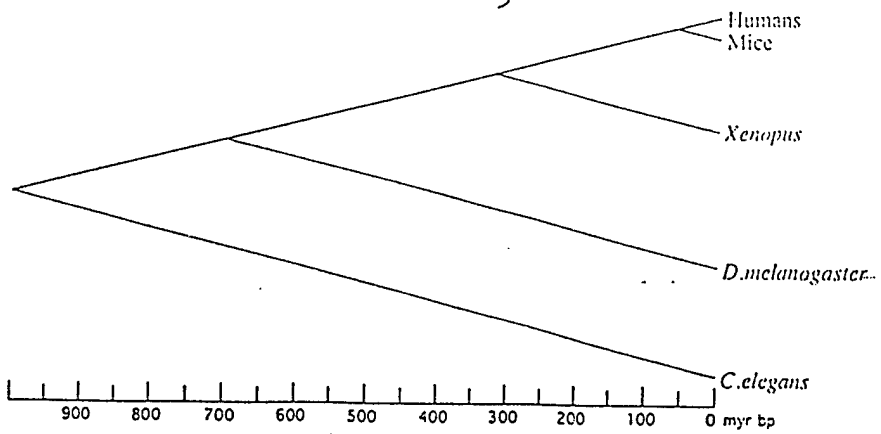

Figure 1.3 Evolutionary relationships among commonly used model organisms. The approximate times of divergence of humans, mice, frogs (*Xenopus*), flies (*D. melanogaster*), and nematodes (*C. elegans*) from common ancestors is indicated along the time scale in millions of years before present.

(IV. Mice as a Model System . . . [continued])

mouse = Latin mus; Greek mys; Sanskrit: mush = to steal

early records of mouse domestication and even worship

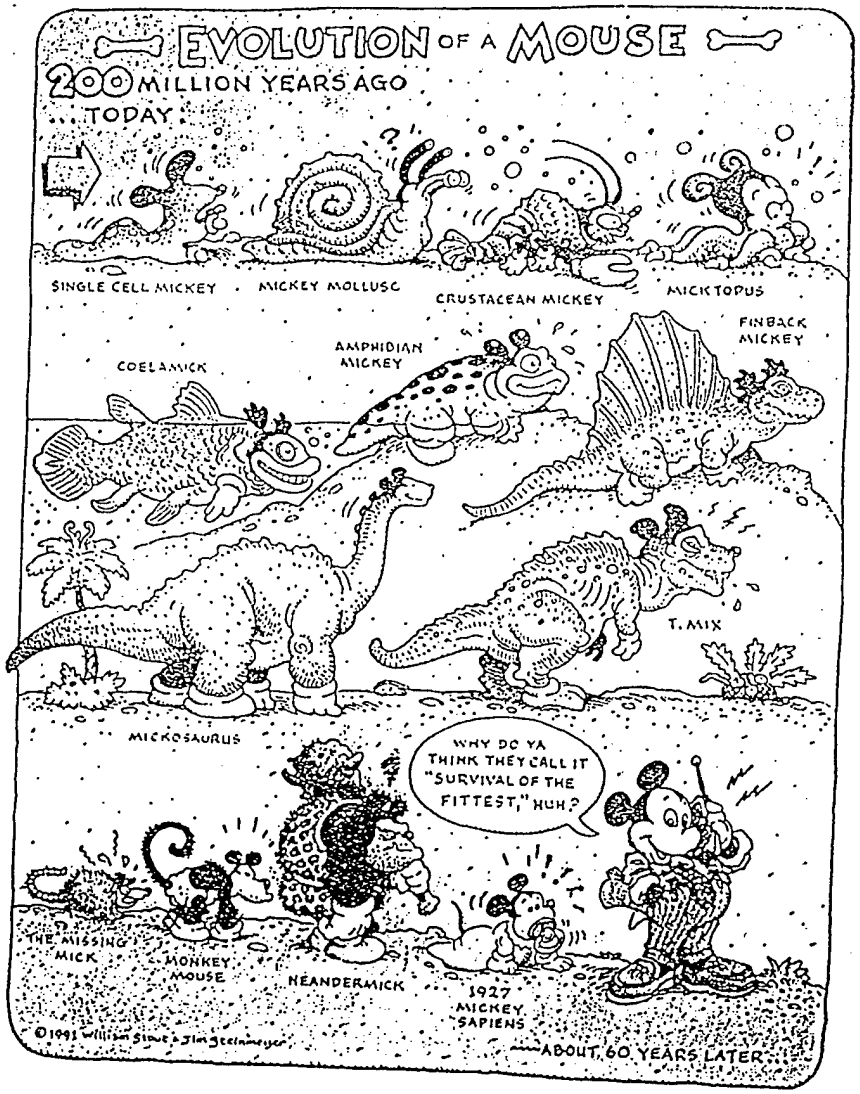

Figure 2.1 - "Evolution of a mouse" by William Stout and Jim Steinmeyer. Pen and Ink, watercolor. From *The Art of Mickey Mouse* compiled by Craig Yoe and Janet Morra-Yoe. ©1991 The Walt Disney Company (Yoe and Morra-Yoe, 1991). Reprinted by permission of Hyperion.

(IV. Mice as a Model System . . . [continued])

Laboratory mice: Asian cultures had a fondness for unusual looking mice. Hence, mouse breeders developed mutant lines with different colors. These lines were the forerunners of our laboratory mice

Miss Abbie Lathrop (~1900), a retired school teacher, provided the critical link between "fancy" mouse breeders and American mouse geneticists. She began to breed mice for sale as pets on her farm I Grandby, MA. Her farm was near the Bussey Inst. (Harvard University), directed by Prof. William Castle. She provided mice to Castle (Harvard), Leo Loeb (Univ. of PA), and others. She also conducted her own experiments witha s many as 11,000 animals breeding on her farm at any one time (1910-1918). (see H.C. Morse, 1978, Origins of Inbred Mice, Acad. Press, N.Y,).

- Many of the common inbred lines so important to mouse genetics today were derived entirely from animals provided by Ms. Lathrop, e.g., C57BL/6 and C57BL/10 (=B6 & B10)

founders of mouse genetics:
(Pre WWII)

Ceunot (early 1900's); Frency geneticist who geneticist who provided the first evidence for the applicability of Mendel's laws to mammals (and by implication to humans) using inheritance of coat color phenotypes

William Ernest Castle: brought the "fancy" mouse into his lab in 1902, and began a systematic analysis of inheritance and genetic variation

over 28 years the Bussey Institute trained 49 students, including Dunn, Little, Wright, Snell; 13 were elected to the U.S. NAS

(founders of mouse genetics - continued)

Clarence Little: (Bussey) developed *inbred* genetically homogeneous lines

- 1909 - "DBA" strain, which had mutant alleles in 3 coat colors (loci)

  dilute (d)
  brown (b)
  nonagouti (a)

- 1918 - moved to CSHL, and with his colleagues Leonell Strong, E.C. Mac developed the most famous early inbred lines:

B6, B10, C3H, CBA, Balb/C {$^{Bagg/alb}$}
(see next page for table)

their rationale for these studies at CSHL was to demonstrate the genetic basis of cancer

Table 3.1 Some important inbred strains

Strain	Color	Major use	Other characterstics	Origin	Generation[a]
129/Sv-*Sl*/+,c^+p^+ *(129)*	Agouti	Source of most ES cell lines and genetic material used for homologous recombination. Used for studies of embryology and reproduction.	Relatively high testicular teratoma incidence. Relatively small size. Resistant to radiation.	~1930 (Dunn)	F79 (JAX)
BALB/c	Albino	Used in immunological studies and for the production of hybridomas. A new congenic strain BALB/cByJ-Rb(8.12)5Bnr available from JAX is most efficient for hybridoma production.	Docile females. Males of the J substrain only are extremely aggressive. Relatively poor breeders, but variation among sublines. Sensitive to radiation.	1913 (Bagg)	F105 (CR) F180 (JAX) F195 (Taconic)
C57BL/6 (B6)	Black	Standard strain for genetic studies; common backcross partner for congenic construction and mapping panels.	Relatively long lived and hearty. Excellent breeders. Resistant to radiation.	1921 (Little)	F160 (CR) F187 (JAX) F155 (Taconic)
C57BL/10 (B10)	Black	Commonly used in genetic studies performed outside of the US and for the construction of congenics at the *H-2* complex.	Common ancestry with B6.	1921 (Little)	F192 (JAX)
CAST/Ei	Agouti	Used in matings with traditional inbred strains to create F_1 hybrids with high levels of heterozygosity for linkage studies. Better intercross reproductive performance than *M. spretus* strains.	Derived from wild animals of the subspecies *M. m. castaneus*. Male F_1 hybrids formed with lab strains are fertile.	1971 (Marshall to Eicher)	F53 (JAX)
C3H	Agouti	Used commonly in genetic studies.	High mammary tumor incidence. Large adults.	1920 (Strong)	F167 (CR) F139 (JAX) F160 (Taconic)
DBA/2	Dilute brown	Used in crosses with B6 to produce the best-characterized set of RI strains, and for the production of standard F_1 hybrid animals.		1909 (Little)	F164 (CR) F183 (JAX) F165 (Taconic)
FVB/N	Albino	Recently derived strain with special characteristics that are ideal for the production of transgenic mice. An agouti congenic is currently under construction.	Very large litters, easy to handle, large and prominent pronuclei in zygotes.	1975 (NIH)	>F30 (CR) F57 (JAX) F40 (Taconic)
MOLF/Ei	Agouti	Used in matings with traditional inbred strains to create F_1 hybrids with high levels of heterozygosity for linkage studies. Better intercross reproductive performance than *M. spretus* strains.	Derived from wild animals of the *faux* subspecies *M. m. molossinus* (Section 2.3).	~1975 (Potter to Eicher)	F50 (JAX)
SPRET/Ei	Agouti	Used in matings with traditional inbred strains to create highly heterozygous backcross panels for linkage analysis.	Derived from the species *M. spretus*. Small animals. Difficult to handle.	1988 (Eicher)	F37 (JAX)

[a]As of 1993.

From: Mouse Genetics (ed. L. Silver, 1995; Oxford University Press)

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Salisbury, Jeffrey L.
Appendix Exhibit D

GENETIC VARIANTS AND STRAINS OF THE LABORATORY MOUSE

Third Edition
Volume 2

Edited by
MARY F. LYON
MRC Mammalian Genetics Unit
SOHAILA RASTAN
MRC Head Office
and
S.D.M. BROWN
MRC Mammalian Genetics Unit

for the

International Committee on
Standardized Genetic Nomenclature
for Mice

OXFORD · NEW YORK · TOKYO
OXFORD UNIVERSITY PRESS
1996

(founders of mouse genetics - continued)

In 1929, Little founded the Jackson Laboratory (Bar Harbor, MN)

- 8 researchers; heir to the Bussey Institute original inbred strains

In 1996, three major suppliers of inbred mice:

Jackson Labs
Charles River Labs
Teconic Farms

Post WWII: three laboratories were founded and/or contracted to study the effects of radiation on mice (to understand the consequences of nuclear fallout for humans):

(Jackson Laboratory)

*Oak Ridge National Laboratory (TN)

*Atomic Energy Research Establishment (Harnell, ENG)

additional inbred lines were developed in these laboratories, and are in current use today

preWWII, genetics in mice was overshadowed by Drosophila & C. elegans {development neurobiology '70s}, but mice became recognized as useful models for two experimental systems that couldn't be studied in these beasts: Immunology
Cancer

(founders of mouse genetics - continued)

laboratory mice as genetic models:

- rodents
- small (25 - 40 g)
- short generation time (~10 weeks from being born to giving birth
- average of 5 - 10 pups/litter, with immediate postpartum estrus (and fathers don't eat their young!)
- (1990's; - extensive genetic linkage map ~3,000 loci in '94
  - 100's of inbred lines)
- inbred strains, all practical purposes these mice are homozygous for their entire genome (genetically identical to each other)
- 19 autosomal chromosomes + X and Y (20 vs 23 in humans)

Table 3.2 Categories of genetic crosses

Designation	Types of matings	Offspring genotypes	Major uses
Backcross	(1) $A/a \times A/A$ (2) $A/a \times a/a$	(1) A/a, A/A (2) A/a, a/a	Linkage analysis; production of congenic strains
Incross	(1) $A/A \times A/A$ (2) $a/a \times a/a$	(1) A/A (2) a/a	Maintenance of an inbred strain
Intercross	$A/a \times A/a$	A/a, A/A, a/a	Linkage analysis
Outcross	(1) $A/A \times a/a$ (2) $a^1/a^2 \times a^3/a^4$	(1) A/a (2) $[a^1/a^3, a^1/a^4, a^2/a^3, a^2/a^4]$	Initial step in strain production and linkage analysis; production of F_1 hybrids

V. Production of Tumors in Experimental Animals

DNA	
Viruses	many models
Cells }	{mice
Tissues}	
[Genes]	transgenics/knockouts

- transplantation:
  A basic understanding of transplantation terminology is necessary when discussing methods of transplantation.

  Autograft: A graft of tissue from one sit to another on the same individual. Rejection is rare.
  Allograft: A graft between genetically dissimilar animals of the same species. This graft may undergo rejection.
  **Xenograft*: A graft between animals of different species. Rejection may be quite violent.

- the outcome of transplantation is dependent upon many factors:

  tumor
  - histologic classification
    well: melanoma, colon, lung, kidney, bone
    poorly: breast, prostate, endocrine, lymphoid
  - primary vs. metastasis

  host
  - site (can influence tumor take, subsequent growth, responsiveness to therapy)
  - strain of animal (mouse)
  - sex (no effect on takes; may affect growth)
  - pregnancy (unpredictable)
  - In general, after many transplants, host requirements are less specific.
  - PREPARATION OR SELECTION OF THE HOST TO PREVENT HOST VS. GRAFT REJECTION

(V. Production of Tumors - continued)

methods used to immunosuppress hosts:

- drugs
- ionizing radiation

* immunodeficient animals: nude mouse
SCID mouse

Nude Mice

athymic and hairless; arose during development of inbred strains of mice (see Genet. Res. '66 = hairless
*Nature '68 = athymic)

whn = mutant locus

SCID Mice

severe immune-deficient; defect in stem cell progeny pool that gives rise to B and T cells

still has NK cells, macrophages

can be repopulated (with immune cells) - good for testing novel immunotherapeutics

*handout

10
Cell Proliferation

Ian F. Tannock

10.1 INTRODUCTION

Tumors grow because they contain a population of cells that is expanding as a result of cell division. Growth occurs because the homeostatic control mechanisms that maintain the appropriate number of cells in normal renewal tissues are defective. Development of tritiated thymidine and autoradiography in the 1950s, and the more recent application of flow cytometry, have allowed a detailed analysis of tumor growth in terms of the kinetics of proliferation of their constituent cells. Proliferative rate varies widely among tumors; nonproliferating cells are common, and there is often a high rate of cell death. The rate of cell proliferation in tumors may be an important factor in determining prognosis, or response to radiation or chemotherapy. Several normal tissues, including bone marrow and intestine, contain cells with a high rate of cell proliferation, and damage to these cells may be dose limiting for chemotherapy. Concepts related to the cell cycle and the molecular events that occur during its constituent phases are therefore not only of biological interest, but are key to understanding the interaction of drugs and radiation with tissues.

10.2 TUMOR GROWTH

10.2.1 Concept of Exponential Growth

Tumor growth can be determined by measuring tumor volume as a function of time. Most commonly this is done by making caliper measurements of at least two orthogonal diameters, and by assuming that the tumor is ellipsoid in shape. If tumor volume (V) is then plotted against time (t) the resulting growth curve will often approximate an exponential relationship, at least during part of its growth (Fig. 10.1a). It is usual to plot tumor growth curves using a logarithmic axis for volume and a linear axis for time, since the exponential relationship is then represented as a straight line (Fig. 10.1b).

Exponential growth of tumors will occur if the rates of cell production and of cell loss or death are proportional to the number of cells present in the population (N). The differential equation that describes tumor growth is then given by

$$\frac{dN}{dt} = (K_P - K_L)N. \qquad (10.1)$$

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Appendix Exhibit D

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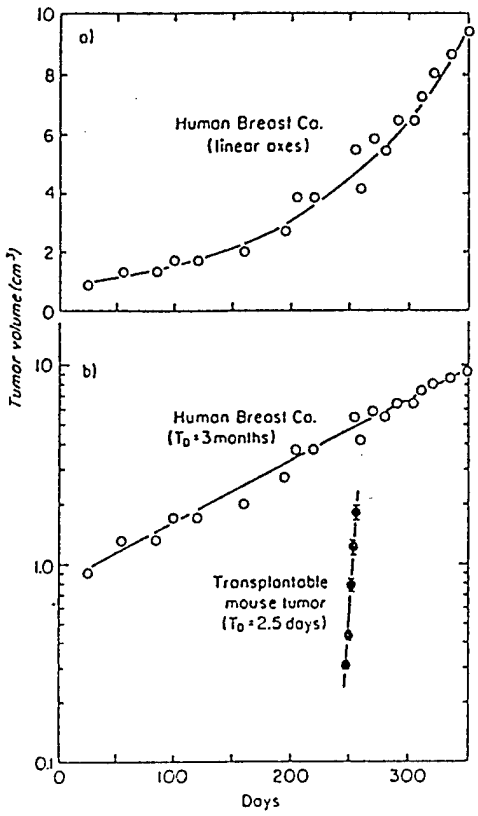


Figure 10.1. Growth curves for a lung metastasis from a human breast cancer: *a*, plotted on linear axes; *b*, same data plotted using a logarithmic scale for tumor volume. (Data of RP Hill and RS Bush, unpublished. Included with permission.) A growth curve for a rapidly growing transplantable tumor in the mouse is included in *b* for comparison. T_D = volume doubling time.

Table 10.1 Volume Doubling Time (T_D) for Representative Human Tumors

Tumor Type	Number of Tumors	Volume Doubling Time (weeks) (geometric mean value)
Primary lung cancer		
Adenocarcinoma	64	21
Squamous-cell carcinoma	85	12
Anaplastic carcinoma	55	11
Breast cancer		
Primary	17	14
Lung metastases	44	11
Soft-tissue metastases	66	3
Colon/rectum		
Primary	19	90
Lung metastases	56	14
Lymphoma		
Lymph node lesions	27	4
Lung metastases of:		
Carcinoma of testis	80	4
Childhood tumors	47	4
Adult sarcomas	58	7

Note: From data reviewed by Steel (1977).

Here K_P and K_L are the rate constants for cell production and cell loss. Equation (10.1) can then be integrated to give

$$N = N_0 \exp[(K_P - K_L)t], \qquad (10.2)$$

where N_0 is the number of cells in the population at the initial time of observation ($t = 0$). Tumor volume (V) will also be related exponentially to time, if the number of cells is the principal determinant of tumor volume (see section 10.2.3). Exponential growth implies that the time taken for a tumor to double its volume is constant. The volume doubling time (T_D) can be obtained by setting $N = 2N_0$ at $t = T_D$ in eq. (10.2). Thus,

$$T_D = \frac{\log_e 2}{(K_P - K_L)} = \frac{0.693}{(K_P - K_L)}, \qquad (10.3)$$

and the equation describing growth of the tumor may then be written

$$V = V_0 \exp(0.693t/T_D). \qquad (10.4)$$

Here V_0 is the tumor volume at time $t = 0$. During the period of exponential growth, doubling times for transplanted murine tumors are typically 1–5 days, while most human tumors grow more slowly with doubling times in the range of 1–3 months (Table 10.1).

Exponential growth often leads to the false impression that the rate of tumor growth is accelerating with time (see Fig. 10.1a). Increase in the diameter of a human tumor from 0.5 to 1.0 cm may escape detection, whereas increase in diameter of a tumor from 5 to 10 cm is more dramatic and is likely to cause new clinical symptoms. Both require three volume doublings, and during exponential growth they will occur over the same period of time.

10.2.2 Growth of Human Tumors

Estimates of the growth rates of untreated human tumors have been limited by the following constraints:

1. Only tumors that tend to be unresponsive to therapy can ethically be followed without treatment, although some data are available from older studies on the growth of tumors such as lymphoma, which are now treated aggressively with drugs.
2. Accurate measurements can only be made on tumors growing in selected sites. The majority of studies have examined lung metastases using serial X-rays,

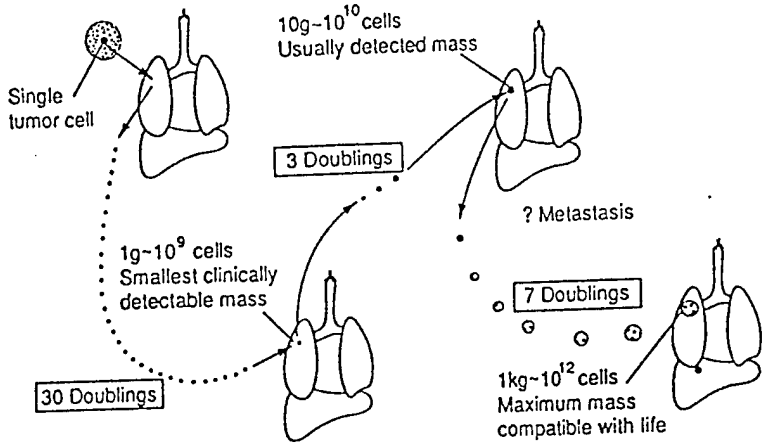


Figure 10.2. A human solid tumor must undergo about 30 to 33 doublings in volume from a single cell before it achieves a detectable size of 1–10 g. Metastases may have been established prior to detection of the primary tumor. Only a few further doublings of volume lead to a tumor whose size is incompatible with life. (Adapted from Tannock, 1983.)

although the availability of computerized tomographic (CT) and magnetic resonance imaging (MRI) scans has expanded the range of sites in which tumor volume can be estimated with reasonable accuracy. There have been few measurements of the growth of primary tumors.

3. The period of observation is restricted to that between the time of detection of the tumor and either death of the host or the initiation of some form of therapy; this time interval is only a small fraction of the history of the tumor's growth (see Figs. 10.2 and 10.3).

Despite the limitations stated above, there is a large number of published estimates of the growth rate of human tumors. Many of these studies have utilized only two or three sequential measurements, so that they do not provide information about the shape of the tumor growth curve. Steel (1977) has reviewed published measurements of the rate of growth of 780 human tumors, and estimates of volume doubling time for several types of tumor are summarized in Table 10.1. A few general conclusions may be stated:

1. There is wide variation in growth rate, even among tumors of the same histological type and site of origin.
2. Representative mean doubling times for lung metastases of common tumors in man are in the range of 2–3 months.
3. There is a tendency for childhood tumors, and adult tumors that are known to be responsive to chemotherapy (e.g., lymphoma, Ca testis), to grow more rapidly than unresponsive tumors (e.g., Ca colon).
4. From the limited data available, it can be noted that metastases of breast and colorectal tumors tend to grow more rapidly than the primary tumor in the same patient.

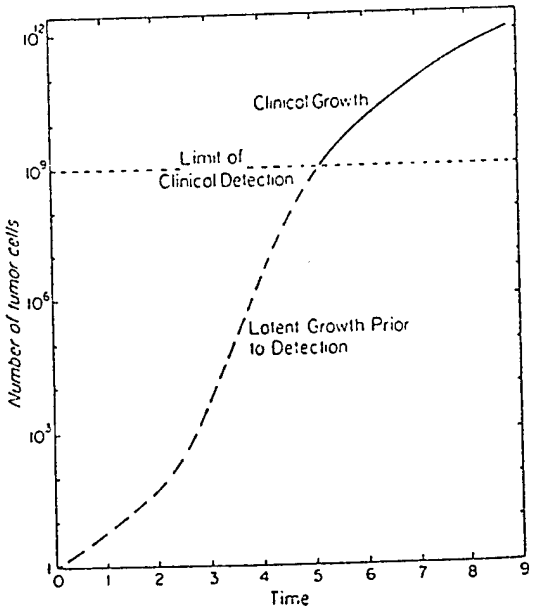


Figure 10.3. Hypothetical growth curve for a human tumor, showing the long latent period prior to detection. Tumors may show an early lag phase, and progressive slowing of growth at large size.

10.2.3 Long Preclinical History of Tumors: Departures from Exponential Growth

paradoxical

Superficial tumors may be detected clinically when they contain about 1 billion (10^9) cells; tumors of internal organs are likely to escape detection until they are considerably larger (Fig. 10.2). There is indirect evidence

(V. Production of Tumors - continued)

physical techniques:

- selection of tumor/host combination
- sterile technique (immunosuppressed animals)
- removal of tumor from host; mince 2-3 mm fragments (in medium) [can disperse here]
- inject (known inoculation volume and cell #):
  *subcutaneous intramuscular/intracranial
  intraperitoneal vein
- tumor "take" requires ~7 days
- measure growth with calipers

requirements for nutrients:

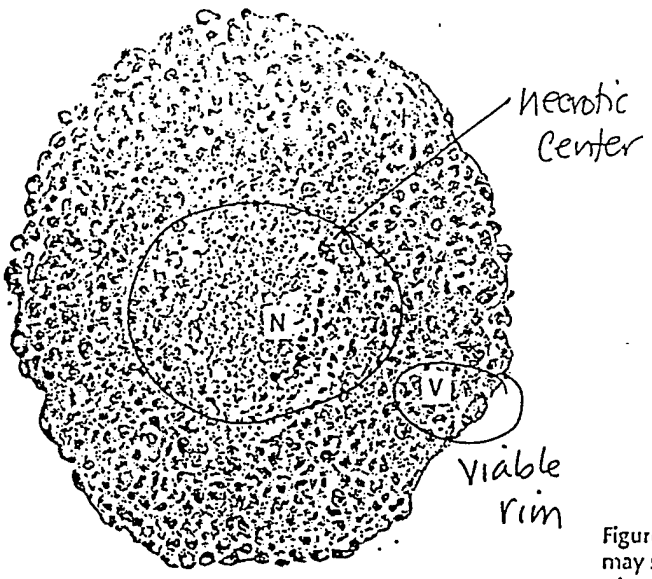


Figure 10.18. Cross section of a spheroid formed from a tumor cell line derived from human bladder cancer, showing the viable rim (V) and central necrosis (N). (Courtesy of Dr. R. M. Sutherland.)

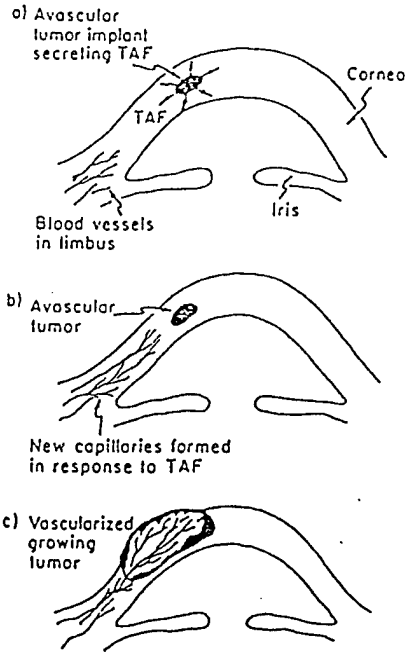


Figure 10.19. Experiment to demonstrate that tumor tissue may stimulate the growth of blood vessels through secretion of growth factors, here designated by tumor angiogenesis factors (TAF). A piece of tumor implanted into the avascular cornea of a rabbit's eye grows to a maximum size of ~1 mm until blood vessels are stimulated to invade it from the surrounding limbus. (Adapted from Folkman, 1975.)

(from: Basic Science of Oncology - Tannak '96)

Current Topics in Tumor Biology

a journal club

Wednesday October 9, 1996
2:30-3:30pm
1093 Guggenheim

"Characteristics of an Assay for Rous Sarcoma Virus and Rous Sarcoma Cells in Tissue Culture"

by

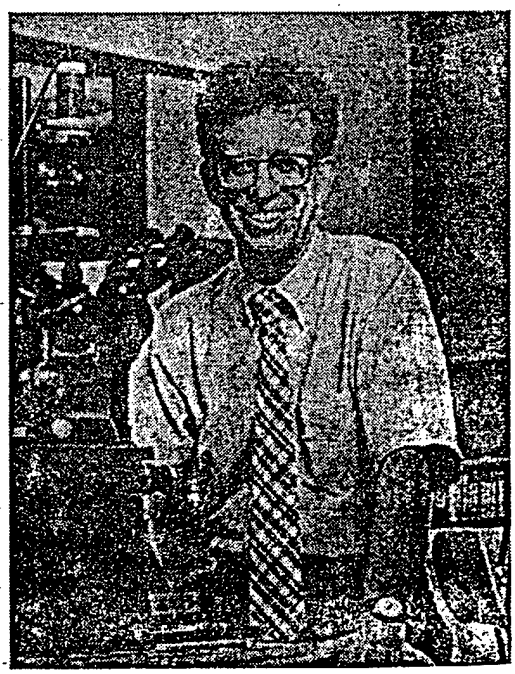
Howard M. Temin and Harry Rubin

Virology 6:669-688 (1958)

The paper will be presented by

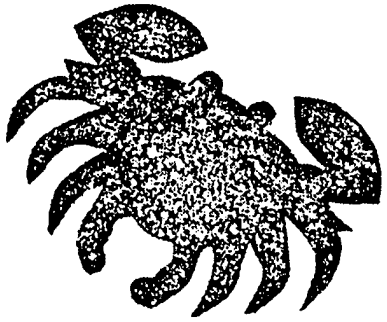
Nicole Ann Becker

Graduate Student



In 1958, Howard Temin (then a graduate student) and Harry Rubin (a postdoctoral fellow) developed the first quantitative assay for the transformation of cultured cells by tumor viruses. Prior to their work, Rous Sarcoma Virus (isolated in 1911 by Peyton Rous) had become the first generally accepted tumor virus because of its ability to cause sarcomas following inoculation of chickens. The simple assay for cell transformation that Temin and Rubin devised has formed the modern basis for studies of tumor viruses and oncogenes, including Temin's subsequent experiments from which the DNA provirus hypothesis was derived. Temin was awarded the Nobel Prize in 1975 along with Baltimore and Dulbecco. Temin died in 1994 at the age of 59 from lung cancer (he was never a smoker).

(Note: Journal club presentations during Fall Quarter will cover papers of fundamental historic interest in Cancer Biology)



Tumor Biology Tea

Please join us for tea, treats, and a relaxed atmosphere of stimulating conversations with anyone interested in the field of tumor biology.

To be held immediately following the tumor biology journal club each Wednesday.

Approximately **4pm**, Room **1008 Guggenheim**

First Tea: October 9th

All are welcome.

Dr. N. Maihle
TBio I, 1996

INDEPENDENT STUDY PROBLEM SET
Week 2/TBio I

1) Provide a brief history of cell cultivation, and how this history has been interwoven with the study of transformed cells.

2) When was the first mammalian cell line established, by whom, and what was it called? Is it still in culture? How was it derived? What characteristic property of rodent cells was determined in the course of these experiments?

3) What is the "Hayflick phenomenon"? What follows cell crisis in culture, and how do rodent cells and human cells differ during this period?

4) What are the properties of transformed cells that can be assayed *in vitro*? Which of these factors is truly unique to transformed cells?

5) What is the relationship between metabolic rate, the rate of cell division, and the transformed phenotype?

6) What is meant by the term "cooperativity between oncogenes"?

7) What is the relationship between immortalization and the transformed phenotype?

TBIO 5000
Small Group Problem Set
10/10/96

1. The oncogene hypothesis, as developed by Bishop and Varmus in the late 1970's suggested that the transforming elements of transforming retroviruses were genetic sequences called viral oncogenes, and that these sequences were pirated by retroviruses via recombination between retroviruses and normal cellular genes (i.e., proto-oncogenes).

   By the early 1980's this model was generally accepted, but only a few viral oncogenes had been cloned, and their genetic and/or functional similarities were unclear. What was the status of tumor suppressor research at this time?

   In 1983, both Land and Ruley, independently proposed that some of these oncogenic sequences could transform cells in culture synergistically. Did these oncogenes have transforming potential independently *in* vitro? What were the oncogenes involved in these studies, and briefly describe the data used to support the concept on oncogene cooperativity.

2. Since these 1983 publications, further studies suggest that additional oncogenes can act synergistically: which classes of oncogenes are generally involved in cooperative transformation? How stringent are the assays that were used to determine the transforming potential of these oncogenes? What is the role of tumor suppressor gene products in oncogene cooperativity?

3. What molecular models have been proposed to explain the phenomenon of "oncogene collaboration"? Have any of these models been tested and/or proven to exist at the molecular level?

4. What is the relationship between *in vitro* transformation assays using primary cell cultures *vs.* established cell lines (e.g., 3T3 cells). What is meant by the expression that '3T3 cells are halfway there' in transformation assays?

5. What is the relationship between immortalization and the transformed phenotype?

6. What are the implications of the concept of oncogene cooperativity for the multistep model of carcinogenesis?

MAYO CANCER CENTER
"Works in Progress"
1996

Noon - 1:00 p.m.

ROOM	DATE	TITLE	SPEAKER
Guggenheim 1008/1093	January 26, 1996	"Molecular Basis of Pediatric Brain Tumors"	Dr. Corey Raffel
Guggenheim 1008/1093	February 23, 1996	"Pediatric Marrow Transplantation"	Dr. Peter Anderson
Guggenheim 1008/1093	March 22, 1996	"Molecular Studies on the Pathogenesis and Treatment of Myeloma"	Dr. John Lust
Guggenheim 1008/1093	April 19, 1996	"A Young Patient with Anal Cancer and a Strong Family History of Colon Cancer: A Review of Clinical Considerations, Medical Genetics, and Molecular Biology"	Dr. James Martenson
Guggenheim 1008/1093	May 17, 1996	"Magnetic Resonance Elastrography Via Direct Visualization of Acoustic Strain Waves"	Dr. Richard Ehman
	NO WORKSHOPS 6/96 - 8/96		
Guggenheim 1008/1093	September 27, 1996	"Serine Proteases: Targets for Chemotherapeutic Agents"	Dr. Matthew Ames
Guggenheim 1008/1093	October 25, 1996	"Target of Rapamycin: Immunosuppressive Drugs Uncover a Novel Family of Eukaryotic Cell Cycle Regulators"	Dr. Robert Abraham
Guggenheim 1008/1093	November 22, 1996	"Growth Factor-Regulated Transcription Factor Encoding Genes from Exocrine Pancreatic Cell Populations"	Dr. Raul Urrutia
Guggenheim 1008/1093	December 20, 1996	"Application of Retroviral Vectors to Molecular Medicine"	Dr. Mark Federspiel

MAYO CANCER CENTER
GRAND ROUNDS

WINTER QUARTER, 1996
Noon - 1:00 p.m.

ROOM	DATE	TITLE	SPEAKER
Kendall-Hench Lecture Hall	January 10, 1996	"Cyclooxygenase-2 Reversibly Alters Intestinal Epithelial Adhesion and Apoptosis"	Dr. Raymond DuBois Vanderbilt Cancer Center
Leighton Auditorium	January 18, 1996	"Ras Prenylation: A Novel Target for Cancer Chemotherapy"	Dr. Said Sebti University of Pittsburgh
Guggenheim 1093	January 22, 1996	"Chemoprevention of Liver Cancer With Oltipraz: Experimental Models and Clinical Trials"	Dr. Thomas Kensler Johns Hopkins University
Leighton Auditorium	February 1, 1996	"Molecular Genetics of Endometrial Cancer"	Dr. Lora Hedrick Johns Hopkins University
Leighton Auditorium	February 8, 1996	"Utility of the human Multidrug Resistance Gene and Promoter for Gene Therapy"	Dr. A. Christie King Glaxo-Wellcome Research
Leighton Auditorium	February 15, 1996	"The Minnesota Cancer Surveillance System: Past, Present, and Olmsted County"	Dr. Alan Bender Dr. Sally Bushhouse Minnesota Department of Health
Leighton Auditorium	February 29, 1996	"Co-deletion of CDKN2 (p16INK4) and Methylthioadenosine Phosphorylase (MTAP) Genes in Multiple Tumor Types: Implications for Chemoselectivity in Cancer Therapy"	Dr. Funmi Olopade University of Chicago Medical Center
East 12 Seminar Room	March 1, 1996	"Moving into the Age of Genetics in Clinical Cancer Care: The Example of Breast Cancer"	Dr. Funmi Olopade University of Chicago Medical Center

Leighton Auditorium	March 7, 1996	"Molecular Characterization of the 3p14.2 Common Fragile Site, FRA3B; Its Role in Chromosomal Breakage in Solid Tumors"	Dr. David I. Smith Wayne State Univesity School of Medicine
Kendall-Hench Lecture Hall	March 14, 1996	"Role of Angiogenic Growth Factors in Breast Cancer Progression"	Dr. Francis Kern Lombardi Cancer Center Georgetown University
Leighton Auditorium	March 18, 1996	"DNA Methylation as a Mechanism for Control of Estrogen Receptor Expression"	Dr. Nancy Davidson Johns Hopkins University
Guggenheim 1093	March 21, 1996	"A Novel Mammary Specific Gene and Its Implication to Breast Cancer"	Dr. Timothy Fleming Washington University School of Medicine

MAYO CANCER CENTER GRAND ROUNDS

SPRING QUARTER, 1996
Noon - 1:00 p.m.

ROOM	DATE	TITLE	SPEAKER
Leighton Auditorium	April 4, 1996	"Nuclear Matrix Proteins as Diagnostic and Monitoring Tools in Cancer"	Dr. Cheryl Hayden Matritech, Inc.
Leighton Auditorium	April 11, 1996	"Functional Dissection of elk-1 Onco-Protein and a Glimpse into the Function of BRCA1 Involved in Breast and Ovarian Cancers"	Dr. M. Veena N. Rao Jefferson Cancer Institute Thomas Jefferson University
South Lecture Hall	April 12, 1996	"Role of Fusion Proteins in Human Leukemias and Solid Tumors"	Dr. E. Shyam P. Reddy Jefferson Cancer Institute Thomas Jefferson University
Kendall-Hench Lecture Hall	April 25, 1996	"The HER-2/neu Oncogene in Cancer"	Dr. Mien-Chie Hung M.D. Anderson Cancer Center

Leighton Auditorium	May 2, 1996	"Telomerase and Cancer: Diagnostic, Prognostic, and Therapeutic Implications"	Dr. Jerry Shay
Leighton Auditorium	May 16, 1996	"Genetic Therapy of Cancer: The Potential Use of T-cell Receptor Genes for the Treatment of Melanoma"	Dr. Michael Nishimura Surgery Branch, NCI
Mann Hall, Medical Sciences Building	May 23, 1996	"Detecting Genetic Effects in Epidemiologic Studies of Complex Diseases"	Dr. Ping Yang University of Pittsburgh Medical Center
South Lecture Hall	June 3, 1996	"Chromosomal Breakage and Rearrangements in FRA3B in Many Human Tumors: New Targets in Tumorigenesis"	Dr. David I. Smith Wayne State University School of Medicine
Leighton Auditorium	June 6, 1996	"Studies of the DCC (deleted in colorectal cancer) Gene in Cancer and Development"	Dr. Eric Fearon University of Michigan Comprehensive Cancer Center
Leighton Auditorium	June 20, 1996	"Camptothecin-based Topoisomerase I Targeted Therapies: Some Rules of the Game"	Dr. Peter Houghton St. Jude Children's Research Hospital
Kendall-Hench Lecture Hall	July 19, 1996	"Cell Cycle Regulation of Receptor Tyrosine Kinases"	Dr. Mien-Chie Hung M.D. Anderson Cancer Center

Seminars Co-Sponsored by the MAYO CANCER CENTER

SUMMER/FALL QUARTERS, 1996

ROOM	DATE	TITLE	SPEAKER
Guggenheim 1008/1093	June 7, 1996	"The 1996 Mayo-Luther Forum on Hematopoietic Stem Cells"	Dr. L. A. Solberg DR. J. E. Wagner Dr. B. B. Aggarwal Dr. P. J. Cagnoni Dr. R. Sackstein
Guggenheim 1093	August 16, 1996	"Alteration of the HER-2/neu Gene in Human Breast Cancer: Diagnositc and Therapeutic Implications"	Dr. D. J. Slamon Johnson Comprehensive Cancer Center

Foundation House	September 11 - 12, 1996	"Comfort Symposium: Pancreatic Carcinogenesis"	Dr. R. J. MacDonald Dr. E. P. DiMagno Dr. S. Githens Dr. C. D. Ulrich, II Dr. D. Bockman Dr. J. K. Reddy Dr. D. S. Longnecker Dr. P. Pour Dr. J. A. Williams Dr. C. D. Lodgson Dr. R. Urrutia Dr. S. N. Thibodeau Dr. C. Raffel
Phillips Hall, Siebens 1	October 16, 1996	"New and Future Directions in Predicting Prostate Tumor Behavior"	Dr. D. S. Coffey
Phillips Hall, Siebens 1	October 30, 1996	"Harold W. Siebens Symposium on Molecular Medicine"	Dr. E. R. Dickson Dr. M. M. Ames Dr. G. J. Nabel Dr. J. M. Heard Dr. E. G. Nabel Dr. M. K. Brenner
Guggenheim 1498	November 20, 1996	"Regulation of Transcription and V(D)J Recombination of the Kappa Immunoglobulin Light Chain Locus"	Mr. D. O'Brien University of Minnesota
Kendall-Hench Lecture Hall	November 26, 1996	"Mechanisms of HIV-1 Reverse Transcriptase Resistance to Nucleoside and Nonnucleoside Inhibitors"	Dr. S. H. Hughes NCI-Frederick Cancer Research and Development Center

clinic bulletin

Salisbury, Jeffrey L.
Appendix Exhibit E

VISITING FACULTY -- SECTION GUEST

April 5, 1996

BIOCHEMISTRY AND MOLECULAR BIOLOGY — Visiting Faculty Member — Dr. John Adam, professor, Mathematics and Statistics, Old Dominion University, Norfolk, Va. (See Tues.)

CARDIOVASCULAR DISEASES — Visiting Faculty Member — Dr. David J. Skorton, professor of medicine and engineering, vice president for research, The University of Iowa, Iowa City. (See Wed.)

DERMATOLOGY — Visiting Faculty Member — Dr. Francisco A. Kerdel, University of Miami School of Medicine, Cedars Medical Center. (See Thurs. and Fri.)

HEALTH SCIENCES RESEARCH — Visiting Faculty Member — Mr. Victor Cohn, science reporter, Washington, D.C. (See Thurs.)

MAYO CANCER CENTER — Visiting Faculty Member — Dr. M. Veena N. Rao, Jefferson Cancer Institute, Philadelphia. (See Thurs.)

MAYO CANCER CENTER — Visiting Faculty Member — Dr. E. Shyam P. Reddy, Jefferson Cancer Institute, Philadelphia. (See Fri.)

PHARMACOLOGY — Visiting Faculty Member — Dr. Alessandra d'Azzo, associate member, Department of Genetics, St. Jude's Children's Hospital, Memphis, Tenn. (See Fri.)

† Certified for Category I, CME Credit on an hour-for-hour basis for purposes of Minnesota Relicensure and the Physician's Recognition Award of AMA.

CONFERENCES, LECTURES, SEMINARS

Saturday, April 6

CARDIOVASCULAR DISEASES--8:30 a.m., Walters Hall, 8 Alfred, Saint Marys Hospital-- Edwards — Cardiac Transplantation: Update 1996.

† GYNECOLOGICAL SURGERY--7:30 a.m., Room 4N-103, Charlton Bldg. -- Kho — Ovarian Tumors of Low Malignant Potential — Podratz — Case Presentation.

† NEURO-ONCOLOGY WORK CONFERENCE, Case Conference--7 a.m., Room 2-651, Mary Brigh, Saint Marys.

† ORTHOPEDIC SURGERY -- 9 a.m., Judd Hall, Mayo Bldg.-- No Conference.

OTORHINOLARYNGOLOGY--Core Curriculum--8 a.m., Methodist, Dining Room 5 -- Trastek — Tracheal and Cervical Esophageal Tumors.

-- 9 a.m., Dining Room 5, Methodist -- Vickers — Surgical Anatomy of the TMJ and Infratemporal Fossa.

PLASTIC SURGERY -- 9 a.m., Room 1093, Guggenheim Bldg.

THORACIC AND CARDIOVASCULAR SURGERY, Congenital Heart Surgery Conference--7:30 a.m., Room 5-193, Saint Marys -- Theodoro — TAPVC.

Monday, April 8

† CARDIAC SURGERY TEACHING SESSION -- 7 a.m., Room H and J, Saint Marys Cafeteria -- Crescenzo/Mullany —Case Presentation.

DERMATOLOGY, Dermatopathology Conference -- 11 a.m., Room 1-507, Baldwin Bldg.

† DIAGNOSTIC RADIOLOGY, Conference -- noon, 2nd Floor Lecture Hall, Mayo Bldg.-- Kiely — Radiology of Stroke.

INTERNAL MEDICINE PATHOLOGY MORTALITY AND MORBIDITY CONFERENCE--12:30 p.m., Room M-459, Saint Marys.

NEUROLOGY, Basic Neurology Course--4:30 p.m., Room 1093, Guggenheim Bldg.-- Petersen — Cortical Maps.

PATHOLOGY -- 5 p.m., 11th Floor, Hilton Bldg.-- Gaffey.

VASCULAR MEDICINE -- 7 a.m., Room M-459, Alfred Bldg., Saint Marys--Case Presentations.

Tuesday, April 9

BIOCHEMISTRY AND MOLECULAR BIOLOGY — Visiting Faculty Member — 11 a.m., Mann Hall, Medical Sciences Bldg. — J. Adam —Mathematical Models and Metaphors in Cancer Biology.

† DIAGNOSTIC RADIOLOGY, Conference -- noon, 2nd Floor Lecture Hall, Mayo Bldg.-- Hartman — CT of the Airways (Chest).

— 4 p.m., 2nd Floor Lecture Hall, Mayo Bldg. — Bonelli — Bone.

Tuesday, April 9 (Continued)

ENDOCRINOLOGY/INTERNAL MEDICINE--12:30 p.m., Room M-59, Joseph Bldg., Saint Marys-- Chini — Cyclic ADP Ribose and NAADP, Novel Regulators of Intracellular Calcium.

FAMILY MEDICINE --12:30 p.m., Dining Room H & J, Saint Marys.

† HYPERTENSION -- 12:30 p.m., 9th Floor Lecture Hall, Mayo Bldg.-- Morgenstern — A Potpourri of Issues in Juvenile Hypertension.

INTERNAL MEDICINE, Community Medicine--7:30 a.m., 1st Floor Lecture Hall, Baldwin Bldg.-- O'Meara - The Use of Oral and Sublingual Nifedipine for the Acute Treatment of Severe Hypertension — Vizenor — Evaluating Plasma Acetaminophen Levels After Acute Ingestion of Acetaminophen.

† NEPHROLOGY -- 7:45 a.m., Weld Hall, 3rd Floor, Eisenberg Bldg, Methodist -- Burnett — Advanced in our Understanding of the Natriuretic Peptide System in Congestive Heart Failure.

ORTHODONTICS--7:30 a.m., Room 482-W, Mayo Bldg.-- Technique.

† ORTHOPEDICS--6 p.m., Judd Hall, Mayo Bldg.-- McGrory -- Femoral Shaft Fractures in Children — Ortiguera — Fractures in Child Abuse.

PEDIATRICS--7 a.m., Room 2-651, Mary Brigh Bldg.--Saint Marys.

PEDIATRICS, Cardiac Catheterization Conference--7:30 a.m., Walters Hall, Saint Marys.

PERIPHERAL VASCULAR SURGERY--7:30 a.m., Mayo Lecture Hall, 1st Floor, Alfred Bldg., Saint Marys.

† PHYSICAL MEDICINE AND REHABILITATION, Clinical Conference--7:15 a.m., 10th Floor Conference Room, Mayo Bldg.-- Showalter — Acute Quadriplegic Myopathy.

— 11 a.m., Room 3-716, Saint Marys — Spine Discussion Group.

PREVENTIVE MEDICINE — 12:15 p.m., Room 1-507, Baldwin Bldg. — Orford — Pilots and Passengers - Problems in the Air.

† PSYCHIATRY & PSYCHOLOGY -- 7:30 a.m., Judd Auditorium, Mayo Bldg. -- Saracino — Psychiatry in the Alaskan Bush.

RADIATION ONCOLOGY NEW PATIENT CONFERENCE--8 a.m., Room C-100-5, Charlton Bldg.

† UROLOGY, (EX. U) Conference--5:30 p.m., 17th Floor Seminar Room, Mayo Bldg.-- Kletscher/Patterson.

Wednesday, April 10

† ANESTHESIOLOGY--7 a.m., Kendall-Hench Hall, Guggenheim Bldg.-- Dietz — Nitric Oxide in Human Vasomotor Control.

CARDIOVASCULAR DISEASES, Echocardiography--7:30 a.m., Judd Hall, Mayo Bldg. -- Seward — Adult Ebstein's Anomaly — Ammash — Pseudo-Ebstein's.

CARDIOVASCULAR DISEASES — Visiting Faculty Member — 12:30 p.m., 19th Floor Lecture Hall, Mayo Bldg. — D. Skorton — The Government/University Partnership in Research: In Search of New Principles.

— 7 p.m., Mayo Foundation House — Cardiac Imaging: Progress and Prospects.

† CARDIOVASCULAR SURGERY--7:30 a.m., Walters Hall, Alfred Bldg., Saint Marys-- Puga — Chief Resident/Morbidity and Mortality Conference.

† COLON AND RECTAL SURGERY--7 a.m., Room 402, Siebens Bldg.-- Martenson — Radiation Enteritis/Proctitis.

† DIAGNOSTIC RADIOLOGY, Conference--noon, 2nd Floor Lecture Hall, Mayo Bldg.-- King — Adrenal Pathology.

ENDOCRINOLOGY, Grand Rounds--7:30a.m., 18th Floor Lecture Hall, Mayo Bldg.

† MEDICAL GRAND ROUNDS--12:30 p.m., Phillips Lecture Hall, Siebens Bldg.--Will Also be Televised Mayo Lecture Hall, Room M-459, Saint Marys -- Ahlskog — Medication Strategies for Early Parkinson's Disease? Recipe to Slow Progression?

NEUROLOGY, Basic Neurology Course--4:30 p.m., Room 1093, Guggenheim Bldg.-- Lagerlund —Cortical Neuron Circuits.

† NEUROLOGY, Saint Marys Clinical Case Conference -- 7:00 a.m., Mayo Lecture Hall, Room M-459, Alfred Bldg., Saint Marys -- Child Neuro.

† OPHTHALMOLOGY, Grand Rounds -- 7:15 a.m., 7th Floor Seminar Room, Mayo Bldg.

Wednesday, April 10 (Continued)

ORAL SURGERY--7:30 a.m., Dining Room #4, Methodist.

ORTHODONTICS--7:30 a.m., Room 110, Harwick Bldg.--Literature Review.

† ORTHOPEDICS, Fracture Conference--7:15 a.m., Mann Hall, Medical Sciences Bldg.-- Trousdale — Complications Following Hip Fracture.

OTORHINOLARYNGOLOGY--7:30 a.m., 10th Floor Seminar Room, Mayo Bldg.-- Pathology Conference.

† PLASTIC SURGERY -- 6:45 a.m., Room G-21, Saint Marys Hospital.

PULMONARY/CRITICAL CARE MEDICINE CONFERENCE, Medical Surgical Clinical Conference--7:30 a.m., 19th Floor Lecture Hall, Mayo Bldg.--Case Presentation.

PSYCHIATRY AND PSYCHOLOGY, Multidisciplinary Pain Group, 12:15 P.M., 10th Floor Seminar Room, Mayo Bldg. — Gay — Spinal Manipulation in Back Pain Treatment.

SURGICAL ORTHODONTIC Clinic--4 p.m., W-4A Laboratory--B.A. Lund, A. H. Sather.

Thursday, April 11

COMBINED CRITICAL CARE--11 a.m., Mayo Lecture Hall, Room M-459, Alfred Bldg., Saint Marys-- Simon/Johnson/Tobert — Interactive Multidisciplinary Conference.

DERMATOLOGY, Hospital Conference--7:30 a.m., Judd Auditorium, Mayo Bldg.

DERMATOLOGY — Visiting Faculty Member— noon, 12th Floor Seminar Room, Mayo Bldg. — F. Kerdel — Inpatient Dermatology in a Generic Fashion.

† DIAGNOSTIC RADIOLOGY, Conference--noon, 2nd Floor Lecture Hall, Mayo Bldg.-- Carlson — GI.

— 4 p.m., 2nd Floor Lecture Hall, Mayo Bldg. — Baldwin — Vasc. Intervention.

ENDOCRINOLOGY, Pituitary-Gonad-Adrenal Conference--12:30 p.m., 18th Floor Lecture Hall, Mayo Bldg.

FAMILY MEDICINE--12:30 p.m., Dining Room H & J, Saint Marys.

† GASTROENTEROLOGY, Liver Conference — 12:30 p.m., 19th Floor Lecture Hall, Mayo Bldg. — Raimondo/Saslow.

HEALTH SCIENCES RESEARCH — Visiting Faculty Member — 10 a.m., Leighton Auditorium, Siebens Bldg. — V. Cohn — How to Help Reporters Tell the Truth (Sometimes).

† HEMATOLOGY, Clinical Case Conference--7:45 a.m., 10th Floor Seminar Room, Mayo Bldg.

MAYO CANCER CENTER — Visiting Faculty Member — noon, Leighton Auditorium, Siebens Bldg. — M. Rao —Functional Dissection of elk-1 Onco-Protein and a Glimpse into the Function of BRCA1 Involved in Breast and Ovarian Cancer.

NEUROLOGY, Basic Neurology Course -- 4:30 p.m., Room 1093, Guggenheim Bldg.-- McLaren — Visual System.

ORTHODONTICS--7:30 a.m., Room 110, Harwick Cafeteria--Case Presentation.

† ORTHOPEDICS, Oncology Tumor Conference -- 7 a.m., East 2 Conference Room, Mayo Bldg.

† PEDIATRICS, Core Conference--12:30 p.m., 1st Floor Lecture Hall, Baldwin Bldg.-- No Conference.

PHYSICAL MEDICINE AND REHABILITATION, Sports Medicine Conference--7:15 a.m., 10th Floor Seminar Room, Mayo Bldg.-- E10 Discussion Group.

— 10:30 a.m., South Dining Room, Saint Marys Cafeteria — Brain Discussion Group.

RADIATION ONCOLOGY NEW PATIENT CONFERENCE--8 a.m., Room C-100-5, Charlton Bldg.

† RHEUMATOLOGY--7:30 a.m., Room 1093, Guggenheim Bldg. — No Conference.

† UROLOGY, Academic Seminar--5:30 p.m., 17th Floor Seminar Room, Mayo Bldg.-- Kramer — Pediatric GU Sarcomas.

Friday, April 12

BREAST Case Conference--7 a.m., Second Floor Lecture Hall, Mayo Bldg.

† CARDIOVASCULAR GRAND ROUNDS -- 7:30 a.m., 16th Floor Lecture Hall, Mayo Bldg.-- Meyers/Frye.

CLINICAL BIOCHEMISTRY AND IMMUNOLOGY SEMINAR--7:45 a.m., Room 1061, Hilton Bldg.-- Snyder — TBA.

DERMATOLOGY — Visiting Faculty Member — 7:45 a.m., 6th Floor Lecture Hall, Mayo Bldg. — F. Kerdel — Toxic Epidermal Necrolysis.

Friday, April 12 (Continued)

† DIAGNOSTIC RADIOLOGY, Conference-- 7 a.m., Multidisciplinary Breast Conference.

— noon, 2nd Floor Lecture Hall, Mayo Bldg.— Breen — Cardiac.

ENDOCRINOLOGY, Thyroid Conference--12:30 p.m., 18th Floor Lecture Hall, Mayo Bldg.

GASTROENTEROLOGY, GI Conference--12:30 p.m., 19th Floor Lecture Hall, Mayo Bldg. -- Pathology Conference.

† GENERAL THORACIC SURGERY--7 a.m., Room G-21, Saint Marys Cafeteria -- Case Presentations.

HAND Clinic--6:30 a.m., Dining Room 6, Methodist-- Amadio — Review of Hand Papers At AAOS Meeting.

† INTERNAL MEDICINE, General Medicine Residents' Conference -- 7:30 a.m., Walters Hall, Saint Marys -- Gen Med 1&2.

LABORATORY SOCIETY--noon, Mayo Foundation House--Bleimeyer - The Information Superhighway as a Laboratory Tool.

MAYO CANCER CENTER — Visiting Faculty Member— noon, South Hall, Guggenheim Bldg. — E. Reddy — Role of Fusion Proteins in Human Leukemias and Solid Tumors.

† NEPHROLOGY--12:30 p.m., Room 1132, Hilton Bldg. -- Renal Parenchymal Conference.

† NEUROLOGY, Resident Research Conference -- 12:30 p.m., 8th Floor Conference Room, Mayo Bldg.-- Boes — CNS Aspergillosis.

† PEDIATRICS--7:45 a.m., Mayo Lecture Hall, M-459, Alfred Bldg., Saint Marys-- Crifasi — The Use of FISH in the Diagnosis of Pediatric Disorders.

PHARMACOLOGY — Visiting Faculty Member— 11 a.m., Room 1093, Guggenheim Bldg. — A. d'Azzo — Animal Models of Lysosomal Diseases and Therapy.

PULMONARY/CRITICAL CARE MEDICINE CONFERENCE -- noon, 16th Floor Lecture Hall, Mayo Bldg.-- Patel — Asthma Clinic Update.

RADIATION ONCOLOGY SEMINAR--8 a.m., Room C-100-5, Charlton Bldg. -- Kresl — Journal Club.

† RHEUMATOLOGY, Clinical Case Conference --7:30 a.m., 15th Floor Lecture Hall, Mayo Bldg. — No Conference.

† SPORTS MEDICINE CENTER CONFERENCE, 6:45 a.m., Dining Room 5, Methodist.

— 12:15 p.m., Judd Auditorium, Mayo Bldg. — Clinical Conference.

Saturday, April 13

CARDIOVASCULAR DISEASES--8:30 a.m., Walters Hall, 8 Alfred, Saint Marys Hospital-- Packer — Electrophysiology of the Heart - Cellular.

† GYNECOLOGICAL SURGERY--7:30 a.m., Room 4N-103, Charlton Bldg. -- Sims — TBA — Wilson -- Case Presentation.

† NEURO-ONCOLOGY WORK CONFERENCE, Case Conference--7 a.m., Room 2-651, Mary Brigh, Saint Marys.

† ORTHOPEDIC SURGERY -- 9 a.m., Judd Hall, Mayo Bldg.-- Beckenbaugh — Injection Techniques in Hand Surgery.

PHYSICAL MEDICINE AND REHABILITATION, 8 a.m., Room 406, Siebens Bldg. — Resident Seminar Day.

PLASTIC SURGERY -- 9 a.m., Room 1093, Guggenheim Bldg.

THORACIC AND CARDIOVASCULAR SURGERY, Congenital Heart Surgery Conference--7:30 a.m., Room 5-193, Saint Marys -- Larrain — Truncus Arteriosus.

Salisbury, Jeffrey L.
Appendix exhibit F

1

Current Topics in Tumor Biology

a Journal club

Monday 2/15/96
12:15 -1:15 pm (Rochester) Room 1093 Guggenheim
11:15-12:15 pm (Scottsdale) Room 149 J

paper presented by

Jeffrey L. SALISBURY

Mice lacking cyclin D1 are small and show defects in eye and mammary gland development.

Fantl et al., 1995.
Genes and Development 9:2364-2372

AND

Cyclin D1 provides a link between development and oncogenesis in the retina and breast.

Sicinski et al., 1995. Cell 82:621-630

2

Current Topics in Tumor Biology

a Journal club

Monday 2/29/96
12:15 -1:15 pm (Rochester) Room 1093 Guggenheim
11:15-12:15 pm (Scottsdale) Room 149 J

paper presented by

Richard WHITE

A p53-dependent mouse spindle checkpoint.

Cross et al., 1995. Science 267:1353-1356.

3

Current Topics in Tumor Biology

a Journal club

Monday 3/4/96
12:15 -1:15 pm (Rochester) Room 1093 Guggenheim
11:15-12:15 pm (Scottsdale) Room 149 J

paper presented by
Steve RITLAND

Nature 378: 789-792 (1995)
Science 266: 66-71 (1994)

BRCA1 and BRCA2
Breast Cancer Susceptibility Genes

4

Current Topics in Tumor Biology

a Journal club

Monday 2/12/96
1:00 -2:00 pm (Rochester) Room F Mayo II
12:00-1:00 pm (Scottsdale) Room AUD

paper presented by
Taruna ARORA

Science 270:789-791 (1995)

Aberrant Subcellular Localization of BRCA1 in Breast Cancer

5

Current Topics in Tumor Biology

a Journal club

Monday 2/26/96
1:00 -2:00 pm (Rochester) Guggenheim 1093
12:00-1:00 pm (Scottsdale) 149 J

paper presented by
Raja MUTHUPILLAI

Chromosoma 103:401-407

Organization Of Heterologous DNA Inserts On The Mouse Meiotic Chromosome.

6

Current Topics in Tumor Biology

a Journal club

Monday 3/4/96
12:00 -1:00 pm (Rochester) Guggenheim 1093
11:00-12:00 noon (Scottsdale) 2C 20

paper presented by
Javad PARVIZI

Science 269:1854-1857

Magnetic Resonance Elastography by Direct Visualization of Propagating Acoustic Strain Waves

7

Current Topics in Tumor Biology

a Journal club

Monday 3/11/96
12:00 -1:00 pm (Rochester) Guggenheim 1093
11:00-12:00 noon (Scottsdale) 2C 20

paper presented by
Mike ROGERS

Proc. Natl. Acad. Sci. 1996. 93:274-278
Berg, van Kranen, Rebel et al.,

Early p53 alterations in mouse skin carcinogenesis by UVB radiation.

8

Current Topics in Tumor Biology

a Journal club

Tuesday April 23, 1996
12:00 -1:00 pm (Rochester) Guggenheim 1093
11:00-12:00 noon (Scottsdale) 2C 20

paper presented by
André BARON

Proc. Natl. Acad. Sci. 1996. 93:2002-2007

Parangi, O'Reilly, Christofori et al.,

Antianglogenic therapy of transgenic mice impairs *de novo* tumor growth

9

Current Topics in Tumor Biology

a Journal club

Tuesday April 30, 1996
12:00 -1:00 pm (Rochester) Guggenheim 1093
11:00-12:00 noon (Scottsdale) 2C 20

paper presented by
Jill Reiter

Cell 85:27-37 (1996)

Serrano, Lee, Chin, et al.,

Role of the INK4a locus in tumor suppression and cell mortality.

Salisbury, Jeffrey L.
Appendix exhibit F

1

Current Topics in Tumor Biology

a Journal club

Wednesday October 2, 1996
2:30-4:00pm
1093 Guggenheim

"The Origin of Malignant Tumors"

by
Theodor Boveri
1914

The Paper will be presented by

Dr. Wilma Lingle
Instructor in Tumor Biology

2

Current Topics in Tumor Biology

a Journal club

Wednesday October 9, 1996
2:30-3:30pm
1093 Guggenheim

"Characteristics of an Assay for Rous Sarcoma Virus and Rous Sarcoma Cells in Tissue Culture"

by
Howard M. Temin and Harry Rubin

The paper will be presented by

Nicole Ann Becker
Graduate Student

3

Current Topics in Tumor Biology

a Journal club

Wednesday October 16, 1996
2:15-3:20pm
Phillips Hall, Siebens 1

Second Annual
Charles G. Moertel, M.D. Lecture

New and Future Directions in Predicting Prostate Tumor Behavior

Dr. Donald Coffey
Department of Urology
Johns Hopkins University

4

Current Topics in Tumor Biology

a Journal club
Wednesday October 23, 1996
2:30-3:30pm
1093 Guggenheim

"Metastasis and Tumor Immunity" Peyton Rous, 1918, JAMA 55:1885
"Transmission of a Malignant New Growth by Means of a Cell-Free Filtrate" Peyton Rous, 1911, JAMA 56:198
"RNA-dependent DNA Polymerase in Virions of Rous Sarcoma Virus" Howard M. Temin and Satoshi Mizutani
1970, Nature 226:1211-1213

The papers will be presented by

Jonathan Baines
Graduate Student

5

Current Topics in Tumor Biology

a Journal club

Wednesday October 30, 1996
12:30-5:30 P.M.
Phillips Hall, Siebens Building

Harold W. Siebens Symposium on Molecular Medicine

12:45 P.M. G. Nabel, M.D., Ph.D.
"Human Gene Therapy: Lessons from Viruses and Clinical Applications"
1:45 P.M. J. Heard, M.D., Ph.D.
"Regulation of the Delivery of Therapeutic Proteins from Genetically Engineered Tissues"
3:20 P.M. E. Nabel, M.D.
"Gene Transfer and Cardiovascular Disease"
4:20 P.M. M. Brenner, M.B., Ph.D.
"Cell and Gene Therapy of Blood Diseases"
5:30 P.M.
Reception in Hoge Atrium, Siebens Building

6

Current Topics in Tumor Biology

a Journal club

Wednesday November 6, 1996
2:30-3:30pm
1093 Guggenheim

"High Incidence of lung, bone, and lymphoid tumors in transgenic mice overexpressing mutant alleles of the p53 oncogene."
(1989) Lavigueur et al., Mol. Cell. Biol. 9:3982-3991.
"Mice deficient for p53 are developmentally normal but susceptible to spontaneous tumors."
(1992) Donehower et al., Nature 356: 215-221
"p53 loss of function: implications for the processes of immortalization and tumorigenesis"
(1992) Finlay, BioEssays 14:557-560

The papers will be presented by

Dr. Brad Silverman
Postdoctoral Fellow

7

Current Topics in Tumor Biology

a Journal club
Wednesday November 13, 1996
2:30-3:30pm
1093 Guggenheim

Antitumor activity of a phosphorothioate antisense oligodeoxynucleotide targeted against C-*raf* kinase

B.P. Monia, J.F. Johnston, T. Geiger, M. Muller, and D. Fabbro
Nature Medicine 2:668-675

paper presented by:
Ms. Julie Johnson
Graduate Student

8

Current Topics in Tumor Biology

a Journal club

Wednesday November 20, 1996
2:30-3:30pm
1068 Guggenheim
⇦ New Room Change

Aberrant subcellular localization of BRCA1 in breast cancer.
Chen *et al.*, 1995, Science 270:789-791.
BRCA1 is secreted and exhibits properties of a granin.
Jensen *et al.*, 1996, Nature Genetics 12:303-308.
Location of BRCA1 in human breast and ovarian cells.
Scully *et al.*, 1996, Science 272:123-125.
(response, Chen *et al.*, Science 272:125-126).

paper presented by:
Mr. Mike Rogers
Graduate Student

9

Current Topics in Tumor Biology

a Journal club
TUESDAY, NOVEMBER 26, 1996
12:00 (Noon)
KENDALL-HENCH HALL
(GUGGENHEIM 2)

"Mechanisms of HIV-1 Reverse Transcriptase Resistance to Nucleoside and Nonnucleoside Inhibitors"

STEPHEN H. HUGHES, Ph.D.

Director, Molecular Basis of Carcinogenesis Laboratory
ABL-Basic Research Program
NCI-Frederick Cancer Research and Development Center
Frederick, Maryland

JOURNAL OF VIROLOGY, Apr. 1996, p. 2533–2544
0022-538X/96/$04.00+0

Vol. 70, No. 4

Ligand-Independent Dimerization of Oncogenic v-*erbB* Products Involves Covalent Interactions

MARGARET A. ADELSMAN, BRENDA K. HUNTLEY, AND NITA J. MAIHLE*
Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, Minnesota 55905

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Mutant v-*erbB* products of avian c-*erbB1* have previously been used to correlate structural domains of the receptor encoded by this proto-oncogene with tissue-specific transformation potential. In these studies, deletion of the ligand-binding domain of the receptor has been shown to be required for transformation of erythroblasts, fibroblasts, and endothelial cells. It has, therefore, been postulated that deletion of this domain results in an allosteric change in the receptor analogous to the ligand-bound state of the epidermal growth factor receptor; i.e., it induces a receptor conformation that is constitutively active with respect to mitogenic signaling. While oncogenic v-*erbB* products have been shown to be expressed on the cell surface of both fibroblasts and erythroblasts, no comprehensive analysis of the oligomeric potential of these products has been conducted. Since the first event known to follow epidermal growth factor binding to its receptor is oligomerization, and receptor dimerization has been correlated with mitogenic signaling, we have carefully analyzed the ability of several v-*erbB* products to oligomerize in the three target cell types transformed by these oncogenes. In this report, we demonstrate that v-*erbB* products can efficiently homodimerize in all three target tissues, that this dimerization is ligand independent and occurs at the cell surface, and that there is no apparent correlation between v-*erbB* dimerization and transformation of avian fibroblasts. Furthermore, both oncogenic and nononcogenic v-*erbB* products can heterodimerize with the native c-*erbB1* product in chicken embryo fibroblasts, suggesting that heterodimerization between v-*erbB* and native c-*erbB1* is not sufficient to result in c-*erbB1*-mediated sarcomagenesis.

While the signaling properties and biochemistry of the human epidermal growth factor receptor (EGFR) have been studied extensively, little is known concerning the function of oncogenic c-*erbB1* mutants in malignant transformation. Several viral mutants of avian c-*erbB1* have been characterized and have been demonstrated to transform erythroblasts, fibroblasts, and endothelial cells (13, 39). All of these v-*erbB* mutants exhibit truncation of the majority of the extracellular ligand-binding domain, rendering them insensitive to regulation by ligand (32).

In contrast to the EGFR, little is known about the dimerization status of oncogenic v-*erbB* products. Ligand-induced dimerization has been demonstrated for the EGF receptor and has been postulated to be a prerequisite for normal receptor signaling of cell division (36). An alternative model exists, however, which suggests that monomeric receptors are themselves active tyrosine kinases, capable of transmitting signals to the interior of the cell (9, 31, 44). It has been suggested that deletion of the ligand-binding domain in oncogenic mutants of c-*erbB1* results in a conformational change analogous to the change associated with the EGFR upon binding ligand (24). In the absence of a ligand-binding domain, however, the oligomeric potential of v-*erbB* receptor products has been unclear. Native gel electrophoresis of the partially purified avian erythroblastosis virus strain R (AEVR) v-*erbB* product has suggested that this mutant receptor form exists in a monomeric state (65). More recently, however, sucrose gradient centrifugation analysis of a truncated EGFR from glioblastoma cells suggested that analogous human mutant EGFR can dimerize in the absence of a ligand-binding domain (33).

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The potential for ligand-independent dimerization has been demonstrated previously for diverse tyrosine and serine/threonine receptor kinases. For example, an oncogenic form of the $p185^{neu}$ receptor tyrosine kinase exists largely in a dimeric form because of a point mutation in its transmembrane domain (63). A constitutively active form of the erythropoietin receptor also has been described that forms ligand-independent homodimers due to a single amino acid change in the extracellular domain (62). In addition, a mutant colony-stimulating factor 1 receptor has been shown to undergo ligand-independent dimerization in a manner requiring both deletion of the ligand-binding domain and a carboxy-terminal alteration (11). Finally, transforming growth factor β (TGF-β) receptors also have been demonstrated to heterodimerize in the absence of ligand (61). These studies clearly demonstrate the potential for receptor dimerization to occur in the absence of ligand stimulation and also suggest a possible correlation between oncogenic activity and ligand-independent receptor dimerization.

We have, therefore, hypothesized that similar ligand-independent complexes may exist between v-*erbB*-encoded products and that such receptor interactions may be important in oncogenic signaling. In this report, we have investigated the dimerization potential of the avian c-*erbB1* receptor tyrosine kinase and its oncogenic mutants. Specifically, we have analyzed the E1 v-*erbB* product, a ligand-binding domain truncation mutant capable of inducing erythroleukemia, and S3 v-*erbB*, a c-*erbB1* mutant similar in structure to E1 v-*erbB* that has sustained an additional internal deletion in the carboxy-terminal regulatory region that abrogates erythroblast-transforming potential but activates the induction of both fibrosarcomas and hemangiosarcomas (15, 48). Using chemical cross-linkers, we have confirmed that wild-type avian c-*erbB1* undergoes ligand-induced receptor homodimerization. In contrast, both the E1 and S3 v-*erbB* mutants exhibit ligand-independent homodimerization. Moreover, both mutants are capa-

ble of heterodimerizing with the wild-type receptor in a ligand-independent fashion. In contrast to the wild-type c-*erbB1* product, both v-*erbB* mutants exhibit significant disulfide-mediated receptor interactions. These results suggest that neither v-*erbB* homodimerization nor v-*erbB* heterodimerization with the wild-type receptor is sufficient to induce transformation. Furthermore, these results demonstrate that at least two distinct mechanisms, ligand dependent and ligand independent, are involved in c-*erbB1* oligomerization.

MATERIALS AND METHODS

Cell culture, transfections, and retroviral constructs. Chicken embryo fibroblasts (CEF) were prepared from 10-day-old chicken embryos (line 0), obtained from the U.S. Department of Agriculture Avian Disease and Oncology Laboratory, East Lansing, Mich. QT6 is a chemically transformed quail fibroblast line (43). The v-*erbB*-transformed avian erythroblast line, 6C2, was derived from AEVR-infected chick erythroid precursors (7). S3 v-*erbB*-transformed endothelial cells were obtained by primary culture of hemangiosarcomas resulting from in vivo infection of chicks with REBS3 (15). CEF and 6C2 cells were maintained in Dulbecco's modified Eagle's medium (BioWhittaker) supplemented with 10% fetal calf serum (Gibco), 1% chick serum (Gibco), 100 U of penicillin per ml (BioWhittaker), 100 μg of streptomycin per ml (BioWhittaker), and 0.1% amphotericin B (fungizone; Gibco). QT6 cells and S3 v-*erbB*-transformed endothelial cells were cultured in Dulbecco's modified Eagle's medium supplemented with 5 or 15% fetal calf serum, respectively.

QT6 cells stably expressing E1 v-*erbB* (E1 v-*erbB*/QT6) and S3 v-*erbB* (S3 v-*erbB*/QT6) products have been described previously (15). E1 v-*erbB*/QT6-BH cells were similarly generated by stable transfection of QT6 cells with E1 v-*erbB* cDNA in the Bryan high-titer form of the RCAN vector (RCANBH) (26, 54). Expression of the E1 v-*erbB* and S3 v-*erbB* products in CEF was accomplished by infecting primary cultures of low-passage CEF with filtered viral supernatants as previously described (15). Cells were fully infected at approximately 2 weeks postinfection as determined by immunoprecipitation of v-*erbB* products (data not shown). pCMV/c-*erbB1* was generated by subcloning the *Not*I-*Kpn*I c-*erbB1* cDNA fragment from pTF1 (19) into pCMV (Invitrogen). QT6 cells stably expressing wild-type c-*erbB1* were generated by cotransfection of pCMV/c-*erbB1* with the selectable marker pSV2neo (55). Transient expression of c-*erbB1* was achieved by calcium phosphate precipitation (22) using the same expression vector. A kinase-inactive c-*erbB1* mutant was generated by cloning the *Stu*I-*Sph*I fragment of pGK- (15) into the *Stu*I-*Xho*I site of pCMV/c-*erbB1*. Cells were typically analyzed 48 h posttransfection.

Chemical cross-linking studies. Cells expressing wild-type c-*erbB1* or v-*erbB* mutant proteins were grown to subconfluency and then serum starved for 24 h. Cells were transferred to 4°C and selected samples were exposed to 100 ng of human TGF-α (Gibco) per ml for 30 or 60 min, as indicated. After ligand stimulation, cells were washed twice in cold phosphate-buffered saline (PBS). The membrane-impermeable cross-linkers bis(sulfosuccinimidyl)suberate (BS^3) or 3,3′-dithiobis(sulfosuccinimidyl)propionate (DTSSP; Pierce) were dissolved in PBS and added to a final concentration of 2 mM for 30 or 60 min at 4°C. The reaction was quenched with the addition of 1 M glycine, pH 8.0 (final concentration of 50 mM), for an additional 15 min. After washing with cold PBS, cells were scraped in lysis buffer {50 mM HEPES [*N*-2-hydroxyethylpiperazine-*N*′-2-ethanesulfonic acid], pH 7.5, 10% glycerol, 0.5% Triton X-100, 1.5 mM $MgCl_2$, 1 mM EGTA [ethylene glycol-bis(β-aminoethyl ether)-*N,N,N′,N′*-tetraacetic acid]} containing protease inhibitors (1 mM phenylmethylsulfonyl fluoride [PMSF], 50 μg of aprotinin per ml, 400 nM orthovanadate) and were rocked at 4°C for 20 min followed by centrifugation at 4°C for 20 min. For DTSSP cross-linking experiments, 10 mM iodoacetamide was included in the lysis buffer to inhibit nonspecific disulfide interactions.

Postnuclear supernatants were immunoprecipitated with polyclonal antisera recognizing distinct regions of avian c-*erbB1* (40). Immunoprecipitations with T2, recognizing the carboxy terminus of c-*erbB1*, or E4, an anti-c-*erbB1* kinase domain antibody, were carried out at 4°C for a minimum of 2 h. Immunopure protein A/G-Sepharose beads (Pierce) were added to each sample, followed by incubation at 4°C for 2 h. Immobilized complexes were washed three times in HTG buffer (20 mM HEPES, pH 7.5, 0.1% Triton X-100, 10% glycerol), twice in a high-stringency wash (50 mM borate, pH 8.3, 0.7 M NaCl, 0.3 M $MgCl_2$, 10% glycerol, 0.1% Triton X-100), and once in HTG buffer, all containing protease inhibitors. Immobilized complexes were then eluted from the beads by addition of 2× sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) sample buffer (125 mM Tris, pH 6.8, 4% SDS, 2 mM EDTA, 20% glycerol, 10% β-mercaptoethanol [β-ME], 0.6% bromophenol blue, pH 6.8), and samples were resolved by electrophoresis on 5% or 3 to 9% linear gradient polyacrylamide gels.

For analysis of DTSSP-cross-linked receptor complexes, β-ME was omitted from the sample buffer. Bands of interest were excised from dried gels and were rehydrated in 50 mM ammonium bicarbonate. Samples were then homogenized and brought to a final concentration of 5% β-ME and 0.1% SDS. Samples were heated for 5 min at 100°C, followed by overnight incubation at 37°C with gentle agitation. Supernatants were removed from gel pieces by centrifugation, followed by lyophilization. Eluted protein samples were resuspended in 50 to 100 μl of distilled H_2O and were reduced in the presence of 100 mM dithiothreitol, pH 8.0, for 2 h at 50°C. An equal volume of 4× sample buffer was added, and samples were loaded onto 3 to 9% polyacrylamide gradient gels.

In vitro kinase assays. Washed immunoprecipitates were incubated in 100 μl of HTG buffer. A final concentration of 15 mM $MnCl_2$ was added immediately prior to addition of 5 μCi of [γ-^{33}P]ATP. Samples were incubated on ice for 15 min, and reactions were stopped by the addition of 2× SDS-PAGE sample buffer. Kinase reactions were analyzed by autoradiography following SDS-PAGE electrophoresis.

Western blotting (immunoblotting). Washed immunoprecipitates were separated by SDS-PAGE and transferred to nitrocellulose (Schleicher & Schuell) in transfer buffer (49.6 mM Tris, 384 mM glycine, 20% methanol, 0.01% SDS) as described (45). Nitrocellulose filters were blocked in BSA-TBS-T (5% bovine serum albumin, 20 mM Tris, pH 7.6, 137 mM NaCl, 0.1% Tween 20) at room temperature for at least 1 h. Blots were rinsed in TBS-T prior to incubation with primary antibody (monoclonal anti-c-*erbB1* C13, provided by H. S. Wiley, monoclonal antiphosphotyrosine 4G10 [UBI], or polyclonal anti-c-erbB1 T2 or E4). After subsequent incubation with a secondary goat anti-rabbit or anti-mouse immunoglobulin G antibody conjugated to horseradish peroxidase (Amersham), protein bands were visualized by enhanced chemiluminescence.

RESULTS

The focus of this study was to examine the oligomeric state of avian c-*erbB1* and the E1 v-*erbB* and S3 v-*erbB* tissue-specific oncogenic forms of this receptor. We also have analyzed the dimerization potential of the AEVR v-erbB mutant. Figure 1 summarizes the structural characteristics of these receptors and their transforming capacities.

Ligand-dependent dimerization of c-*erbB1*. As the human EGFR has been well documented in its ability to undergo ligand-induced homodimerization, we began our study by investigating the oligomeric potential of the avian c-*erbB1* receptor overexpressed in the chemically transformed quail fibroblast cell line, QT6 (c-*erbB1*/QT6). Because the cognate ligand for the avian c-*erbB1* receptor is unknown, we used human TGF-α, which has been shown to bind with high affinity to the avian receptor (34). As shown in Fig. 2A, when receptors were stimulated with ligand prior to cross-linking and immunoprecipitation, a homodimeric c-*erbB1* species that migrated at an apparent molecular size of 340 kDa when analyzed by reducing SDS-PAGE could be detected. Under these conditions both monomeric and dimeric c-*erbB1* species were enzymatically active as determined using an in vitro kinase assay (Fig. 2A). Probing blots of parallel immunoprecipitates with an anti-*erbB* antibody identified the primary component of both the monomeric and dimeric species as c-*erbB1* (Fig. 2B). Furthermore, TGF-α stimulated the phosphorylation of both monomeric and dimeric receptors on tyrosine as demonstrated by antiphosphotyrosine Western blotting (Fig. 2C).

In CEF, c-*erbB1* is naturally expressed at much lower levels than those represented by the overexpressed receptor in QT6 cells. To address the possibility that receptor dimerization was influenced by overexpression in these transfected cells, we analyzed native c-*erbB1* dimerization in CEF following TGF-α stimulation. Figure 2D shows that c-*erbB1* dimerized in a ligand-dependent fashion when expressed at physiologic levels in CEF. To be sure that stimulation of the receptors was optimal in both QT6 and CEF cells, the dimerization assays were repeated over a range of ligand concentrations and with increasing exposure time to TGF-α (data not shown). These data demonstrated that c-*erbB1* receptors were maximally stimulated by approximately 50 to 100 ng of TGF-α per ml and that ligand stimulation resulted in very rapid receptor dimerization, measured as early as 30 s post-ligand stimulation.

Ligand-independent homodimerization of E1 v-*erbB*. The erythroblastosis-inducing E1 v-*erbB* oncogene product was ex-

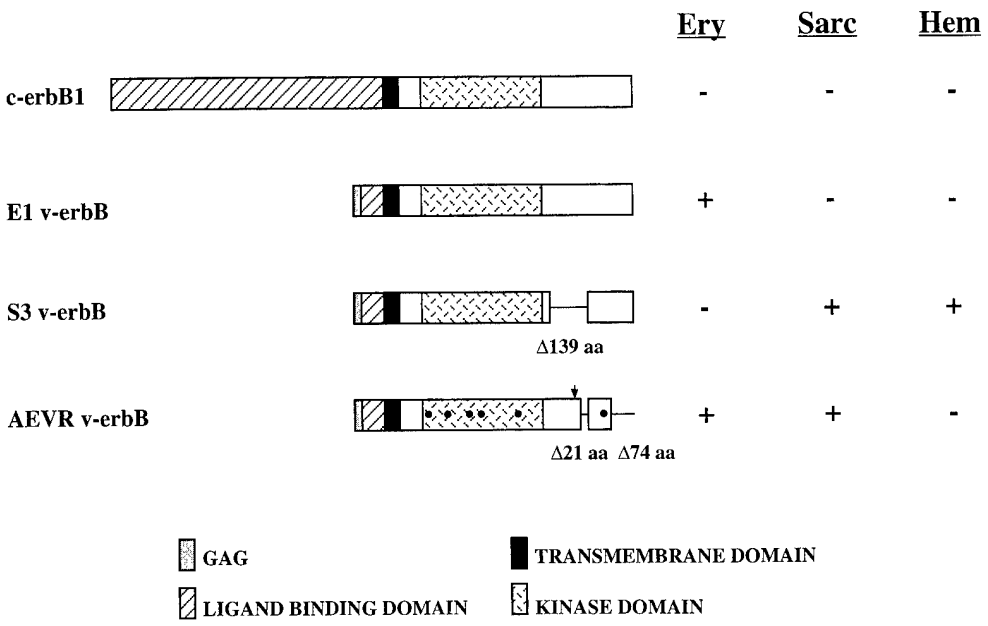

FIG. 1. Tissue-specific transformation by c-*erbB1* mutants. Mutants of the avian c-*erbB1* receptor tyrosine kinase arising from retroviral transduction are compared schematically with the full-length wild-type c-*erbB1* receptor. The ability of these mutants to induce erythroblastosis (Ery), fibrosarcomas (Sarc), and hemangiosarcomas (Hem) is shown at right. The transmembrane, ligand-binding, and protein tyrosine kinase domains are indicated. Dark circles and an arrowhead indicate point mutations and a single amino acid deletion, respectively, in the AEVR v-*erbB* gene product.

amined for its ability to homodimerize in the presence or absence of ligand. QT6 cells stably expressing this mutant receptor (E1 v-*erbB*/QT6) were exposed to the membrane-impermeable cross-linker BS^3 following ligand stimulation. As shown in Fig. 3A, dimers of this truncated receptor were evident in the presence of cross-linker regardless of whether or not cells were stimulated with TGF-α (lanes 6 and 8). The broad migration pattern of monomeric E1 v-*erbB* in these gels reflects the complex glycosylation characteristic of this and other v-*erbB* proteins. Tyrosine phosphorylation of both monomeric and dimeric E1 v-*erbB* receptor species was also ligand independent as demonstrated by antiphosphotyrosine immunoblotting of parallel samples (Fig. 3B, lanes 6 and 8). In contrast, no v-*erbB*-immunoreactive complexes were immunoprecipitated from parental QT6 cells as analyzed by in vitro kinase assay (Fig. 3A, lanes 1 to 4), or by antiphosphotyrosine blotting (Fig. 3B, lanes 1 to 4).

Although E1 v-*erbB* is not capable of transforming fibroblasts (15, 48), the previous experiments analyzed E1 v-*erbB* in the context of chemically transformed QT6 cells. Therefore, we investigated the oligomeric potential of E1 v-*erbB* in primary CEF. Cross-linking analysis was performed on CEF infected with the RCANBH retroviral expression vector that contained the E1 v-*erbB* gene. As shown in Fig. 3C, an apparent complex of the predicted molecular size (160 to 180 kDa) was immunoprecipitated in a cross-linker-dependent, ligand-independent fashion in E1 v-*erbB*/CEF. Because the endogenous c-erbB1 monomeric glycoprotein migrates at approximately 170 kDa in CEF, it was difficult to distinguish between monomeric c-*erbB1* and dimeric E1 v-*erbB* complexes. Therefore, we employed a reducible cross-linker, DTSSP, to examine the individual components of these putative homodimeric complexes. Following ligand stimulation, chemical cross-linking was performed on CEF expressing E1 v-*erbB*. Nonreducing SDS-PAGE analysis of immunoprecipitated receptor complexes is illustrated in Fig. 4A. Under these conditions the distinction could be made between the c-*erbB1* monomeric (Fig. 4A, a) and E1 v-erbB homodimeric receptor forms (Fig. 4A, b). Following excision and reduction of band a, two bands appeared by SDS-PAGE analysis: the predominant upper band was the 170-kDa monomeric c-*erbB1* receptor, while the diffusely migrating E1 v-*erbB* monomer was also visible because of close migration of bands a and b under nonreducing conditions (Fig. 4B, lanes 1 and 3). Following excision and reduction of the b complex (Fig. 4A), two bands were also generated: the major reduction product was the 85-kDa E1 v-*erbB* monomer; a second band (asterisk) apparently resulted from the incomplete reduction of the complex (Fig. 4B, lanes 2 and 4). Identification of incompletely reduced complexes and complex components was supported by comigration with the c-*erbB1* monomer, the E1 v-*erbB* monomer, or unreduced bands a and b (data not shown). Therefore, E1 v-*erbB* forms homodimers in both QT6 and CEF in a ligand-independent fashion. These data further demonstrate that under nonreducing conditions, E1 v-*erbB* oligomerization is cross-linker independent and is mediated, at least in part, by disulfide interactions.

Ligand-independent homodimerization of S3 v-*erbB*. In addition to the ligand-binding domain deletion found in the E1 v-*erbB* product, S3 v-erbB has sustained an internal carboxy-terminal deletion of 139 amino acids, abrogating its erythroblast-transforming potential but activating its ability to transform fibroblasts and endothelial cells (15, 48). We examined the oligomeric potential of S3 v-*erbB*, stably expressed in QT6 cells (S3 v-*erbB*/QT6) or expressed by retroviral infection of CEF (S3 v-*erbB*/CEF). Chemical cross-linking studies were performed on cells following exposure to TGF-α as before. In vitro kinase assays on immunoprecipitated products from these experiments are shown in Fig. 5A. Similar to E1 v-*erbB*, the S3 v-*erbB* receptor showed ligand-independent homodimerization as evidenced by a cross-linked band migrating at approximately 150 kDa in both S3 v-*erbB*/QT6 and S3 v-*erbB*/CEF. Wild-type

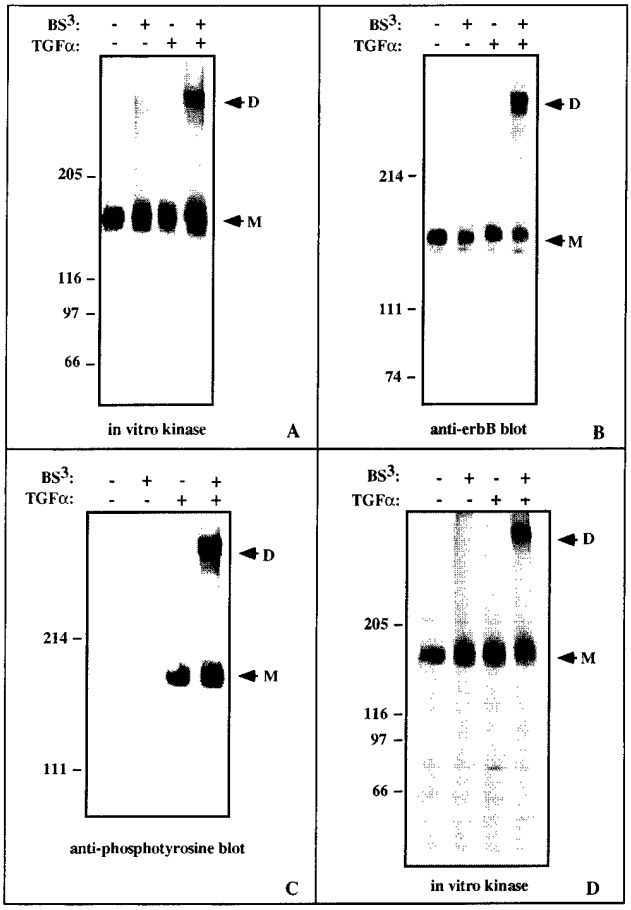

FIG. 2. Ligand-dependent homodimerization of avian c-*erbB1*. QT6 cells overexpressing exogenous c-erbB1 (panels A to C) or CEF expressing endogenous c-*erbB1* (panel D) were serum starved for 24 h and then placed at 4°C in the presence or absence of 100 ng of TGF-α per ml for 1 h. Cell surface receptor oligomers were then cross-linked in the presence of 2 mM BS^3 for 1 h at 4°C. Cells were lysed and immunoprecipitated with the T2 anti-*erbB* polyclonal antibody (40). An in vitro kinase assay was performed on washed immunoprecipitates, and samples were analyzed on SDS-PAGE gels (5% polyacrylamide). Monomeric (M) and cross-linked dimeric (D) c-*erbB1* complexes in QT6 cells are represented by the autoradiograph in panel A. Parallel immunoprecipitates were separated by SDS-PAGE and analyzed by immunoblotting with the C13 monoclonal antibody directed against the carboxy-terminal domain of c-*erbB1* (panel B) or with the antiphosphotyrosine antibody 4G10 (panel C). CEF cells (panel D) were cross-linked and analyzed by in vitro kinase activity as described above. The autoradiograph shown in panel D was exposed approximately 4 times longer than the autoradiograph illustrated in panel A.

c-*erbB1* monomer and ligand-dependent c-*erbB1* homodimers were also apparent in S3 v-*erbB*/CEF (open arrows), while an additional band of approximately 225 kDa (asterisk) appeared in a ligand-independent fashion (Fig. 5A, even-numbered lanes). Phosphotyrosine analysis of parallel samples (Fig. 5B) indicated that the 225-kDa complex as well as the S3 v-*erbB* monomeric and dimeric complexes were tyrosine phosphorylated. Because of the much lower levels of endogenous c-*erbB1* compared to S3 v-*erbB* in these cells, tyrosine-phosphorylated c-*erbB1* monomer and dimer were not readily detected in lanes 3 and 4 of Fig. 5B but were apparent upon longer exposure (data not shown). These data suggest that the S3 v-*erbB* product is able to undergo ligand-independent oligomerization, yielding dimeric and possibly trimeric forms. In contrast, trimeric forms (or multimeric forms other than dimers) of the E1 v-*erbB* product were not observed.

To address the nature of the higher-order oligomers observed for S3 v-*erbB*, we used the reducible cross-linker DTSSP and analyzed the pattern of receptor complex formation in S3 v-*erbB*/CEF under nonreducing conditions. Similar to E1 v-*erbB*, S3 v-*erbB* oligomerized in both a ligand- and cross-linker-independent fashion under these conditions (Fig. 5C). Extensive oligomerization was observed even in the absence of DTSSP, and excision and reduction of each of the indicated bands revealed that all four excised bands (Fig. 5C, bands a to d) consist of S3 v-*erbB* (Fig. 5D). A homodimeric c-*erbB1* complex from DTSSP-cross-linked c-*erbB1*/QT6 cells (see Fig. 6) was excised, reduced, and electrophoresed under reducing conditions for comparison (Fig. 5D, lane 1). Remaining higher-molecular-weight oligomeric bands were apparently due to incomplete reduction of the original excised bands.

Covalent interactions utilizing disulfide bridges have not been thought to be involved significantly in ligand-mediated EGFR homodimerization (37, 65), yet our results (Fig. 4, 5C, and 5D) provide evidence for v-*erbB* associations via this mechanism. Thus, we analyzed the TGF-α-induced homodimerization of avian c-erbB1 under nonreducing conditions. Figure 6 demonstrates cross-linking of ligand-induced c-*erbB1* homodimers in the presence of DTSSP (lanes 4 and 8). While high-molecular-weight complexes were also visible at reduced levels in lanes 1 to 3 and 5 to 7, the addition of 10 mM iodoacetamide in the lysis buffer (lanes 5 to 8) inhibited nonspecific disulfide-mediated complex formation (open arrows). The low levels of ligand- and/or cross-linker-independent complexes remaining in lanes 5 to 7 apparently represent a small population of disulfide-mediated c-*erbB1* homodimers, as excision and reduction of these bands revealed monomeric c-*erbB1* (data not shown). We have also observed this phenomenon in CEF expressing physiologic levels of c-*erbB1* (data not shown). In contrast, the addition of iodoacetamide to S3 v-*erbB* or E1 v-*erbB* lysis conditions did not reduce the formation of the large fraction of covalently linked mutant homodimers (Fig. 4A and 5C and data not shown).

To address the possibility that high levels of oncogenic receptors expressed in these cells were influencing receptor interactions, we performed transient transfections of QT6, using a range of E1 v-*erbB* plasmid DNA concentrations (0.5 to 10 μg of DNA/10^6 cells), followed by expression and cross-linking analyses. Results of these experiments indicated that v-*erbB*-encoded receptors dimerize even when expressed at low levels (data not shown). In addition, further control experiments indicated that high ligand concentrations (500 ng/ml) or lengthy incubation times (1 h) did not affect E1 or S3 v-*erbB* homodimerization (data not shown).

Heterodimerization of E1 v-*erbB* with c-*erbB1*. The expression of E1 or S3 v-*erbB*-encoded receptors in CEF raised the possibility of heterodimerization between the full-length c-*erbB1* and mutant v-*erbB* receptors. One factor, however, that had the potential to influence our ability to detect potential heterodimers was the difference in expression levels between the endogenous wild-type c-*erbB1*- and the v-*erbB*-encoded receptors introduced by retroviral infection of CEF. We addressed this question by using E1 v-*erbB*/QT6 cells transiently transfected with wild-type c-*erbB1*. Immunoprecipitation analysis of receptor expression under these conditions demonstrated that both c-*erbB1* and E1 v-*erbB* were expressed at similar levels (data not shown). Cross-linking experiments with DTSSP revealed at least two unique molecular weight complexes in receptor immunoprecipitates when samples were resolved under nonreducing conditions (Fig. 7A). As described above (Fig. 4A), complex formation was cross-linker and ligand independent but was not evident when samples were

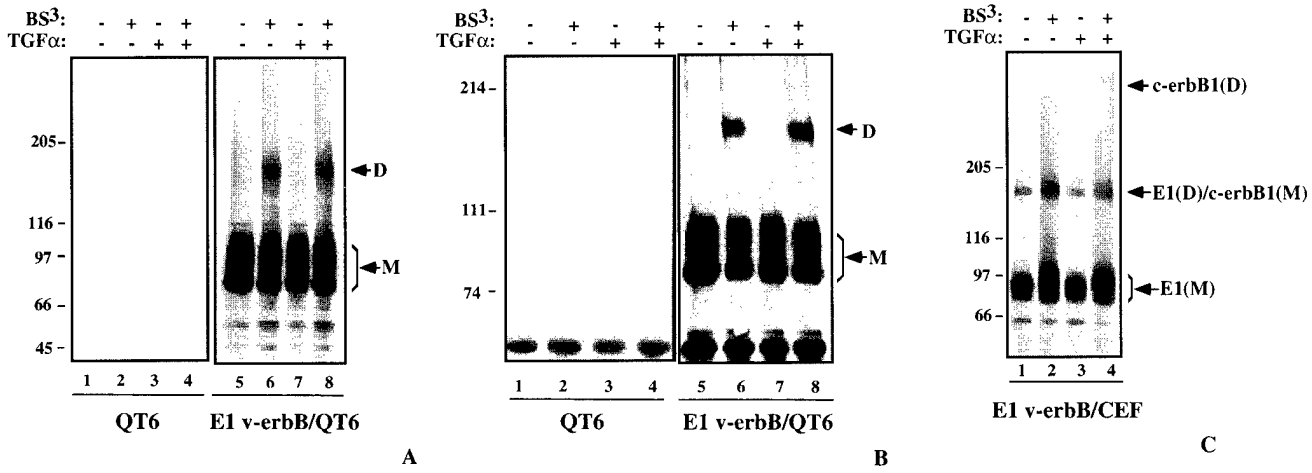

FIG. 3. Ligand-independent homodimerization of E1 v-*erbB*. QT6 cells stably expressing the E1 v-*erbB* gene product (E1 v-*erbB*/QT6) or E1 v-*erbB*-infected CEF (E1 v-*erbB*/CEF) were serum starved for 24 h and then placed at 4°C in the presence or absence of 100 ng of TGF-α per ml for 30 min. Parental QT6 cells were treated in parallel as a control. Cells were cross-linked in the presence of 2 mM BS^3 for 30 min at 4°C. In vitro kinase reactions were performed on washed immunoprecipitates as described previously, and representative autoradiographs of 3 to 9% gradient gels are shown in panels A and C. Parallel samples were transferred to nitrocellulose and probed with the antiphosphotyrosine antibody 4G10 followed by ECL detection (panel B). Monomeric (M) and homodimeric (D) complexes of E1 v-*erbB* and endogenous c-*erbB1* are indicated with arrowheads.

resolved under reducing conditions (data not shown). In contrast, ligand- and cross-linker-mediated homodimerization of transfected c-*erbB1* occurred under these conditions (Fig. 7A, lane 8). We analyzed the content of these receptor complexes by excising the two unique bands described above. Complex reduction followed by electrophoretic analysis (Fig. 7B) demonstrated the presence of both E1 v-*erbB* and wild-type c-*erbB1* products in these excised bands. The full-length c-*erbB1* receptor was excised and reduced for comparison, and it comigrated with the reduced c-*erbB1* monomer from the heterodimeric complexes. The nature of the migration difference between these two heteromeric complexes is currently unclear but may represent alternative stoichiometries or contributions from intramolecular disulfide bonding in each complex. Similar analyses using S3 v-*erbB*/QT6 transiently overexpressing c-*erbB1* did not reveal apparent heterodimeric complexes (data not shown). Therefore, we conclude that E1 v-*erbB* and the wild type c-*erbB1* receptor tyrosine kinases are capable of forming heterodimers in fibroblasts. Moreover, this heterodimerization event is not dependent upon ligand stimulation or the presence of cross-linker and is mediated, at least in part, by disulfide interactions.

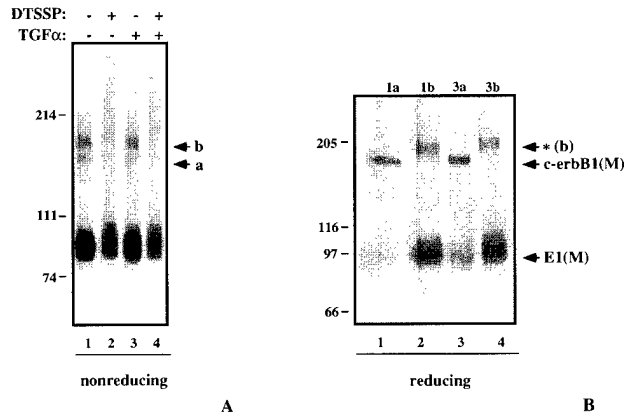

FIG. 4. Ligand-independent homodimerization of E1 v-*erbB* in CEF. The RCANBH retroviral vector (26, 54) was used to express E1 v-*erbB* in CEF. Infected cells were treated as described for Fig. 3 except that the reducible cross-linker DTSSP (2 mM) was used and 10 mM iodoacetamide was included during cell lysis. Immunoprecipitates were labeled by using an in vitro kinase assay, and samples were separated by SDS-PAGE under nonreducing conditions (panel A). Putative monomeric c-*erbB1* (a) and homodimeric E1 v-*erbB* (b) receptor complexes were excised from the dried gel. Protein complexes were eluted from the gel slices and reduced in the presence of 100 mM dithiothreitol, followed by reducing SDS-PAGE (panel B). Bands originating from the gel in panel A are designated by lane number and band letter. Incompletely reduced complexes are visible (panel B, lanes 2 and 4, uppermost band), and small amounts of reduced E1 dimer are obtained from the excised c-*erbB1* bands because of the diffuse migration of bands a and b on the nonreducing gel (panel B, lanes 1 and 3).

Transphosphorylation of kinase-inactive c-*erbB1* by E1 and S3 v-*erbB* products. We further examined the potential for heterodimeric interaction between v-*erbB* mutants and c-*erbB1* by using a full-length c-*erbB1* cDNA clone mutated at the ATP binding site (c-*erbB1*/K^-). This receptor was not enzymatically active when expressed alone in QT6 cells, as assessed by both in vitro kinase assay and antiphosphotyrosine blotting (data not shown). Transient expression of c-*erbB1*/K^- in E1 v-*erbB*/QT6 (Fig. 8A) or S3 v-*erbB*/QT6 (Fig. 8B) followed by cross-linking and in vitro kinase assays revealed transphosphorylation of the c-*erbB1*/K^- receptor in a manner that was dependent upon the coexpression of kinase-active v-*erbB* (Fig. 8A and B, lanes 5 to 8). Analysis of parallel immunocomplexes by antiphosphotyrosine blotting (Fig. 9) further indicated ligand-independent transactivation of the c-*erbB1*/K^- receptor in cells expressing E1 v-*erbB* and S3 v-*erbB* (lanes 5 to 8). Thus, while we have not been able to physically capture heterodimers between S3 v-*erbB* and c-*erbB1*, it is apparent that in fibroblasts expressing either E1 v-*erbB* or S3 v-*erbB*, a kinase-inactive c-*erbB1* receptor becomes transactivated in a ligand-independent manner.

Homodimerization of v-*erbB* mutants is not tissue or transformation specific. Since oncogenic products of c-*erbB1* exhibit tissue specificity in their transforming capabilities, we asked whether ligand-independent dimerization of v-*erbB* products was conserved in tissues other than fibroblasts. Figure 10 analyzes the potential for v-*erbB* products to homodimerize in erythroblasts and endothelial cells. Figure 10A demonstrates

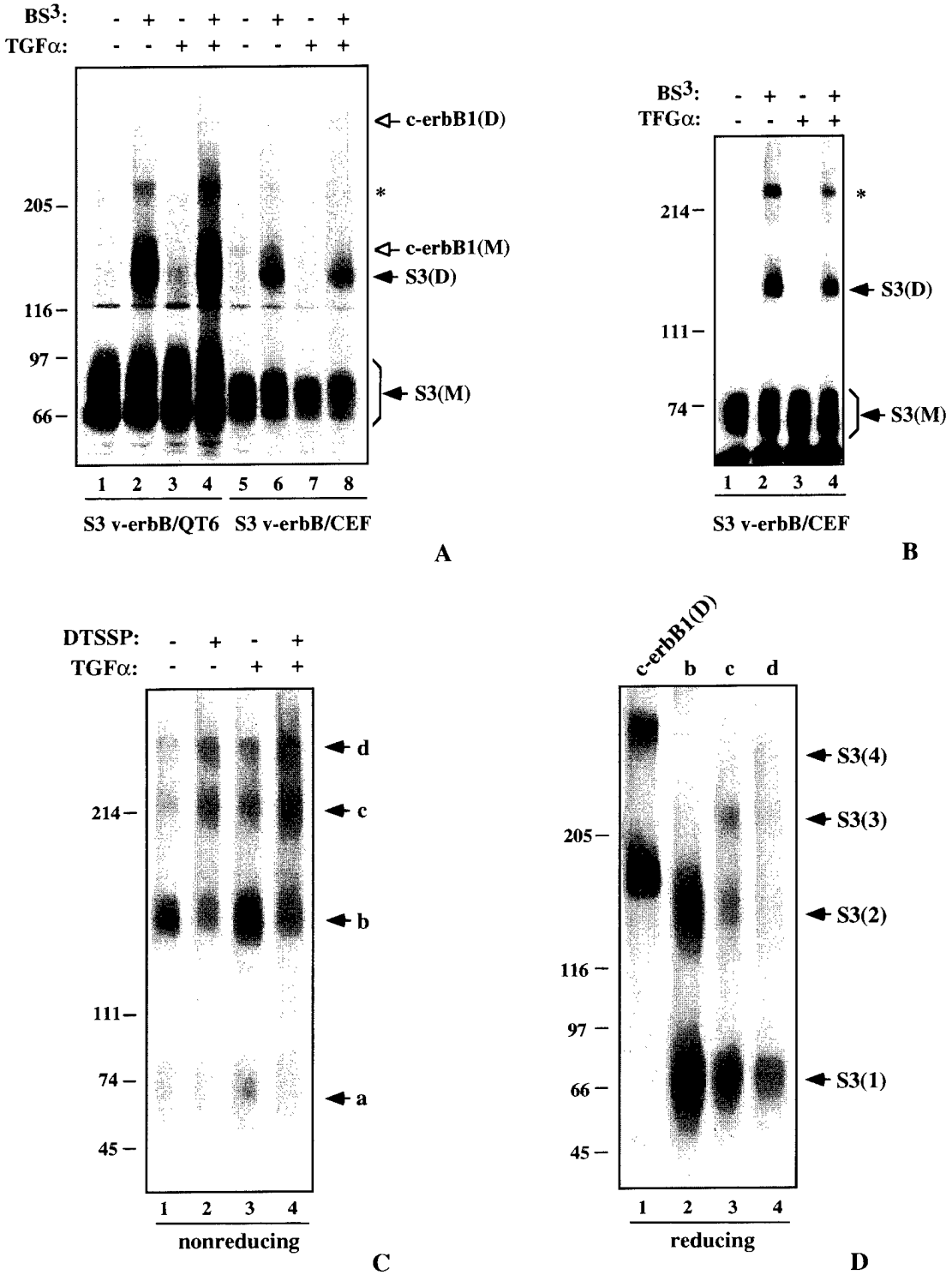

FIG. 5. Ligand-independent homodimerization of S3 v-*erbB* in fibroblasts. QT6 cells stably expressing the S3 v-*erbB* mutant or S3 v-*erbB*-infected CEF were cross-linked with BS^3 (panels A and B) or DTSSP (panel C) after ligand stimulation as previously described. Panel A compares in vitro phosphorylated immunoprecipitated S3 v-*erbB* complexes from S3 v-*erbB*/QT6 and S3 v-*erbB*/CEF after BS^3 cross-linking. Parallel S3 v-*erbB*/CEF samples were analyzed by antiphosphotyrosine immunoblotting in panel B. Monomeric (M) and homodimeric (D) forms of v-*erbB* are indicated, as well as a putative S3 v-*erbB* trimer (asterisk). In vitro phosphorylated monomers and homodimers of c-*erbB1* are indicated in panel A (open arrows). In vitro phosphorylated immunocomplexes from S3 v-*erbB*/CEF are analyzed in panel C under nonreducing conditions. Iodoacetamide was included during lysis as described in Fig. 4. Bands indicated (b to d) in panel C were excised and reduced for SDS-PAGE analysis (panel D). A DTSSP-cross-linked c-erbB1 homodimeric complex was excised from an accompanying gel (see Fig. 6) and reduced for comparison. Apparent incomplete reduction of excised bands is evident in each of the lanes in panel D.

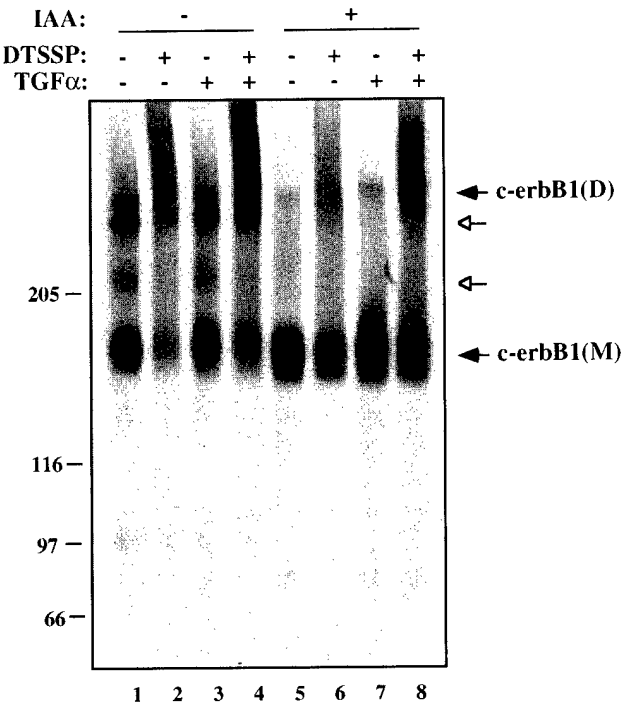

FIG. 6. Analysis of c-*erbB1* homodimeric complexes under nonreducing conditions. c-*erbB1*/QT6 cells were stimulated with ligand (lanes 3, 4, 7, and 8), followed by exposure to 2 mM DTSSP. Cells were then lysed in the absence (lanes 1 to 4) or presence (lanes 5 to 8) of 10 mM iodoacetamide. Immunocomplexes were labeled by in vitro kinase assay and analyzed by nonreducing SDS-PAGE. Monomeric (M) and homodimeric (D) receptor forms are indicated. The open arrows indicate apparent nonspecific complexes formed in the absence of iodoacetamide (lanes 1 to 4).

the ligand-independent homodimerization of the leukemogenic AEVR v-*erbB* product in 6C2 erythroblast cells. Ligand-dependent homodimerization of the native c-*erbB1* product was also apparent in these cells (Fig. 10B). Furthermore, a unique cross-linker-dependent receptor complex which may represent a heterodimeric complex analogous to that formed between E1 v-*erbB* and c-*erbB1* in fibroblasts, was apparent in lane 2 (Fig. 10B, open arrow). Examination of primary cultures of cells obtained from an S3 v-*erbB*-induced hemangiosarcoma also revealed significant homodimerization of the S3 v-*erbB* product in this tumor (Fig. 10C). Thus, ligand-dependent homodimerization of the avian c-*erbB1* receptor and ligand-independent homodimerization of various v-*erbB* products, including E1 v-*erbB*, S3 v-*erbB*, and AEVR v-*erbB*, do not appear to be tissue or transformation specific.

DISCUSSION

Previous studies have focused primarily on ligand-mediated EGFR interactions, and many elegant studies have demonstrated both ligand-induced homo- and heterodimerization events associated with the activation of EGFR family members (36). Although loss of the ligand-binding domain in various avian v-*erbB* mutants renders these proteins oncogenic and has been postulated to induce a constitutively "active" form of the receptor (24), no studies have thoroughly analyzed the dimerization potential of these naturally occurring viral oncogene products. It has been reported that native gel electrophoresis of partially purified AEVR v-*erbB* detects mutant receptors that are apparently monomeric (65). Recently, an EGFR mutant strikingly similar in structure to the E1 v-*erbB* product has been isolated from glioblastoma cells (64). Sucrose gradient centrifugation analysis of this receptor suggests the existence of a dimeric truncated receptor population (33). While ligand-mediated induction of receptor dimerization is thought to be critical for full-length EGFR activation, the potential for this receptor to activate signals in a monomeric state has remained controversial (9, 31, 44). Since no previous studies have clearly addressed the oligomeric potential of oncogenic v-*erbB* proteins that have lost the ability to be regulated by ligand (32), in this study we have analyzed the dimerization potential of tissue-specific transforming v-*erbB* mutant receptors. Here, we demonstrate, for the first time, the ligand-independent, cell surface homodimerization of v-*erbB* mutants in three different target tissues. We also demonstrate the formation of ligand-independent heterodimers between the erythroblastosis-inducing E1 v-*erbB* and the wild-type avian c-*erbB1* product. Surprisingly, the formation of these ligand-independent receptor complexes results from covalent receptor-receptor interactions, suggesting that a distinct mechanism of receptor dimerization occurs in the absence of the c-*erbB1* ligand-binding domain.

In contrast to the ligand-dependent dimerization shown in this study for avian c-*erbB1* and previously for the EGFR (36), v-*erbB* mutants clearly exhibit ligand-independent homodimerization in fibroblasts, erythroblasts, and endothelial cells. The cross-linkers used in this study, BS^3 and DTSSP, are membrane impermeable and, as such, are limited to reacting with available cell surface free amines, predominantly on lysine residues (56). This limitation, combined with the relatively rapid hydrolysis of chemical cross-linkers in aqueous solution, may result in the underestimation of the actual number of ligand-independent homodimers present in these cells. Nonetheless, these studies clearly reveal cross-linked v-*erbB* homodimers at the cell surface by using both in vitro kinase and immunoblotting detection methods. This is an important observation, since cell surface expression of these mutant receptors is thought to be required for transformation (8, 52, 53). Furthermore, while only a small fraction of the AEVR v-*erbB* receptor population is terminally glycosylated and expressed on the cell surface (23, 25, 40, 46), we can detect homodimers of this mutant in transformed erythroblasts with a membrane-impermeable cross-linker, suggesting that much of the cell surface AEVR v-*erbB* population exists in a ligand-independent homodimeric form.

Analysis of v-*erbB* mutants under nonreducing conditions resulted in the unexpected observation of significant ligand-independent covalent homodimeric interactions between both E1 v-*erbB* and S3 v-*erbB* products. Furthermore, S3 v-*erbB* consistently showed a potential for higher-order oligomeric complex formation that was not apparent in our analyses of E1 v-*erbB*. DTSSP did not markedly enhance homodimerization of either E1 v-*erbB* or S3 v-*erbB*, suggesting that the covalent disulfide-mediated homodimers we observe result from the dominant mechanism of interaction for these mutant receptors. In contrast to the v-*erbB*-encoded receptors, wild-type c-*erbB1* products formed ligand-dependent, cross-linker-dependent (i.e., DTSSP) homodimers when analyzed by nonreducing SDS-PAGE. Although covalent interactions have generally not been implicated in EGFR dimerization (37, 65), cross-linker-independent homodimerization has been reported for the EGFR in A431 cells when analyzed under nonreducing conditions (47). In this study, we observed that a small population of wild-type c-*erbB1* receptors dimerize in the absence of ligand or cross-linker. Ligand-induced disulfide-mediated dimerization has been described previously for the PDGF (37)

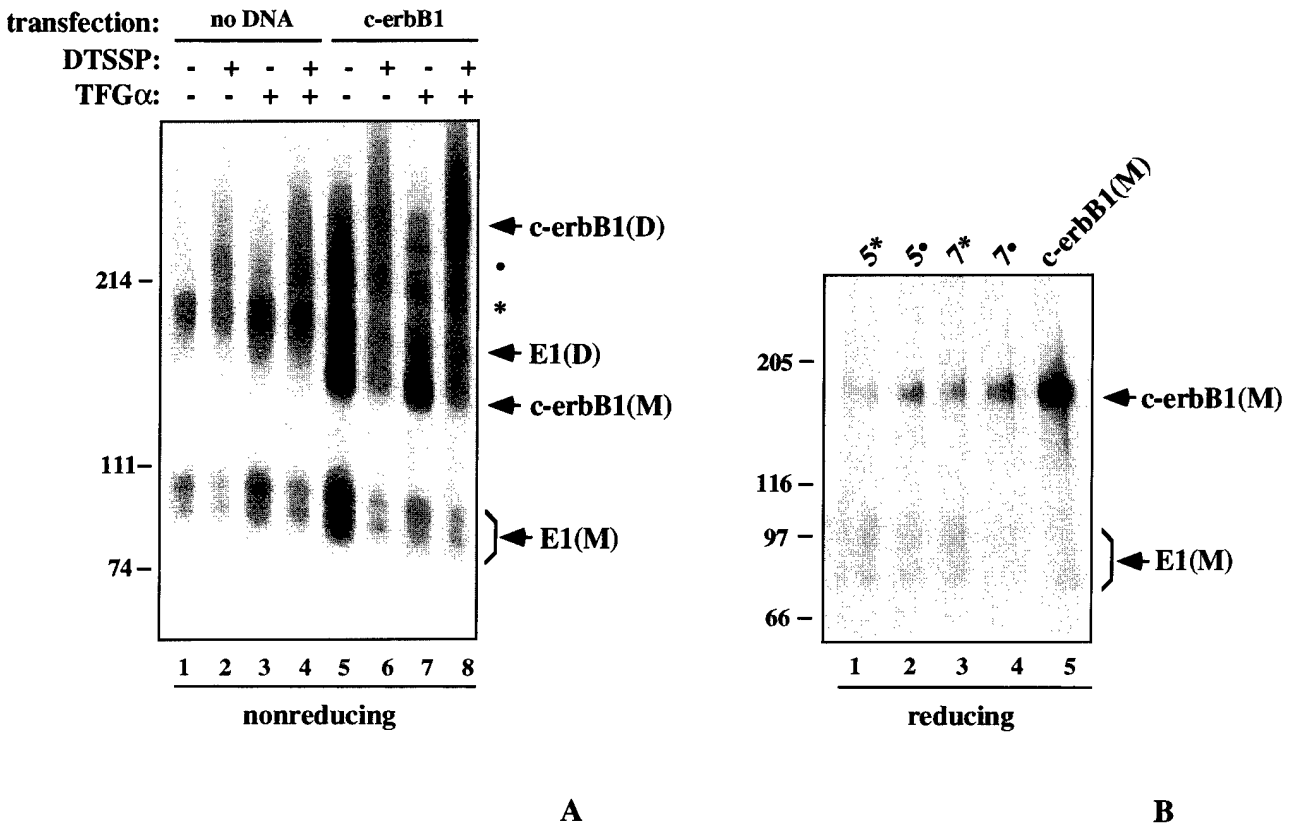

FIG. 7. Ligand-independent heterodimerization of E1 v-*erbB* with wild-type c-*erbB1*. E1 v-*erbB*/QT6 cells were transiently transfected with an expression vector carrying the full-length c-*erbB1* cDNA. Cells were serum starved 24 h posttransfection. After another 24 h, cells were incubated in the presence or absence of ligand and exposed to the cross-linker DTSSP, as described previously. Immunoprecipitated receptor complexes were labeled by in vitro kinase assays and separated by nonreducing SDS-PAGE on 3 to 9% gradient gels (panel A). Multimeric c-*erbB1* and E1 v-*erbB* complexes are indicated by arrows, while putative heterodimeric bands are indicated by * and •. Putative heterodimeric bands were excised and reduced prior to electrophoresis under reducing conditions (panel B). Bands excised from panel A are indicated by lane number and corresponding symbol. Monomeric transfected c-*erbB1* was excised and reduced for comparison (panel B, lane 5).

and CSF1 (38) receptors, as well as for the growth hormone receptor (20). In contrast, ligand-independent disulfide-mediated dimerization has been described for oncogenic p185^{neu} (63), for an oncogenic erythropoietin receptor mutant (62), and for the activated RET receptor-like tyrosine kinase (51). The activating mutations in these proteins reside in the transmembrane (2, 3, 57) or ligand-binding (51, 66) domains, and all three oncogenic mutant receptors are constitutively dimeric, utilize covalent disulfide interactions, and transform cells in a ligand-independent fashion. Therefore, the observation of disulfide-mediated homodimeric interactions between E1 v-*erbB* and S3 v-*erbB* products, which also have sustained an alteration in the extracellular domain, may be significant with respect to the oncogenic signals transmitted by these mutant receptors.

It previously has been shown that coexpression of AEVR v-*erbB* with a kinase-inactive human EGFR results in phosphorylation of the EGFR (49). More recently, experiments in CEF showed that the presence of a mutated form of insertionally activated c-*erbB1* appears to induce tyrosine phosphorylation of endogenous avian c-*erbB1* in the absence of ligand (54). In our current study, we have observed the ligand-independent stimulation of kinase-inactive c-*erbB1* in a manner that required the presence of either E1 v-*erbB* or S3 v-*erbB* (Fig. 8 and 9). Together, these data suggest that these oncogenic v-*erbB* mutants are capable of transactivating wild-type c-*erbB1*. We have also described a covalent heterodimeric complex of E1 v-*erbB* and c-*erbB1*, observed under nonreducing electrophoretic conditions. A putative S3 v-*erbB*/c-*erbB1* heterodimeric complex has been more elusive, using our current experimental conditions, and we are continuing to pursue the characterization of this complex.

Analysis of various EGFR mutants has been informative regarding the receptor domains that may be involved in ligand-dependent receptor dimerization. For example, several studies have used the soluble EGFR extracellular domain to demonstrate that the ligand-binding domain is sufficient for ligand-dependent EGFR interactions (10, 27, 35, 67). Recent studies also have demonstrated that various structural mutations within the transmembrane domain of the EGFR do not affect ligand-induced receptor dimerization (12, 29), suggesting that the integrity of this EGFR domain may be less critical for ligand-mediated receptor aggregation. Furthermore, mutant EGFR truncated proximal to the kinase domain are able to undergo ligand-dependent heterodimerization with wild-type EGFR (30), indicating that the kinase and carboxy-terminal domains are not required for ligand-dependent dimerization.

While little is known about growth factor receptor domains involved in ligand-independent dimerization, a recent study (14) presents new data suggesting that both the EGFR transmembrane and kinase domains may be required for ligand-independent receptor heterodimerization. In this study, the ability of full-length EGFR to interact with various recombinant EGFR truncation mutants was assessed. Coimmunoprecipitation analysis suggested that ligand-independent het-

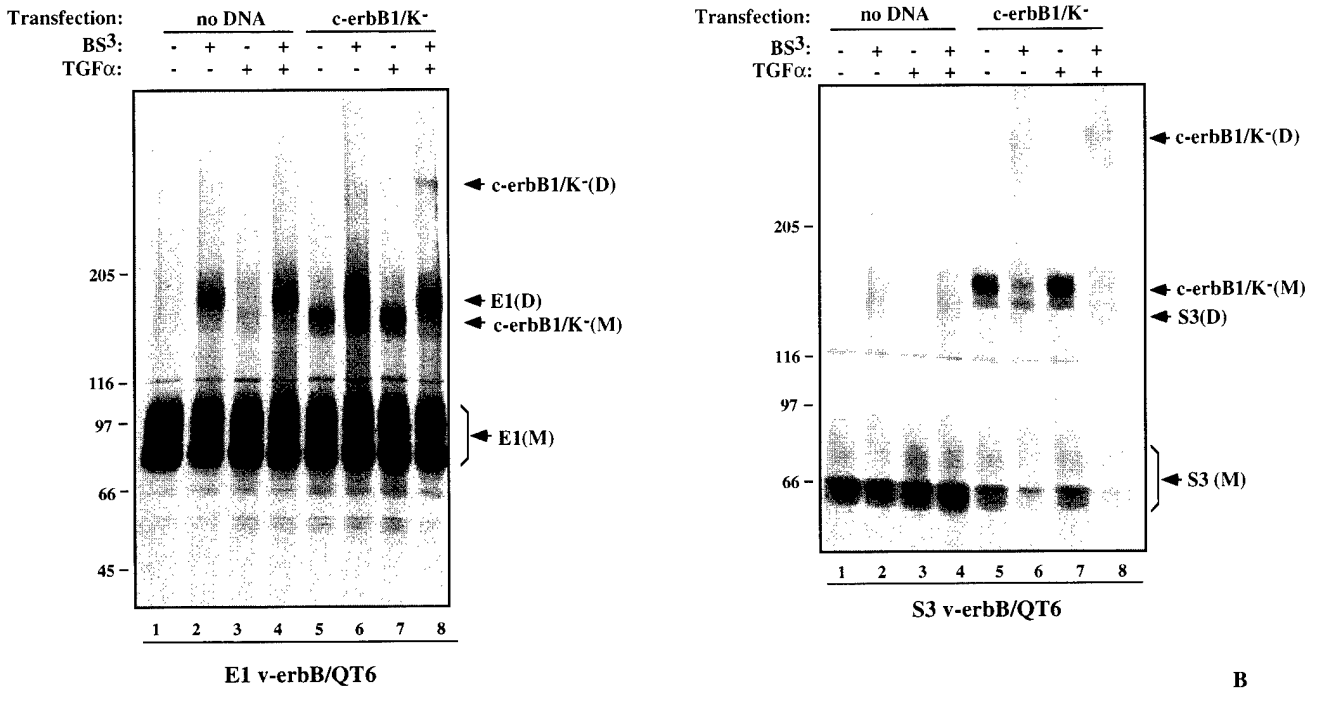

FIG. 8. Transphosphorylation of c-*erbB1* by E1 v-*erbB* and S3 v-*erbB* in vitro. E1 v-*erbB*/QT6 (panel A) or S3 v-*erbB*/QT6 (panel B) were transiently transfected with kinase-inactive c-*erbB1* (c-*erbB1*/K$^-$). Cells were serum starved prior to ligand stimulation and exposure to 2 mM BS^3. Cell lysates were immunoprecipitated and in vitro kinase assays were performed followed by reducing SDS-PAGE analysis.

erodimeric interactions may occur between the wild-type human EGFR and various EGFR mutants lacking the entire extracellular domain. While no direct cell surface interactions were demonstrated in this study, truncated mutant receptors could be coimmunoprecipitated with full-length EGFR. Our results support the interpretation of these recent observations and further demonstrate a direct covalent heterodimeric interaction between the naturally occurring E1 v-*erbB* receptor mutant and avian c-*erbB1*. We also directly demonstrate the cell surface nature of v-*erbB* homodimers. Clearly, the ligand-binding domain of avian c-*erbB1* is not required for homo- or heterodimerization of mutant v-*erbB* receptors, nor does the

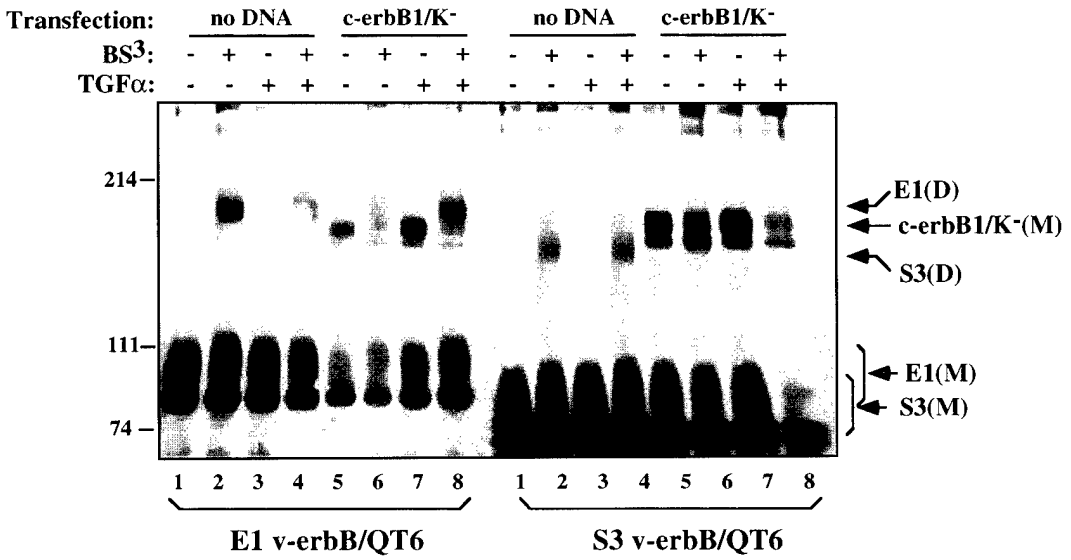

FIG. 9. Transphosphorylation of c-*erbB1* by E1 v-*erbB* and S3 v-*erbB* in situ. Parallel immunoprecipitates of transfected samples in Fig. 8 were separated by SDS-PAGE and transferred to nitrocellulose for antiphosphotyrosine immunoblotting with monoclonal antibody 4G10.

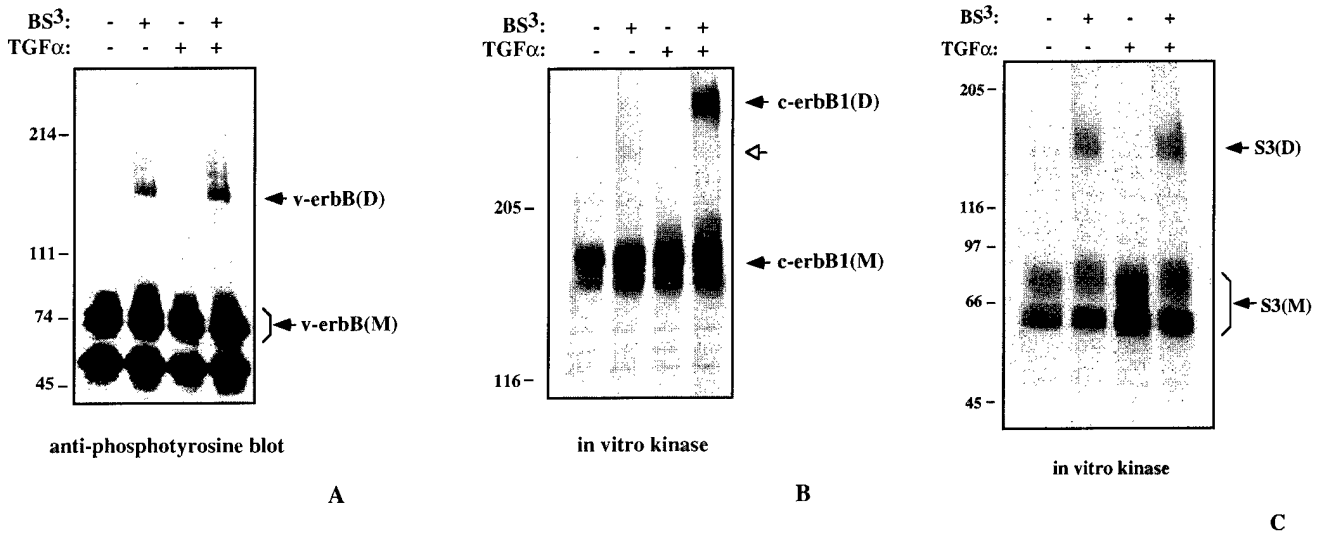

FIG. 10. Homodimerization of c-*erbB1* and v-*erbB* products in erythroblasts and endothelial cells. 6C2 erythroblasts expressing the AEVR form of v-erbB (panels A and B) or endothelial cells from S3 v-*erbB*-induced hemangiosarcoma tissue (panel C) were cross-linked with BS^3 following TGF-α stimulation. AEVR v-*erbB* dimers were detected by immunoprecipitation with an anti-*erbB* kinase domain antibody (panel A) followed by antiphosphotyrosine immunoblotting with monoclonal antibody 4G10. Wild-type c-*erbB1* dimers were detected by immunoprecipitation with T2 (panel B) followed by in vitro kinase assay. S3 v-*erbB*/endothelial cells in panel C were cross-linked and immunoprecipitated as in panel B. A band migrating with the appropriate electrophoretic mobility for a heterodimer (c-*erbB1* + AEVR v-*erbB*) is indicated in cross-linked 6C2 cells by an open arrow (panel B, lane 2).

139-amino-acid carboxy-terminal deletion in S3 v-*erbB* affect this receptor's ability to dimerize. In fact, S3 v-*erbB* consistently demonstrated higher-order oligomerization than did E1 v-*erbB* under both reducing and nonreducing conditions. Together, these results suggest that multiple domains contribute to receptor homo- and heterodimerization and that the mechanisms involved in ligand-dependent versus ligand-independent EGFR dimerization are distinct.

Our current work also demonstrates that ligand-independent homodimerization of v-*erbB* occurs in all three of the target tissues previously described to be transformed by these mutant receptors. S3 v-*erbB* homodimerizes in both fibroblasts and endothelial cells, suggesting that v-*erbB* homodimerization is not regulated by tissue-specific factors. Furthermore, E1 v-*erbB* homodimerizes and the dimeric form of this receptor is an active kinase in nontransformed CEF. While the differences we have observed in the dimerization characteristics of E1 v-*erbB* and S3 v-*erbB* may be important with respect to their transforming capabilities, the present study demonstrates that receptor dimerization, per se, is not sufficient for transformation. However, since all three v-*erbB* mutants analyzed here, E1 v-*erbB*, S3 v-*erbB*, and AEVR v-*erbB*, undergo ligand-independent homodimerization, it remains possible that ligand-independent receptor dimerization is required for transformation by these mutants, and this hypothesis is experimentally testable.

While v-*erbB* has been described as a constitutively active form of the EGFR (24), recent studies to elucidate the characteristics of ligand-independent growth factor receptor signaling suggest that aspects of ligand-dependent versus ligand-independent signaling may be distinct. For example, previous studies have shown that while overexpression of the human EGFR (17, 50, 60) or the avian c-*erbB1* product (54) in cultured cells can cause anchorage-independent growth in a ligand-dependent fashion, mere overexpression of these receptors is not tumorigenic in any animal model. Furthermore, while overexpression of EGFR family members has been correlated with a variety of human malignancies (1, 5, 6, 16, 21, 42, 58, 59), in no case has overexpression been attributed to the etiology of the tumor. In sharp contrast, v-*erbB*-encoded mutant receptors are highly tumorigenic in vivo as well as being mediators of ligand-independent transformation of primary cells in culture (15, 48). In addition, wild-type EGFR has been shown to activate transcription of urokinase plasminogen activator in an EGF-dependent fashion (28), while analogous studies have demonstrated that v-*erbB* does not activate this pathway (4). Recent studies also have demonstrated both quantitative and qualitative differences between ligand-dependent and ligand-independent patterns of tyrosine phosphorylation in primary fibroblast cultures expressing c-*erbB1* and oncogenic v-*erbB* products (41). Thus, several differences between the signals and biological endpoints initiated by ligand binding to wild-type EGFR versus those initiated by oncogenic v-*erbB* mutant receptors in the absence of ligand recently have been demonstrated. The receptor dimerization data presented in this study further illustrate the unique characteristics of ligand-independent signaling mediated by mutant c-*erbB1*-encoded receptors.

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M A Y O

GRADUATE SCHOOL
DEGREE PROGRAMS
1996 - 1997

mayo

The Mayo Vision

Mayo aspires to provide the highest quality, compassionate care at a reasonable cost through a physician-led team of diverse people working together in clinical practice, education and research in a unified multi-campus system.

The Mayo Pledge

Mayo pledges to conduct its interdependent programs of medical care, research and education in keeping with the highest standards of ethics and quality. Fundamental to this pledge is the absolute need to combine the science and art of medicine and technology with personalized care. Excellence in all endeavors with respect for the individual—both patient and employee—is the primary goal. Mayo will achieve this pledge through:

Comprehensive and compassionate patient care delivered through an integrated, multispecialty group paractice.

Superior biomedical research.

Scholarly educational programs to teach and train medical and scientific professionals for national and Mayo needs and to be a health information resource for the public.

Institutional Principles

To realize the vision, and in keeping with the pledge, Mayo has as its principles:

1. To honor the commitment that "the needs of the patient come first."
2. To be local, regional, national and international in service.
3. To emphasize access for patients who may most benefit from Mayo's practice characteristics.
4. To be a unified, integrated medical system in multiple locations offering the Mayo style of group practice.
5. To recruit and retain outstanding people to work as a team in an interdisciplinary setting.
6. To respect the individual contributions of each member of the Mayo family and to reaffirm the importance of "continuing interest by every member of the staff in the professional progress of every other member."
7. To promote cultural diversity and equality of opportunity within the Mayo family.
8. To serve appropriately those patients whose financial circumstances indicate that payment of normal charges would be a dificult burden.
9. To be a leader in conducting our activities in a manner which protects, conserves and reuses natural resources.
10. To consider resource allocation at Mayo within the perspective of a system rather than its individual entities.
11. To conduct our activities in a manner that permits a financial return sufficient to meet present and future requirements, both operational and capital, for its programs in practice, education and research.
12. To measure success in terms of quality and not quantity; service and not self-serving; financial security and not accumulated wealth; system in contrast to individual entity.

1996-97 ACADEMIC CALENDAR

Fall Quarter

Registration for fall quarter courses due - September 6, 1996.*
Fall quarter begins - September 30, 1996.
Last date to withdraw - November 8, 1996.
Thanksgiving Holiday - November 28, 1996.
Last day of quarter - December 20, 1996.
Christmas Holiday - December 25, 1996.
Break - December 23 - January 3, 1997.

Winter Quarter

Registration for winter quarter courses due - December 13, 1996.*
Winter quarter begins - January 6, 1997.
Last date to withdraw - February 14, 1997.
Last day of quarter - March 28, 1997.
Break - March 31 - April 4, 1997.

Spring Quarter

Registration for spring quarter courses due - March 14, 1997.*
Spring quarter begins - April 7, 1997.
Last date to withdraw - May 16, 1997.
Memorial Day Holiday - May 26, 1997.
Last day of quarter - June 27, 1997.

Summer Quarter

Registration for summer quarter courses due - June 6, 1997.*
Summer quarter begins - June 30, 1997.
Independence Day Holiday - July 4, 1997.
Last date to withdraw - August 8, 1997.
Labor Day Holiday - September 1, 1997.
Last day of quarter - September 19, 1997.
Break - September 22 - 26, 1997.

*Later registration allowed, with permission of instructor, if course less than 15% completed.

1997-98 ACADEMIC CALENDAR

Fall Quarter

Registration for fall quarter courses due - September 5, 1997.*
Fall quarter begins - September 29, 1997.
Last date to withdraw - November 7, 1997.
Thanksgiving Holiday - November 27, 1997.
Last day of quarter - December 19, 1997.
Break - December 20, 1997 - January 4, 1998.

Winter Quarter

Registration for winter quarter courses due - December 12, 1997.*
Winter quarter begins - January 5, 1998.
Last date to withdraw - February 13, 1998.
Last day of quarter - March 27, 1998.
Break - March 28 - April 5, 1998.

Spring Quarter

Registration for spring quarter courses due - March 13, 1998.*
Spring quarter begins - April 6, 1998.
Last date to withdraw - May 15, 1998.
Memorial Day Holiday - May 25, 1998.
Last day of quarter - June 26, 1998.

Summer Quarter

Registration for summer quarter courses due - June 5, 1998.*
Summer quarter begins - June 29, 1998.
Independence Day Holiday - July 3, 1998.
Last date to withdraw - August 7, 1998.
Labor Day Holiday - September 7, 1998.
Last day of quarter - September 18, 1998.
Break - September 19 - 27, 1998.

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*Later registration allowed, with permission of instructor, if course less than 15% completed.

Mayo Foundation
Department of Education Services

Richard M. Weinshilboum, M.D.
Director for Education

Marsha M. Hall
Chair, Department of Education Services

Richard McGee, Ph.D., Director
Office of Minority Affairs

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Mayo Graduate School

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Dean

Richard McGee, Ph.D.
Associate Dean for Student Affairs

Catharine J. Chellgren
Registrar/Administrator

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INTRODUCTION

History

The Mayo Foundation, of which the Mayo Clinic is a part, developed gradually from the family medical practice of Dr. William Worrall Mayo and his sons, Dr. William James Mayo and Dr. Charles Horace Mayo. The elder Dr. Mayo came to Rochester in 1863 to practice medicine. His sons assisted him during their boyhood and later joined him in the practice of medicine. As the demand for their services increased, the Mayos invited other physicians to work with them.

This pioneering venture in the private group practice of medicine became known in the early 1900s as Mayo Clinic. This name today describes an organization of over 1700 scientists and medical and surgical specialists working together as a team for the advancement of medical and biomedical education, research in medicine and related sciences and medical care.

The Mayo Graduate School originally was organized under the auspices of Mayo Graduate School of Medicine. In January, 1989, Mayo Graduate School became a separate unit that administers Mayo Ph.D. and Master's degree programs in the basic sciences and Master's degree programs in the clinical sciences. Enrollment currently includes approximately 120 Ph.D. or M.D.-Ph.D. candidates in basic science fields and 15 master's candidates in clinical fields. Other educational components of Mayo Foundation include:

- Mayo Graduate School of Medicine, organized in 1915 to offer programs of graduate medical education. Enrollment currently includes more than 1000 residents and fellows in clinical fields and 230 research fellows involved in postdoctoral basic science research training.
- Mayo Medical School, an undergraduate medical school offering the M.D. degree, opened in 1972, with a current enrollment of 160 students.
- Mayo School of Health-Related Sciences, organized in 1972 to provide training and certification in the health professions allied to medicine. Twenty-one programs are offered with a total enrollment of over 300. Two of the 21 programs include a Masters in Physical Therapy and and Masters in Nurse Anesthesia.
- Section of Continuing and International Education, organized in 1977 to provide continuing education for physicians, through the staff of Mayo Clinic.

Mayo Foundation is accredited by the Commission on Institutions of Higher Education of the North Central Association of Colleges and Schools.

Research Opportunities

Outstanding research opportunities are open to those accepted into the educational programs of the Mayo Graduate School and Mayo Graduate School of Medicine. Two modern buildings with a total of more than 965,000 square feet of space are largely devoted to research programs and related services. Other research space and facilities are scattered throughout the institution. State of the art facilities are available in each of the basic science departments.

Mayo research programs offer a spectrum of diverse opportunities for individuals in nearly all aspects of biomedical sciences. Mayo has a long history of internationally recognized research in areas as diverse as: the biochemistry of endocrine hormones; the physiology of respiratory, cardiovascular and gastrointestinal systems; the molecular mechanisms that regulate the immune response; analysis of the genes encoding blood clotting factors; and three dimensional computer-based magnetic resonance imaging.

The research programs have been open from their inception to graduate students, medical students, research fellows, and residents.

FACULTY

All staff appointments are made to Mayo Clinic/Mayo Foundation and this staff constitutes the faculty for the educational programs of Mayo Foundation. The 1700-plus faculty members include full-time investigators in the sciences related to medicine, clinician-investigators and clinicians. Each member of the staff is full-time salaried, and individual staff members have ample opportunity to teach. Members of the staff have the overall responsibility for undergraduate and graduate education in medicine and the medical sciences, for continuing education and research as well as for the care of patients. Graduate faculty privileges are awarded to qualified faculty members with interest in delivering graduate level courses and in supervising candidates for graduate degrees (see listing of graduate faculty, last section of the catalog).

FACILITIES

The majority of the educational programs, clinical practice and research are conducted in Rocherster within the facilities of Mayo Foundtion. Mayo facilities in Jacksonville, Florida and Scottsdale, Arizona, which were opened in 1986 and 1987, also participate in Mayo's clinical practice, education and research programs.

Rochester

Mayo Foundation's Rochester facilities are located in a seven-block area in downtown Rochester. The 22-story Murry and Leonie Guggenheim Building houses a large proportion of the research laboratories and lecture halls. The Medical Sciences Building is devoted largely to research and educational activities in anatomic pathology, biophysics and surgery, among others. The Plummer Building is home for the Medical Library and many support services as well as some research and diagnostic laboratories. Rochester Methodist Hopsital is within the same area and St. Marys Hospital, which includes additional research facilities, is about a mile away.

The 20-story Mayo Building is the heart of the Mayo complex. It houses most of the medical and surgical deparments and is the center for outpatient diagnosis. The administrative offices of the Graduate School, Mayo Graduate School of Medicine and Mayo School of Health-Related Sciences are located in the Siebens Building. Most of Mayo's clinical laboratories are in the Conrad N. Hilton

Building. The Harwick Building contains medical and x-ray records, the computer center and full-service cafeteria. Mayo Medical School's administrative offices, learning resource center and student lounge are contained in the Mitchell Student Center Building. The Baldwin Building for Community Medicine is the center of care for Rochester area patients.

Jacksonville

Mayo Clinic Jacksonville is a comprehensive outpatient medical facility located on 240 acres near the Intracoastal Waterway in eastern Jacksonville. It includes a full-service laboratory, an on-site pharmacy, an ambulatory surgical center and a radiation-oncology center. A state-of-the-art medical research building houses researchers conducting a large-scale study of Alzheimer's disease.

St. Luke's Hospital, located nine miles inland from the clinic, is a modern 289-bed facility with 16 operating rooms, two ICUs, a bone marrow transplant unit, an epilepsy unit, two cardiac catheterization laboratories and a stereotactic neurosurgery suite.

Scottsdale

Mayo Clinic Scottsdale is a comprehensive outpatient clinical facility located on 149 acres in northern Scottsdale. It includes an ambulatory surgical center, a pain clinic, a full-service laboratory, an on-site pharmacy, a patient library, and a 188-seat auditorium used for physician and patient education programs. The 75,000-square-foot Johnson Medical Research Center houses researchers focusing on molecular genetics, molecular immunology, molecular and cell biology, and molecular chemistry.

Telecommunications System

Mayo's clinics in Rochester, Scottsdale and Jacksonville are linked via a sophisticated video telecommunications system, which provides video teleconferencing and data transmission. Staff in Rochester, Scottsdale and Jacksonville can have live, interactive consultations at the other sites via TV monitors. Clinical and research test results can be transmitted between sites. In addition, Mayo has a five-digit telephone dialing and pager system that ties together all three practice sites.

Office of Minority Student Affairs

The Office of Minority Student Affairs assists and supports minority students in all of the educational programs at Mayo. Located on the fifth floor of the Siebens Building, it is staffed by Dr. Richard McGee, Director of the Office and Associate Dean for Student Affairs in the Graduate School and Ms. Jackie Johnson, Minority Student Adviser. Both are available to answer questions and provide assistance with any issue related to the needs of minority students in Mayo and the Rochester community.

Emergency Loans

Limited short-term financial help for graduate students is available to help alleviate financial hardship resulting from an emergency. Details are available in the Graduate School Office, telephone 284-3163.

Rochester

Rochester provides many cultural, educational and other activities not usually found in cities of similar size. Local people provide the talent and support for a symphony orchestra and chorale, a civic theater, an independent repertory theater, a community art center and a historical society. The Minnesota Orchestra, the Saint Paul Chamber Orchestra, and other nationally known entertainers perform regularly at Mayo Civic Auditorium. Eight colleges or universities offer classes in Rochester or at campuses within an hour's drive of the city.

The four seasons enjoyed by Rochester provide opportunities for ice skating, skiing, biking, hiking, and hunting. The local lakes and rivers are utilized for a variety of water sports. Attractions in the Twin Cities, Minneapolis and St. Paul (80 miles to the north of Rochester), include the Tyrone Guthrie Repertory Theater, Minnesota Orchestra, Mall of America, professional baseball, basketball, and football.

Rochester offers a variety of apartments at rates comparable to those in other cities of similar size.

Graduate Student Association

The Mayo Graduate Student Association is composed of all students pursuing graduate degrees at the Mayo Graduate School. Its purpose is to facilitate interaction among graduate students, and between students, faculty and administration. It provides a means for students to give input to departments concerning coursework and curriculum. A graduate student is chosen each year by the Graduate Student Association to serve on the Mayo Graduate School Education Committee.

POLICIES

STIPENDS

Students with baccalaureate or Master's degrees who are accepted into the Ph.D. program receive a regular bi-weekly stipend beginning at commencement of the program. The stipend continues for an expected duration of four years contingent upon satisfactory performance. Extensions for additional years may be requested from the Mayo Graduate School Education Committee and are granted if performance is satisfactory and funding is available from the program, laboratory or extramurally. The stipend for all graduate students is set at a uniform level ($15,500 for 1996-97) and is reviewed at regular intervals.

Students who are accepted into a combined M.D.-Ph.D. program are provided a stipend ($15,500 for 1996-97). The stipend continues throughout the student's M.D.-Ph.D. program. Medical School and Graduate School tuition and fees are provided by a full scholarship for students accepted into this combined M.D.-Ph.D. program, with satisfactory performance.

Clinical residents accepted into the Master's program receive the usual stipend for clinical fellows at their level of training.

Employees pursuing master's degrees on a part-time basis receive their usual employee salary.

TUITION

Annual tuition for Ph.D. graduate students is $17,900. Tuition for non-degree candidates is $100 per quarter credit. Tuition is provided by a full scholarship for students who are enrolled in a degree program of Mayo Graduate School. Extramural sources of funds are used to defray tuition when appropriate.

REGISTRATION

Registration for Mayo Graduate School courses is accomplished through the Graduate School Office and must be made in writing before the applicable deadline (see Academic Calendar). Mayo courses are primarily intended for individuals appointed to the educational programs of Mayo Graduate School. Others can enroll if they show appropriate prerequisites and secure the course chair's approval. Openings in some courses are severely limited; degree candidates are given preference for these courses.

Registration for credit - Unless waived, payment of tuition is required at the time of registration. Tuition is refunded if a course is cancelled.

Changes in registration

- If a student withdraws within the first one-half of a course, tuition is refunded and a grade of "W" is recorded on the transcript. Later withdrawals result in a grade of "F", and tuition is not refunded.
- **Retroactive registration after a course is completed is not permitted.**
- Students who wish to register for a course after the deadline date must get written permission from the instructor of the course. Late registration forms are available in the Graduate School office.

Grading System

Mayo Graduate School uses two grading systems:

A	Outstanding	S	Satisfactory
A-	Excellent	N	No credit
B+	Very Good		
B	Acceptable		
B-	Marginal/below standards expected		
C+	Below standards		
C	Poor/lowest performance to receive credit		
F	Unsatisfactory		

The Grade Point (GPA) average is based on:

A	=	4.0	B-	=	2.7
A-	=	3.7	C+	=	2.3
B+	=	3.3	C	=	2.0
B	=	3.0	F	=	0.0

The grading system to be used is determined at the time the course is established. A grade of S or N is not considered in determination of GPA. The GPA, which is recorded on the official transcript, is calculated by dividing the sum of all grade points earned by the sum of all credits assigned grade points.

In addition to the grades the transcripts show the following, if applicable:

W – Withdraw

I – Incomplete. Students have, at the option of the faculty, a maximum of one year to make up any deficiency. If the deficiency is not corrected within the year, the transcript will show an "F" for the course.

X – The course is continued over more than one quarter and the grade assigned at the end of the final quarter.

Students may retake courses to improve their grades with the permission of their adviser and the course chair. Both grades will appear on the transcript and the higher grade will be used in computation of the GPA.

Transcript Request

Official transcripts will be issued by the Graduate School office only upon receipt of a written request.

Definition of Credit Hour

Credit is determined by the number of contact hours per week. A one-hour lecture per week equals one credit per quarter. A quarter is usually 12 weeks. Credit is also given for laboratory time in some courses.

Course Numbering

Courses at the 5—- and 8—- levels are graduate level courses that may be used in fulfillment of degree program requirements. Courses at the 8—- level are considered to be at the boundary of what is known or done in a particular field. They can be expected to be exceptionally rigorous.

Student Responsibility

Each graduate student must complete all requirements established for his or her degree by the Graduate School and the Program. **It is the student's personal responsibility to be aware of and understand these requirements.** A student's adviser may not assume these responsibilities, nor may substitute, waive, or exempt the student from any established requirement or academic standard. Such exemptions may, however, be proposed for consideration by the Graduate School, which reserves the right to modify requirements at any time.

Transfer Credits

Students who wish to transfer credits to substitute for a Mayo course must contact the Mayo course director. If the course director determines that a student has the knowledge equivalent to satisfactory performance in the Mayo course, the student will receive the transfer credits.

Students who wish to transfer credits for courses not offered at Mayo may request credit for graduate courses taken at other institutions if they received a grade of A or B. The request must have the approval of the student's education coordinator and the Graduate School. A description of the course from the course catalog or a course outline must accompany the request. The time interval since the credits were earned is a consideration in such decisions. Credits must normally have been earned within the previous ten years (more recently in the case of rapidly advancing subjects).

Residence Requirement

Regardless of how many transfer credits are awarded, candidates for graduate degrees from Mayo Graduate School must complete a minimum period in residence after admission to their degree program. For Ph.D. degree candidates, the minimum period of residence will be two years, and for Master's degree candidates the period is one year.

Extensions

Graduate student appointments are for four years and M.D.-Ph.D. appointments

are for three years in the graduate program. Extensions beyond the fourth year for Ph.D. students and beyond three years for M.D.-Ph.D. students, with stipend support, are permitted with evidence of satisfactory performance and a recommendation signed by at least four of the five members of the student's advisory committee. Each extension is for a maximum of one year.

Confidentiality of Student Records

The Family Educational Rights and Privacy Act (FERPA) affords students certain rights with respect to their education records. They are:

1. The right to inspect and review their education record.
2. The right to request the amendment of the education record to ensure that it is not inaccurate, misleading, or otherwise in violation of the student's privacy or other rights.
3. The right to consent to disclosure of personally identifiable information contained in the education records, except to the extent FERPA authorizes disclosure without consent.
4. The right to file with the U.S. Deparment of Education a complaint concerning alleged failures by Mayo Graduate School to comply with the requiremnts of FERPA.
5. The right to obtain a copy of Mayo Graduate School's student records policy.

The complete FERPA policy is available in the Student/Faculty Handbook.

Equal Opportunity/Affirmative Action

Mayo Graduate School is committed to equal opportunity and affirmative action in the appointment process. This policy is in accord with the policy of Mayo Clinic and Mayo Foundation, which is to seek and select persons for appointment, employment or admission, and to train, advance, promote, transfer and compensate such persons on the basis of individual capability, potential or contribution to the programs and goals of the institution. In making these selections and subsequent personnel decisions, Mayo actively encourages the recognition, development and optimal use of the capabilities of women, racial minorities, persons with disabilities and veterans of the Vietnam era.

Additionally, Mayo observes, respects and supports stated policies of the State and Federal governments that preclude discrimination. Each department chair, administrator, supervisor and employee of Mayo Clinic and Mayo Foundation is responsible for conducting appointment and employment activities in compliance with this policy.

A Student/Faculty Handbook with Mayo Graduate School policies and procedures is available in the Mayo Graduate School office.

Description of Ph.D. Degree Program and Basic Science Track Requirements

The Doctor of Philosophy Program in Biomedical Sciences

Purpose and Philosophy

The Biomedical Sciences Ph.D. Program is intended to train students in the most modern approaches to biomedical research, and to assist with development of analytical, technical, oral and written communication skills which allow students to become independent investigators of the most important and challenging problems in biomedical research.

Students are provided with a supportive atmosphere where they can find role models and mentors to emulate in the development of their research skills and begin acculturation into the biomedical research community. Courses introduce students to the body of information most important to their subsequent research endeavors, and other educational activities facilitate the development of independent learning skills. Students are assisted with formulation of career goals and pathways which best utilize their individual talents and skills.

Mayo's Ph.D. program places heavier emphasis on research training than it does on course work. This philosophy is a natural outgrowth of the institution's long history as a center for investigation in the life sciences. Courses are nevertheless an integral part of the Ph.D. program, providing the intellectual foundation necessary for a well-rounded scientist. A minimum of forty-two credits are required of all Ph.D. students. Mayo's graduate level courses in specific disciplines of the basic sciences will be adequate preparation for most students. Degree candidates who need to obtain additional specialized course work not available at Mayo will be provided with an opportunity for up to three academic quarters of off-campus study at a cooperating institution of higher learning. In such cases, the normal predoctoral stipend will continue, and full tuition will be reimbursed. All Ph.D. candidates must complete at least two years of full-time registration at Mayo to be eligible for their degree.

Admissions Requirements

To be considered for admission to the Ph.D. program, applicants should:

1. Hold a bachelor's degree from an accredited college or university with a minimum 3.0 Grade Point Average based on the 4.0 scale.
2. Have received scores on the verbal, analytical, and quantitative aptitude tests of the Graduate Record Examination indicating strong academic ability (i.e., above the 75th percentile). Subject Tests (e.g. biology, chemistry, biochemistry) are strongly encouraged.
3. Have a minimum undergraduate background with evidence of superior performance, including:

Two years of college chemistry (includes organic)	One year of biology
One year of calculus	One year of physics

   A course in biochemistry or molecular biology is highly recommended.

4. Supply supporting documents, including:

   Official transcripts
   Official copies of GRE or MCAT scores
   Three letters of recommendation

Foreign applicants must take the Test of English as a Foreign Language (TOEFL) to be considered for an appointment.

Each area of specialization may establish additional requirements.

Inquiries regarding admission to the Ph.D. Program in the Biomedical Sciences should be directed to:

Mayo Graduate School
200 First Street Southwest
Rochester, MN 55905
(507) 284-4356
phd.training@mayo.edu

Completed applications must be submitted by December 31.

Authority to make appointments rests with the Graduate School Education Committee on the recommendation of the individual department or program education committee.

Falsifying or omitting information on or accompanying the application may disqualify an applicant from admission or subject a student to dismissal.

The application and supporting documents become the property of Mayo Graduate School upon receipt.

The average number of years to degree is 5.2.

Core Courses (Minimum 13 Credits)

Students must complete a minimum of 13 credits of didactic course work which will provide a broad-based foundation in the biomedical sciences. The 13 credits must include the required one-credit course entitled, "The Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research." The courses should normally be outside the area of specialization, but exceptions may be approved on an individual basis. A student's program of courses is individually developed in consultation with his or her adviser. A series of basic graduate level courses are available to students so they may obtain a comprehensive background in the fundamental disciplines of biochemistry, cell biology and molecular biology. Seminars and journal clubs are not permitted as core courses.

Area of Specialization (Minimum of 18 Credits)

The core courses are followed by course work in the area of specialization (minimum of 18 credits). These courses are chosen with the aid and approval of the student's adviser. Courses appropriate to the different areas of specialization are outlined in the next section. The remaining 11 credits can be selected from any area that the student and adviser deem appropriate and necessary.

The typical program structure is as follows:

Year I - Core, area of specialization coursework, and laboratory rotations

Year II - Advanced courses and commencement of thesis research

Year III & IV - Primarily thesis research with some additional advanced courses

Students in their research phase must register for research each quarter. Research will be graded on the S-N scale, no credit will be given and, therefore, research is not calculated in the GPA.

Laboratory Rotations

Each student must complete at least three laboratory rotations and a minimum of six credits. One rotation can be outside the area of specialization.

M.D.-Ph.D. Program

The M.D.-Ph.D. program is a highly competitive program for students with exceptional academic records and previous research experience. Both the M.D. and Ph.D. degrees may be obtained in an integrated seven to eight-year program.

The elements of the Ph.D. program for students enrolled in the M.D.-Ph.D. program are generally the same as those for non-M.D. candidates, except for laboratory rotations. The laboratory rotation requirement for M.D.-Ph.D. students is satisfied by completing three one-month rotations. It is recommended that two rotations be completed before entering medical school and one between the first and second year of medical school. After the first two laboratory rotations, students follow the Mayo Medical School curriculum for two years. After taking the United States Medical Licensing Examination Step I in June of the second year, students begin their graduate school training. The advanced course work in the area of specialization and the thesis research are undertaken and usually completed in the next three to four years. During the final two years students complete years three and four of the medical school curriculum.

The appointment to the M.D.-Ph.D. program includes a full tuition scholarship for both medical school and graduate school and stipend ($15,500 for 1996-97) for the seven to eight years of training.

Official Degree Program Form

Students are expected to file their Official Degree Program form describing all course work completed and proposed, that will be used in fulfillment of degree requirements, including transfer credits, before the end of their second academic year. The members of the student's qualifying oral examining committee will be appointed on the basis of the information on the cover page of the Degree Program.

Changes in Approved Program

Once approved, the Degree Program must be fulfilled in every detail to meet graduation requirements unless alterations are requested in writing and approved by the graduate education coordinator and the Graduate School.

Minimum Grade Requirements

Students are expected to maintain a grade point average of 3.0 in didactic course work. Students whose performance falls below this standard in a given quarter may be placed on academic probation, as provided for in the Guidelines for Probation and Dismissal (outlined in the Student/Faculty Handbook).

Qualifying Examinations

The qualifying examinations are intended to test the student's fund of information in the sciences related to the chosen field of study and to evaluate the student's ability to reason critically.

Written examination - The qualifying written examination for Ph.D. and M.D.-Ph.D. graduate students must be completed before the end of the second year. The content and format of the examination is determined by each program. The written examination can be taken no more than twice. It must be retaken by the end of the quarter following the quarter in which the exam was first taken. The written examination will test knowledge and critical reasoning in the area of specialization. Material from supporting disciplines may be included.

The Graduate School must be informed of the date of the examination **in advance** so that the written examination report can be sent to the adviser.

Oral examination - When the Graduate School is notified that the written examination has been passed, the oral qualifying examination can be taken. The Graduate School must be informed of the date of the examination in advance so that the Report of Examination form can be sent to the chair. The oral qualifying examination for the Ph.D. and M.D.-Ph.D. students must be completed before the end of the second year. The oral qualifying examination committee will consist of a minimum of four members, three from the track and one from outside the track. The chair of the exam will be recommended to the Graduate School by the department education coordinator. The adviser or any other member of the committee can be the chair. All four members must be present at the exam. Only one dissenting vote will be allowed for a "Pass" or "Conditional Pass." In the event of a Conditional Pass, the specific requirements that must be satisfied by the student will be listed on the Ph.D. Oral Qualifying Examination Report Form. The oral qualifying examination may be taken no more than twice and it must be retaken within six months.

Registration for the ninth quarter is contingent on completion of the qualifying exams.

Thesis

Thesis Advisory Committee - Ph.D. candidates are expected to submit to the Graduate School Office the composition of their thesis advisory committee no later than the end of the first quarter of the student's third year. The Thesis Advisory Committee recommendation form is available from the Graduate School Office.

The Mayo Institutional Review Board must review all protocols for research involving the use of human subjects. It is the candidate's responsibility to secure approval of any such protocols before the research is undertaken.

Thesis Proposal - A written thesis proposal, presentation and thesis committee discussion of the proposal must be completed by the middle of the student's third graduate year. This requirement may be accomplished during the qualifying oral examination. The thesis advisory committee must be approved prior to this committee discussion.

Preparation of thesis - The thesis is the most important document that the Ph.D. candidate will prepare during the course of graduate study and is a record of the scientific accomplishments that justify the awarding of the degree. The thesis is archival. Consequently, the Graduate School has developed standards for its format and style, which should be closely followed. Copies of the guide to preparation of the thesis are available on request from the Graduate School Office. The thesis must be submitted to the final oral examining committee at least three weeks prior to the examination.

Students enrolled in the M.D.-Ph.D. program must submit their final thesis to their advisory committee and the Thesis Readers Report must be signed and submitted to the Graduate School Office before they can resume studies in the Medical School.

Student Progress

Students must have annual meetings with their Thesis Advisory Committee. The first of these meetings, the presentation of the thesis proposal, must be held before the end of the tenth quarter in the program. Registration for the 11th quarter will be contingent upon satisfactory completion of this requirement.

Annual meetings must be held before the end of the 14th and 18th quarters. Registration for subsequent quarters will be contingent upon satisfactory completion of this requirement. Registration forms will include a line for recording the date of these meetings.

If students do not meet deadlines, they will not remain in good standing. Continuation of stipend depends upon remaining in good standing.

Final Oral Examination

The final oral examination will be scheduled after 1) the qualifying written and oral examinations have been taken and passed, 2) all course work shown on the Degree Program form has been completed and 3) a copy of the title page of the thesis is filed in the Graduate School Office. The exam will be open to the Mayo public. The final oral examining committee should receive copies of the thesis at

least three weeks prior to the final oral examination. The examining committee will have at least five members, counting the student's research adviser. The Graduate School strongly encourages the inclusion of an external examiner, i.e., a recognized authority on the thesis topic from another institution. Two members shall come from outside the student's area of specialization. At least two members of the committee, one being the adviser, must have full graduate faculty privileges. Only one dissenting vote will be allowed for a successful defense in the final examination.

Final Thesis Corrections

After a student has passed the final oral examination, members of the thesis advisory committee must sign a form indicating that they are satisfied that the final corrections to the thesis have been made. Four of the five committee members must have signed before the student will be cleared for graduation.

Graduation Deadline

Students are graduated four times a year, the third Friday in February, August and November and mid-May. The latter involves a formal ceremony as part of the Mayo Foundation graduation exercises in conjunction with the Mayo Medical School. No ceremony is held in February, August and November, but students who do graduate at one of these times are encouraged to participate in the May ceremony.

To graduate in February, August or November students must have all requirements completed by the first working day of the month prior to the graduation month. To graduate in May, students must have a draft of the thesis to their adviser by March 15 and their thesis defense scheduled. All other requirements must by completed by April 20, except submission of the thesis. The final copy of the theisis, ready for binding, must be submitted before graduation day.

BIOCHEMISTRY

F. M. Rusnak, Ph.D., *Graduate Education Coordinator*

Z. Bajzer, Ph.D.
M. E. Bolander, M.D.
R. E. Brown, Ph.D.
T. P. Burghardt, Ph.D.
G. W. Dewald, Ph.D.
N. L. Eberhardt, Ph.D.
D. N. Fass, Ph.D.
M. R. Federspiel, Ph.D.
T. A. Felmlee, Ph.D.
L. A. Fitzpatrick, M.D.
S. J. Gendler, Ph.D.
M. J. Getz, Ph.D.
J. P. Grande, M.D. Ph.D.
S. M. Jalal, Ph.D.
R. B. Jenkins, M.D.
J. D. Jones, Ph.D.
C. Kappen, Dr.rer.nat.
B. C. Kline, Ph.D.
R. Kumar, M.D.
V. M. Kumar, Ph.D.
J. J. Lee, Ph.D.
N. A. Lee, Ph.D.
E. B. Leof, Ph.D.
A. H. Limper, M.D.
S. I. Macura, Ph.D.
L. J. Maher, III, Ph. D.
N. J. Maihle, Ph.D.
D. J. McCormick, Ph.D.
J. A. McDonald, M.D., Ph.D.
C. T. McMurray, Ph.D.
M. A. McNiven, Ph.D.
L. J. Miller, M.D.
S. Naylor, Ph.D.
M. Oursler-Velasquez, Ph.D.
W. G. Owen IV, Ph.D.
R. E. Pagano, Ph.D.
L. R. Pease, Ph.D.
J. T. Penniston, Ph.D.
D. R. Pfeifer, Ph.D.
J. F. Poduslo, Ph.D.
F. G. Prendergast, M.D., Ph.D.
J. R. Riordan, Ph.D.
P. C. Roche, Ph.D.
J. L. Salisbury, Ph.D.
H.H.O. Schmid, Ph.D.
T. C. Spelsberg, Ph.D.
E. E. Strehler, Ph.D.
S. N. Thibodeau, Ph.D.
D. J. Tindall, Ph.D.
D. O. Toft, Ph.D.
R. T. Turner, Ph.D.
R. Urrutia, M.D.
G. Vockley, M.D., Ph.D.
S. Vuk-Pavlovic, Ph.D.
Z. Vuk-Pavlovic, Ph.D.
E. D. Wieben, Ph.D.
C.Y.F. Young, Ph.D.

Ph.D. Degree

The requirements for the Biochemistry track conform to the general requirements of the Mayo Graduate School in which a minimum of 24 credits are required in Biochemistry, 13 credits of biomedical core courses, and 5 other credits as deemed appropriate for an individual student's program. **Prerequisites to the track are one year of organic chemistry with laboratory and physical chemistry.** Students lacking the prerequisites will be admitted with the provision that the prerequisites will be rectified during the first year.

The track requirements are:

Bioc	5858	Laboratory Rotations in Biochemistry (2 cr./rotation - 3 rotations req.)	6 cr.
Bioc	8000	General Biochemistry: Structure	3 cr.
Bioc	8001	General Biochemistry: Kinetics, Catalysis and Mechanisms	3 cr.
Bioc	8002	General Biochemistry: Energy Transduction and Signalling	3 cr.

Bioc	8005	Physical Biochemistry	1 cr.
Bioc	8010	Physical Biochemistry	1 cr.
Bioc	8015	Physical Biochemistry	1 cr.
*Bioc	8050	Principles of Cell and Tissue Design	3 cr.
Bioc	8500	Biochemistry and Molecular Biology Journal Club (1 cr./yr. - 3 yrs. required)	3 cr.
*MBio	8101	Replication and Transcription Regulation	3 cr.
*MBio	8102	Regulation of Protein Synthesis	3 cr.

*These courses may be used to satisfy core requirements.

All of these courses, except the Journal Club, must be completed before the student takes the written qualifying examination in year two. At the discretion of the student's committee, one or more advanced topics may be taken during the second year.

Biophysical Sciences Biomedical Imaging Track

R. A. Robb, Ph.D., *Graduate Education Coordinator*

U. Bite, M.D.
J. A. Bonner, M.D.
D. G. Bostwick, M.D.
D.E. Clapham, MD,PhD
R.L. Ehman, M.D.
J.P. Felmlee, Ph.D.
J. M. Fernandez, Ph.D.
B.K. Gilbert, Ph.D.
J.E. Gray, Ph.D.
J.F. Greenleaf, Ph.D.
C.R. Jack, M.D.
M. J. Joyner, M.D.
B. F. King, M.D.
R.W. Kline, Ph.D.
J. Lu, Ph.D.
A. Manduca, Ph.D.
C.H. McCollough, Ph.D.
E.C. McCullough, Ph.D.
R.L. Morin, Ph.D.
H.H. Ottesen, Ph.D.
W. Pavlicek, Ph.D.
J. L. Rae, Ph.D.
S.J. Riederer, Ph.D.
E.L. Ritman, M.D., Ph.D.
G.C. Sieck, Ph.D.
S.M. Sine, Ph.D.
J.H. Szurszewski, Ph.D.
S.R. Taylor, Ph.D.
R.J. Vetter, Ph.D.

Ph.D. Degree

I. Minimum Requirements

A minimum of 42 credits of course work are required for a Ph.D. in the Biophysical Sciences Biomedical Imaging Track. Thirteen core credits are taken outside the student's major area of concentration, as required by the Graduate School. Twenty-nine technical credits are required in the subjects related to the major area, which includes six credits in advanced laboratory methods and three credits in fundamental concepts in Biomedical Imaging, and a minimum of four credits in advanced seminars and/or tutorials.

II. Elective Course Work

A program of course work for both the core and technical components of the Ph.D.

program in the Biomedical Imaging Track may be selected from the following typical curriculum:

Core (13 credit minimum)

BPhy	5500	Fundamentals of Computer Organization and Programming	3 cr.
+Ethic	5000	Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research	1 cr.
HSR	5823	Introductory Statistics I	3 cr.
HSR	5827	Introduction to Regression	1 cr.
Imm	5806	Basic Graduate Immunology	3 cr.
MBio	5000	Introduction to Molecular Biology	3 cr.
Nsci	8300	Concepts in Neurophysiology	2 cr.
Phys	5801	Principles of Biomechanics	3 cr.

Technical (29 credit minimum)

*BPhy	5001	Laboratory Rotations in Biophysical Sciences (4 wks.)	1 cr.
*BPhy	5002	Laboratory Rotations in Biophysical Sciences (8 wks.)	2 cr.
*BPhy	5003	Laboratory Rotations in Biophysical Sciences (12 wks.)	3 cr.
BPhy	5150	Introductory Radiation Biology	2 cr.
BPhy	5225	Introduction to Neural Networks	3 cr.
BPhy	5250	Anatomy for Biomedical Imagers	2 cr.
BPhy	5400	Molecular Electronics	3 cr.
+BPhy	5450	Fundamental Concepts in Biomedical Imaging	3 cr.
BPhy	5520	Algorithms and Problem Solving	2 cr.
BPhy	5610	Imaging and Computers	3 cr.
BPhy	5740	Magnetic Resonance Imaging Systems	3 cr.
BPhy	5800	Physics and Technical Principles of Medical Imaging	3 cr.
BPhy	8100	Medical Health Physics	2 cr.
BPhy	8150	Radiation Therapy Physics	4 cr.
BPhy	8300	Tutorial in Visual Perception and Pychophysics	2 cr.
BPhy	8301	Tutorial in High-Speed Signal Processing	2 cr.
BPhy	8302	Tutorial in Ultrasonic Imaging	2 cr.
BPhy	8304	Tutorial in Physiological Imaging	2 cr.
BPhy	8450	Computer Image Processing	3 cr.
BPhy	8470	Two-Dimensional Digital Signal Processing	3 cr.
BPhy	8490	Advanced Topics in Imaging Science	3 cr.
BPhy	8500	Tutorial in Imaging Science	2 cr.
BPhy	8704	Digital Signal Processing I	3 cr.
BPhy	8705	Digital Signal Processing II	3 cr.
BPhy	8740	Magnetic Resonance Imaging Systems	3 cr.
BPhy	8853	Readings in Biophysical Sciences	2 cr.
CSci	5107	Computer Graphics I	3 cr.
CSci	5117	Computer Graphics II	3 cr.
CSci	5301	Numerical Analysis	4 cr.
CSci	5511	Artificial Intelligence I	4 cr.
CSci	8511	Concepts in Computer Vision	4 cr.
Phy	5551	Topics in Physics for Biology and Medicine	5 cr.

Phy	5552	Topics in Physics for Biology and Medicine	5 cr.
Phy	5553	Topics in Physics for Biology and Medicine	5 cr.
Phys	8300	Concepts in Neurophysiology	3 cr.

+Required course
*At least three different rotations and a minimum of 6 cr. are required.

III. Advanced Studies

Students in the Biomedical Imaging Track are required to take a minimum number of credits in two specific areas of advanced study. These areas are laboratory methods and special tutorials and seminars.

Laboratory Methods (BPhy 5001-3, 6 credits)

Students rotate through the laboratories of senior faculty and become familiar with the techniques, procedures, and projects in the area of research of each laboratory. Laboratory rotations are one, two, or three months (1 cr/mo) and a minimum of six credits and three different laboratories is required.

Tutorials and Seminars

The student is required to take a minimum of four credits in advanced tutorials and/or seminars related to the selected area of dissertation research. Tutorials are arranged with senior faculty. Credit for this requirement can be granted for special off-campus courses. A typical curriculum from which to select the tutorials and seminars follows:

BPhy	8300	Tutorial in Visual Perception and Psychophysics	2 cr.
BPhy	8301	Tutorial in High-Speed Signal Processing	2 cr.
BPhy	8302	Tutorial in Ultrasonic Imaging	2 cr.
BPhy	8304	Tutorial in Physiological Imaging	2 cr.
BPhy	8500	Tutorial in Imaging Science	2 cr.
BPhy	8600	Biodynamics Research Seminars	1 cr.
BPhy	8750	Magnetic Resonance Technical Seminar	1 cr.
BPhy	8852	Seminars in Biophysical Specialties	1 cr.
Phys	8851	Physiology Seminars	1 cr.

IV. Dissertation Research (BPhy 8890)

All students must take and satisfactorily pass a comprehensive qualifying exam, consisting of both written and oral components, before formally beginning their dissertation research. This exam is taken before the end of the second year of the program. As arranged by the adviser, the student may spend several weeks in a laboratory at another institution to learn new or advanced techniques related to the research topic selected. During the third year of the program it is expected that all students will have decided on a dissertation project. By the middle of the third year of study, students must prepare a written prospectus and give a seminar on the background of their proposed dissertation research and present any results they have obtained. At this time, a Thesis Committee chaired by the student's adviser is appointed. Each student meets at least once a year with his/her Committee to discuss their progress. The Committee decides when the research has progressed sufficiently so that a dissertation can be written, and is responsible for coordinating the final thesis defense. The Committee will usually include an outside reviewer from an academic institution other than the Mayo Graduate School. All members of the Department are encouraged to attend any thesis defense, which will include a seminar on the dissertation results by the candidate.

IMMUNOLOGY

L. R. Pease, Ph.D., *Graduate Education Coordinator*

R. T. Abraham, Ph.D.
C. S. David, Ph.D.
G. J. Gleich, M.D.
J. J. Goronzy, M.D., Ph.D.
D. F. Jelinek, Ph.D.
P. J. Leibson, MD,PhD
V. A. Lennon, M.D., Ph.D.
D. J. McKean, Ph.D.
C. V. Paya, M.D.
D. H. Persing, M.D.
M. Rodriguez, M.D
P. J. Wettstein, Ph.D.
C. M. Weyand, M.D., Ph.D.

Ph.D. Degree

Core (Distribution) Credits

Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research	1 cr.
3 credits in each of any two areas other than Immunology	6 cr.
Additional elective (non-seminar) courses in any area other than Immunology	6 cr.

In addition to the core requirement, students are required to take the following combination of courses:

*Imm	5500	Laboratory Methods in Immunology (2 cr./rotation - 3 rotations req.)	6 cr.
Imm	5806	Basic Graduate Immunology	3 cr.

During each of the first and second years, students must elect two different courses from the following. Courses may be repeated in subsequent terms, but at least two different courses must be elected in each of the first two years.

Imm	8862	Current Topics in Cellular Regulation	1 cr.
Imm	8863	Current Topics in Immunology	1 cr.
Imm	8867	Current Topics in Hypersensitivity	1 cr.

Students are required to take the following tutorial courses:

Imm	8876	Tutorial in T Cell Derived Lymphokines	2 cr.
Imm	8877	Tutorial in Molecular Basis of Immune Recognition	2 cr.
Imm	8878	Tutorial in Effector Mechanisms	2 cr.
Imm	8879	Tutorial in Cellular Activation	2 cr.
Imm	8880	Tutorial in Immunopathology	2 cr.
Imm	8882	Tutorial in Cellular Recognition and Development of the Immune Response	2 cr.

Six elective credits from any courses approved for graduate credit.

In addition, before completion of the program, all students are encouraged to attend the one-week-long summer course in Advanced Immunology sponsored by the American Association of Immunologists.

*Not required of M.D.-Ph.D. students.

Molecular Biology

F. M. Rusnak, Ph.D., *Graduate Education Coordinator*

Z. Bajzer, Ph.D.
M. E. Bolander, M.D.
R. E. Brown, Ph.D.
T. P. Burghardt, Ph.D.
G. W. Dewald, Ph.D.
N. L. Eberhardt, Ph.D.
D. N. Fass, Ph.D.
M. R. Federspiel, Ph.D.
T. A. Felmlee, Ph. D.
L. A. Fitzpatrick, MD
S. J. Gendler, Ph.D.
M. J. Getz, Ph.D.
J. P. Grande, M.D., Ph. D.
S. M. Jalal, Ph.D.
R. B. Jenkins, M.D.
J. D. Jones, Ph.D.
C. Kappen, Dr.rer.nat.
B. C. Kline, Ph.D.
R. Kumar, M.D.
V.M. Kumar, Ph.D.
J. J. Lee, Ph.D.
N. A. Lee, Ph.D.
E. B. Leof, Ph.D.
A. H. Limper, M.D.
S. I. Macura, Ph.D.
L. J. Maher, III, Ph.D.
N. J. Maihle, Ph.D.
D. J. McCormick, Ph.D.
J. A. McDonald, M.D., Ph.D.
C. T. McMurray, Ph.D
M. A. McNiven, Ph.D.
L. J. Miller, M.D.
S. Naylor, Ph.D.
M. Oursler-Velasquez, Ph.D.
W. G. Owen, IV, Ph.D.
R. E. Pagano, Ph.D.
L. R. Pease, Ph.D.
J. T. Penniston, Ph.D.
D. R. Pfeifer, Ph.D.
J. F. Poduslo, Ph.D.
F. G. Prendergast, M.D., Ph.D.
J. R. Riordan, Ph.D.
P. C. Roche, Ph.D.
J. L. Salisbury, Ph.D.
H.H.O. Schmid, Ph.D.
T. C. Spelsberg, Ph.D.
E. E. Strehler, Ph.D.
S. N. Thibodeau, Ph.D.
D. J. Tindall, Ph.D.
D. O. Toft, Ph.D.
R. T. Turner, Ph.D.
R. Urrutia, M.D.
G. Vockley, M.D., Ph.D.
S. Vuk-Pavlovic, Ph.D.
Z. Vuk-Pavlovic, Ph.D.
E. D. Wieben, Ph.D.
C.Y.F. Young, Ph.D.

Ph.D. Degree

The requirements for the Molecular Biology track conform to the general requirements of the Mayo Graduate School in which a minimum of 18 credits are required in Molecular Biology, 13 credits of Biomedical core courses, and 11 credits as deemed appropriate for individual student's programs.

The track requirements are:

*Bioc	8000	General Biochemistry: Structure	3 cr.
*Bioc	8001	General Biochemistry: Kinetics, Catalysis and Mechanisms	3 cr.
*Bioc	8002	General Biochemistry: Energy Transduction and Signalling	3 cr.
MBio	5858	Laboratory Rotations in Molecular Biology (2 cr./rotation - 3 rotations req.)	6 cr.
MBio	8050	Principles of Cell and Tissue Design	3 cr.
MBio	8101	Replication and Transcription Regulation	3 cr.

MBio	8102	Regulation of Protein Synthesis	3 cr.
MBio	8500	Biochemistry and Molecular Biology Journal Club (1 cr/yr - 3 yrs required)	3 cr.

*These courses may be used to satisfy core requirements.

Molecular Neuroscience

A. J. Windebank, M.D., *Graduate Education Coordinator*

A. J. Aksamit, M.D.
E. E. Bennaroch, M.D.
W. S. Brimijoin, Ph.D.
T. P. Burghardt, Ph.D.
S. W. Carmichael, Ph.D.
J. L. Carter, M.D.
R. J. Caselli, M.D.
D. E. Clapham, M.D., Ph.D.
J.R. Daube, M.D.
P. J. Dyck, M.D.
A. G. Engel, M.D.
J. M. Fernandez, Ph.D.
N.R. Graff-Radford, M.D.
C. R. Jack, M.D.
R. B. Jenkins, M.D., Ph.D.
C. Kappen, Dr.rer.nat.
D. W. Kimmel, M.D.
L. T. Kurland, M.D.
T. D. Lagerlund, M.D.
J. J. Lee, Ph.D.
V. A. Lennon, M.D., Ph.D.
P. A. Low, M.D.
N. J. Maihle, Ph.D.
K. M. McEvoy, M.D.
R. McGee, Ph.D.
M. McKinney, Ph.D.
J. W. McLaren, Ph.D.
C. J. McMurray, Ph.D.
M. A. McNiven, Ph.D.
F. B. Meyer, M.D.
P. C. O'Brien, M.D.
R. E. Pagano, Ph.D.
R. C. Petersen, M.D., Ph.D.
J. F. Poduslo, Ph.D.
C. Raffel, M.D., Ph.D.
E. Richelson, M.D.
R. A. Robb, Ph.D.
M. Rodriguez, M.D.
C. Shin, M.D.
G. C. Sieck, Ph.D.
S. M. Sine, Ph.D.
E. E. Strehler, Ph.D.
J. H. Szurszewski, Ph.D.
R. Urrutia, M.D.
R. M. Weinshilboum, M.D.
B. J. Westmoreland, M.D.
J. P. Whisnant, M.D.
D. O. Wiebers, M.D.
S. G. Younkin, M.D., Ph.D.

Ph.D. Degree

The requirements for the Molecular Neuroscience Ph.D. Track conform to the general requirements of the Mayo Graduate School in which a minimum of 13 credits are required from the core curriculum. Courses must be selected from at least two areas with a minimum of three credits from each area. None of these courses may be in the area of specialization. We recommend that students select courses after discussion with their adviser.

The track requirements are:

NSci	8400	Neuroanatomy	3 cr.
NSci	8854	Basic Neuroscience	5 cr.
NSci	8300	Concepts in Neurophysiology	3 cr.
*NSci	5001	Laboratory Rotations in Neuroscience (4 wks.)	1 cr.
*NSci	5002	Laboratory Rotations in Neuroscience (8 wks.)	2 cr.
*NSci	5003	Laboratory Rotations in Neuroscience (12 wks.)	3 cr.
NSci	8500	Neuroscience Seminars	1 cr.

NSci	8600	Neuroscience Journal Club	1 cr./yr.
NSci	8650	Molecular Neuroscience Works in Progress	1 cr.

*At least three different rotations and a minimum of 6 cr. are required.

Forty-two credits are required to complete the degree program. In addition to the core and track requirements, additional courses should be selected after consultation between the student and his/her Advisory Committee.

The Qualifying Examination for the Molecular Neuroscience Track has both a written and oral examination. In order to make requirements uniform within each of the tracks of the Graduate School, the Preliminary Qualifying Examination for Molecular Neuroscience is being changed. The new type of comprehensive qualifying examination is being "phased in" over the next two years.

For students matriculating on or before September 1994, the written examination takes the form of a thesis proposal. This proposal must be submitted to the Examining Committee between the beginning of the summer quarter of the first year and the end of the winter quarter of the second year. The proposal should summarize goals, methods, and rationale for a research project. This does not have to be the students' thesis research proposal. The specific guidelines for the form of this proposal are available from the Molecular Neuroscience Secretary.

The oral examination will be conducted no more than six weeks after satisfactory review by the Examining Committee of the written proposal. The oral examination will be composed of three parts. The first part will be an oral presentation by the student of their proposal. The second part will be a discussion between the student and the examiners about this proposal. The third part will be a wide ranging discussion of any course work material covered by the student during their first 1 1/2 years that may be broadly relevant to the proposal.

The Qualifying Examination must be completed before the end of the second year in the program. Students should note that continuation of stipend depends on timely completion of the Qualifying Examination.

For students matriculating after September, 1994, the students will complete a written qualifying examination which will cover the breadth of material in the core courses and track courses which most students will have completed during their first year. This qualifying examination will offer the opportunity to consolidate a broad base of knowledge in biomedical science and insure that students have the necessary foundation to embark on their thesis research. This written examination may contain a mixture of essay-type and multiple choice questions. It will be set and graded by the faculty responsible for teaching the courses.

This examination, the written qualifying examination, will be set once each year in the summer. Students are strongly encouraged to take the examination after the first year while course work is still fresh. The exam must be completed successfully before the end of the second year in the program.

Before the end of 2 1/2 years in the program, the degree candidate must complete a thesis proposal. This proposal must be submitted to the Thesis Advisory Committee before the student has completed 10 quarters in the program. The proposal should summarize the goals, methods, and rationale for a research project. The specific guidelines for the form of this proposal are available from the Molecular Neuroscience Secretary. It is a "mini grant" proposal.

This will be followed by an oral defense which will be conducted no more than 6

weeks after satisfactory review by the Thesis Advisory Committee of the written proposal. The oral defense will be composed of two or three parts. The first part will be an oral presentation by the student of their proposal; the second part will be a discussion between the student and the Committee about this proposal. If there were any conditional elements or weaknesses identified at the time of the written qualifying examination, the Committee may then have a third part to the defense which will include a wide-ranging discussion of either the area of deficiency or course work material covered by the student during the first 2 years. Students will be notified after their Qualifying Examination whether this third component should be expected during the thesis proposal defense.

PHARMACOLOGY

C. T. McMurray, Ph.D., *Graduate Education Coordinator*

R. T. Abraham, Ph.D.
M. M. Ames, Ph.D.
W. S. Brimijoin, Ph.D.
D. E. Clapham, M.D., Ph.D.
Z. Katusic, M.D.
S. H. Kaufmann, M.D., Ph.D.
J. J. Lipsky, M.D.
R. McGee, Ph. D.
M. McKinney, Ph.D.
T .P. Moyer, Ph.D.
S. Naylor, Ph.D.
F. G. Prendergast, MD,PhD
E. Richelson, M.D.
L. A. Stehno-Bittel, Ph.D.
C. Shin, M.D.
J. H. Szurszewski, Ph.D.
S. R. Taylor, Ph.D.
B. M. Velimirovic, M.D. Ph.D.
R. M. Weinshilboum, M.D.

Ph.D. Degree

Core Courses (13 credits minimum)

Bioc	8000	General Biochemistry: Structure	3 cr.
Bioc	8001	General Biochemistry: Kinetics, Catalysis and Mechanisms	3 cr.
Bioc	8002	General Biochemistry: Energy Transduction and Signalling	3 cr.
*Ethic	5000	Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research	1 cr.
Imm	5806	Basic Graduate Immunology	3 cr.
MBio	5000	Introduction to Molecular Biology	3 cr.
MBio	8050	Principles of Cell and Tissue Design	3 cr.

Track (19 credits)

+Phar	5001	Laboratory Rotations in Pharmacology (4 wks.)	1 cr.
+Phar	5002	Laboratory Rotations in Pharmacology (8 wks.)	2 cr.
+Phar	5003	Laboratory Rotations in Pharmacology (12 wks.)	3 cr.
Phar	5100	Pharmacology Seminar Series (4 yrs. req.)	1 cr./yr.
Phar	5800	General Pharmacology	9 cr.
Phar	8800	Research Seminars in Pharmacology	1 cr.
Phar	8805	Drug Metabolism	3 cr.
Phar	8806	Pharmacology of Receptors	3 cr.

*Required

+At least three different rotations and a minimum of 6 cr. are required.

Electives (11 credits)

Students shall complete a total of 11 credits of elective courses. These courses should provide some diversity of exposure to physiological, biochemical, molecular and quantitative approaches. The elective courses may be chosen from the following list or from other course offerings, with the approval of the student's adviser and the Graduate Education Coordinator.

BPhy	5400	Molecular Electronics	3 cr.
BPhy	5500	Fundamentals of Computer Organization and Programming	3 cr.
BPhy	5601	Fundamental Methods in Biomedical Imaging	3 cr.
HSR	5823	Introductory Statistics I	3 cr.
Imm	8862	Current Topics in Cellular Regulation	1 cr.
NSci	8300	Concepts in Neurophysiology	3 cr.
NSci	8854	Basic Neurosciences	5 cr.
Phar	8802	Pharmacology of Heart Muscle	3 cr.
Phar	8803	Biochemical Basis of Neuropharmacology	3 cr.
Phar	8804	Clinical Pharmacology	1 cr.
Phar	8810	Toxicology	3 cr.
Phar	8862	Excitation-Contraction Coupling in Skeletal Muscle	3 cr.
Phar	8863	Molecular Biology: Theory and Application	4 cr.
Phar	8879	Tutorial in Cellular Activation	2 cr.

Research

Phar	8801	Research in Pharmacology

Directed research projects under the supervision of a faculty adviser.

PHYSIOLOGY

R. A. Robb, Ph.D. *Graduate Education Coordinator*

K. An, M.D.
A. G. Andrews, D.M.V.
J. C. Burnett, M.D.
E. P. DiMagno, M.D.
T. P. Dousa, M.D.
J. M. Fernandez, Ph.D.
L. A. Fitzpatrick, M.D.
C. S. Frisk, D.V.M.
P. Gloviczki, M.D.
J. F. Greenleaf, Ph.D.
M. J. Joyner, M.D.
A. A. Khraibi, Ph.D.
S. Khosla, M.D.
D. W. Klass, M.D.
F. G. Knox, M.D., Ph.D.
V. M. Miller, Ph.D.
J. N. Pemberton, M.D.
S. F. Phillips, M.D.
J. L. Rae, Ph.D.
E. L. Ritman, M.D., Ph.D.
M. G. Rock, M.D.
J. C. Romero, M.D.
M.G. Sarr, M.D.
H. V. Schaff, Ph.D.
G. C. Sieck, Ph.D.
S. M. Sine, Ph.D.
J. H. Szurszewski, Ph.D.
S. R. Taylor, Ph.D.
R. T. Turner, Ph.D.

Ph.D. Degree

I. Minimum Requirements

A minimum of 42 credits of course work are required for a Ph.D. in the Physiology

Track. Thirteen core credits are taken outside the student's major area of concentration, as specified by the Graduate School. Twenty-nine technical credits are required in subjects related to the major area, which includes a 3 credit course in **Concepts in Neurophysiology**, a 3 credit course in **Research Animal Experimental Surgery and Methods**, 6 credits in **Laboratory Methods in Physiology**, and a minimum of 6 credits in advanced seminars and readings.

II. Elective Course Work

A program of course work for both the core and technical components of the Ph.D. program in the Physiology track may be selected from the following typical curriculum:

Core (13 credit minimum)

*Ethic	5000	Maintenance of Scientific Integrity and Conduct in Biomedical Research	1 cr.
BPhy	5500	Computer Organization and Programming	3 cr.
BPhy	5601	Fundamental Concepts in Biomedical Imaging	3 cr.
HSR	5823	Introductory Statistics I	3 cr.
HSR	5827	Introduction to Regression	1 cr.
Imm	5806	Basic Graduate Immunology	3 cr.
MBio	5000	Introduction to Molecular Biology	3 cr.

*Required

Technical (29 credit minimum)

*Phys	5001	Laboratory Rotations in Physiology (4 wks.)	1 cr.
*Phys	5002	Laboratory Rotations in Physiology (8 wks.)	2 cr.
*Phys	5003	Laboratory Rotations in Physiology (12 wks.)	3 cr.
BPhy	5150	Introductory Radiation Biology	2 cr.
BPhy	5400	Molecular Electronics	2 cr.
BPhy	8450	Computer Image Processing	3 cr.
BPhy	8600	Biodynamics Research Seminars	1 cr.
Phys	5801	Principles of Biomechanics I	3 cr.
Phys	5802	Principles of Biomechanics II	3 cr.
Phys	8300	Concepts in Neurophysiology	3 cr.
Phys	8851	Physiology Seminars	1 cr.
Phys	8854	Readings in Physiology	2 cr.
Phys	8855	Cardiovascular Physiology	3 cr.
Phys	8856	Respiratory Physiology	2 cr.
Phys	8857	Neurophysiology	2 cr.
Phys	8858	Physiology of Smooth Muscle and its Innervation	2 cr.
Phys	8859	Renal Physiology	2 cr.
Phys	8860	Endocrine Physiology	2 cr.
Phys	8862	Excitation-Contraction Coupling in Skeletal Muscle	3 cr.
Phys	8878	Physiology of Bone I	3 cr.
Phys	8879	Physiology of Bone II	2 cr.
Phys	8880	Principles of Solid Mechanics	3 cr.
Phys	8881	Mechanics of Deformable Materials	3 cr.

*At least three different rotations and a minimum of 6 cr. are required.

III. Advanced Studies

Students in the Physiology Track rotate through the laboratories of senior faculty

and become familiar with the techniques, procedures, and projects in each laboratory. Laboratory rotations may be one, two or three weeks (1 cr/1 mo) and a minimum of six credits and three different laboratories is required.

Students in the Physiology Track are required to take a minimum of three quarters of advanced study in at least two different ongoing seminars, journal clubs, and/or readings courses. Each student must give at least two different seminar presentations. A typical curriculum from which to select such ongoing courses follows:

BPhy	8600	Biodynamics Research Seminars	1 cr.
Phys	8851	Physiology Seminars	1 cr.
Phys	8854	Readings in Physiology	2 cr.

IV. Dissertation Research

All students must take and satisfactorily pass a comprehensive qualifying exam, consisting of both written and oral parts, before formally beginning their dissertation research. This exam must be taken before the end of the second year of the program. Before the middle of the third year of the program, it is expected that all students will have decided on a dissertation project. As arranged by the adviser, the student may spend several weeks in a laboratory of another institution to learn new or advanced techniques related to the research topic selected. During their third year of study, students give a seminar on the background of their proposed dissertation problem and present any results they have obtained. At this time, a Thesis Committee chaired by the dissertation supervisor is appointed. Each student meets at least once a year with his/her Committee to discuss their progress. The Committee decides when the research has progressed sufficiently so that a dissertation can be written, and is responsible for coordinating the final thesis defense. The Committee will usually include an outside reviewer from an academic institution other than the Mayo Graduate School. All members of the Department are encouraged to attend any thesis defense, which will include a seminar on the dissertation results by the candidate.

TUMOR BIOLOGY

Jeffrey L. Salisbury, Ph.D. *Graduate Education Coordinator*

R. T. Abraham, Ph.D.
M. M. Ames, Ph.D.
A. G. Andrews, D.M.V.
K.E. Bennet, M.S.
J. A. Bonner, M.D.
D. E. Clapham, M.D., Ph.D.
C. S. David, Ph.D.
G. W. Dewald, Ph.D.
C. Erlichman, M.D.
M. J. Federspiel, Ph.D.
L. A. Fitzpatrick, M.D.
S. J. Gendler, Ph.D.
M. J. Getz, Ph.D.
J. P. Grande, M.D., Ph.D.
L. C. Hartmann, M.D.
J. N. Ingle, M.D.
D. F. Jelinek, Ph.D.
R. B. Jenkins, M.D., Ph.D.
S. H. Kaufmann, M.D., Ph.D.
P. J. Leibson, M.D., Ph.D.
V. A. Lennon, M.D.
E. B. Leof, Ph.D.
W. L. Lingle, Ph.D.
J. A. Lust, M.D., Ph.D.
L.J. Maher, III, Ph.D.
N. J. Maihle, Ph.D.
R. McGee, Ph.D.
D. J. McKean, Ph.D.
M. A. McNiven, Ph.D.
L. J. Melton, M.D.
H. Nelson, M.D.
J. R. O'Fallon, Ph.D.
D. J. O'Kane, Ph.D.
D. H. Persing, M.D., Ph.D.
M. R. Pittelkow, M.D.
K. C. Podratz, M.D., Ph.D.
F. G. Prendergast, M.D., Ph.D.
C. Raffel, M.D., Ph.D.
T. C. Spelsberg, Ph.D.
E. E. Strehler, Ph.D.
S. N. Thibodeau, Ph.D.
D. J. Tindall, Ph.D.
D. O. Toft, Ph.D.
R. A. Urrutia, M.D.
R. M. Weinshilboum, M.D.
P. J. Wettstein, Ph.D.
A. J. Windebank, M.D.
L. E. Wold, M.D.
C. Y. F. Young, Ph.D.

Ph.D. Degree

Students in the Tumor Biology Track must complete the following, in addition to the 13 core credit requirement.

TBio	5000	Tumor Biology I: Introduction to Tumor Biology	3 cr.
TBio	5100	Research Seminars in Tumor Biology	1 cr.
TBio	5150	Current Topics in Tumor Biology	1 cr.
TBio	5200	Tumor Biology of Pancreatic Cancer	1 cr.
TBio	5250	Gene Therapy and Cancer	1 cr.
TBio	5300	The Business of Science and the Science of Business	1 cr.
TBio	5858	Laboratory Rotations in Tumor Biology (2 cr./rotation - 3 rotations req.)	6 cr.
TBio	8000	Tumor Biology II: Origins of Human Cancer	2 cr.
TBio	8005	Tumor Biology III: Growth Factors, Oncogenes, and Tumor Suppressors	3 cr.
TBio	8200	Cell Biology of Cancer	3 cr.
Path	8875	Cytogenetics	2 cr.

In addition, all students in the Tumor Biology Program shall register for the Animal Care and Use Training Sessions and the American Association of Cancer Research (AACR) course in Histopathology of Cancer. Additional advanced elective courses in any area may be taken to fulfill the overall degree requirements of 42 credits.

Description of Master's Degree Program and Basic Science Track Requirements

Master of Science Program in Biomedical Sciences

The Master of Science (M.S.) Program in Biomedical Sciences is available only to: 1) M.D.s, D.D.S.s and D.M.D.s enrolled in clinical residency programs and/or research fellowships of the Mayo Graduate School of Medicine (basic science specialty requirements described below-clinical science specialty requirements described in a later section); 2) candidates for the Ph.D. in good academic standing but unable to complete all the requirements for the doctorate - requirements available from the Graduate School office; 3) Employees (requirements described in a later section).

Master of Science Program in Biomedical Sciences

(Basic Science Specialties)

The degree requirements include a minimum of 12 credits in biomedical sciences and 12 credits in the area of specialization. Full-time registration for a minimum of one year is required. Fifty percent of the didactic credits must be completed in Mayo Graduate School. General program requirements and specialty track descriptions are outlined later. The equivalent of one year of full-time effort must be devoted to research.

Courses in basic biomedical sciences are required to provide the student with the knowledge to address a research problem, conduct the research and evaluate the results. Courses in the area of specialization are required in addition to provide special skills, techniques or knowledge related to the specialty track.

The primary purpose of the degree program is to enhance the scholarly dimension of the education of physicians and M.D. research fellows who have an interest in academic medicine. Training in research is emphasized. The degree program provides a structure for development of a plan to address a research problem, an orderly approach to the project, assurance of the credentials of the adviser, appropriate supervision and a suitable approach to the analysis and presentation of the results.

General Program Requirements

Eligibility: The program described below is designed chiefly for Mayo residents and research fellows who hold appointments to the programs of Mayo Graduate School of Medicine. Potential candidates for the degree must hold appointments of sufficient duration to complete degree program requirements.

Application: Candidate must complete a Masters Application form. This form, which requires departmental approval of the degree program and research project, is available in the Graduate School Office.

Time Requirement: All requirements must be satisfied within one year after completion of the fellowship.

Thesis Protocol: No later than two months after entering the laboratory, the candidate must submit a protocol to the Mayo Graduate School Education Committee. This protocol must clearly define the candidate's role in his/her

project and must have sufficient detail to permit review by an advisory committee (guidelines are available in the Graduate School Office). If the protocol is not submitted during the first quarter in the laboratory, registration for research credits will not be allowed for the second quarter.

Official Program: Students are encouraged to submit their programs and thesis titles to the Graduate School before the end of the second year of registration. Students and advisers should include on the program forms: a) the minimum number of courses/credits necessary to fulfill degree requirements (credits may vary depending on the chosen area of specialization), b) the thesis title and c) the recommended thesis readers and final oral examining committee. The examining committee consists of a minimum of three individuals, one of whom is the student's adviser, who serves as chair of the committee. One member must be from outside the department and no member other than the chair can be from among a student's research advisers. The recommended committee must be approved by the Graduate School.

Changes in Approved Program: Once approved, the program must be fulfilled in every detail to meet graduation requirements. Alterations in the program should be requested in writing and are subject to approval of the Mayo Graduate School Education Committee.

Minimum Grade Requirements: The minimum grade point average required by the Graduate School for courses included on the official program for the degree is 3.0 (on a 4.0 scale). Grades of A through C, and S are acceptable, but grades of S are not calculated in the grade point average. At least two-thirds of the credits taken and included on any degree program must be graded under the A through F system.

Minimum Credit Requirements: Students must complete a minimum of 12 credits in biomedical sciences and 12 additional credits in the area of specialization (see individual specialty track descriptions for specific course requirements). A minimum of one year in time and effort must be devoted to research. Students are not admitted to a specialty track unless there is reasonable assurance that course work required for completion of degree requirements is available.

Transfer Credits: A total of 12 didactic credits can be transferred into this program. Students who wish to transfer credits to substitute for a Mayo course must contact the Mayo course director. If the course director determines that a student has the knowledge equivalent to satisfactory performance in the Mayo course, the student will receive the transfer credits.

Students who wish to transfer credits for courses not offered at Mayo may request credit for graduate courses taken at other institutions if they received a grade of A or B. The request must have the approval of the student's education coordinator and the Graduate School. A description of the course from the course catalog or a course outline must accompany the request. The time interval since the credits were earned is a consideration in such decisions. Credits must normally have been earned within the previous ten years (more recently in the case of rapidly advancing subjects).

Thesis: The thesis must be submitted to the final oral examining committee at least three weeks before the oral examination.

Written Examination: Must be taken no later than six months before completion of the training program.

Final Examination: Candidates for the M.S. degree must pass a final oral examination, which can be taken only after the written examination has been passed, courses on official program completed, and the thesis reviewed. Successful completion of the final oral examination requires a unanimous decision by all of the members of the committee.

IMMUNOLOGY

L. R. Pease, Ph.D., *Graduate Education Coordinator*

R. T. Abraham, Ph.D.
C. S. David, Ph.D.
G. J. Gleich, M.D.
J. J. Goronzy, M.D., Ph.D.
D. F. Jelinek, Ph.D.
P. J. Leibson, M.D., Ph.D.
V. A. Lennon, M.D., Ph.D.
D. J. McKean, Ph.D.
C. V. Paya, M.D.
D. H. Persing, M.D.
M. Rodriguez, M.D
P. J. Wettstein, Ph.D.
C. M. Weyand, M.D., Ph.D.

Master's Degree

The Master's degree track in Immunology is open only to residents and research fellows in the Mayo Graduate School of Medicine.

Course Requirements

A. Course Work in Biomedical Sciences

Students will be expected to complete 12 credits of course work (or their equivalent) selected from the Biomedical Sciences core curriculum. Students with extensive background in particular areas of the core curriculum will have the opportunity to test out of the core courses.

B. Advanced Courses in Immunology

Each student will be expected to take Imm 5806 Basic Graduate Immunology and a minimum of three tutorials offered by the Immunology faculty in areas specific to the student's research interest. Each student is expected to participate in a minimum of three different Current Topics courses before the degree requirements are completed.

Imm	8862	Current Topics in Cellular Regulation
Imm	8863	Current Topics in Immunology
Imm	8867	Current Topics in Hypersensitivity Reactions

C. Students will register for Imm 8840 Experimental Immunology (6 credits per quarter) for a total of 4 quarters or 24 credits.

Molecular Neuroscience

A.J. Windebank, M.D., *Graduate Education Coordinator*

A. J. Aksamit, M.D.
E. E. Bennaroch, M.D.
W. S. Brimijoin, Ph.D.
T. P. Burghardt, Ph.D.
S. W. Carmichael, Ph.D.
J. L. Carter, M.D.
R. J. Caselli, M.D.
D. E. Clapham, M.D., Ph.D.
J.R. Daube, M.D.
P. J. Dyck, M.D.
A. G. Engel, M.D.
J. M. Fernandez, Ph.D.
N. R. Graff-Radford, M.D.
C. R. Jack, M.D.
R. B. Jenkins, M.D., Ph.D.
C. Kappen, Dr.rer.nat.
D. W. Kimmel, M.D.
L. T. Kurland, M.D.
T. D. Lagerlund, M.D.
J. J. Lee, Ph.D.
V. A. Lennon, M.D., Ph.D.
P. A. Low, M.D.
N. J. Maihle, Ph.D.
K. M. McEvoy, M.D.
R. McGee, Ph.D.
M. McKinney, Ph.D.
J. W. McLaren, Ph.D.
C. J. McMurray, Ph.D.
M. A. McNiven, Ph.D.
F. B. Meyer, M.D.
P. C. O'Brien, M.D.
R. E. Pagano, Ph.D.
R. C. Petersen, M.D., Ph.D.
J.F. Poduslo, Ph.D.
C. Raffel, M.D., Ph.D.
E. Richelson, M.D.
R. A. Robb, Ph.D.
M. Rodriquez, M.D.
C. Shin, M.D.
G. C. Sieck, Ph.D.
S. M. Sine, Ph.D.
E. E. Strehler, Ph.D.
J. H. Szurszewski, Ph.D.
R. Urrutia, M.D.
R. M. Weinshilboum, M.D.
B. J. Westmoreland, M.D.
J. P. Whisnant, M.D.
D. O. Wiebers, M.D.
S. G. Younkin, M.D., Ph.D.

Master's Degree

The Master's degree track in Molecular Neuroscience is open only to residents and research fellows in the Mayo Graduate School of Medicine.

Course Requirements

A. Course work in Biomedical Sciences

Students will be expected to complete 12 credits in biomedical sciences outside the area of specialization.

B. Molecular Neuroscience course requirements

Students will complete 12 credits within molecular neuroscience in addition to a minimum of one year in full-time laboratory research.

PHARMACOLOGY

C. T. McMurray, Ph.D., *Graduate Education Coordinator*

R. T. Abraham, Ph.D.
M. M. Ames, Ph.D.
W. S. Brimijoin, Ph.D.
D. E. Clapham, M.D., Ph.D.
Z. Katusic, M.D.
S. H. Kaufmann, M.D., Ph.D.
J. J. Lipsky, M.D.
M. McKinney, Ph.D.
T. P. Moyer, Ph.D.
F. G. Prendergast, M.D., Ph.D.
E. Richelson, M.D.
C. Shin, M.D.
L. A. Stehno-Bittel, Ph.D.
J. H. Szurszewski, Ph.D.
S. R. Taylor, Ph.D.
R. M. Weinshilboum, M.D.

Master's Degree

General

The Department of Pharmacology offers an M.S. degree track within the Biomedical Sciences Program. This track is open to residents and research fellows in the Mayo Graduate School of Medicine. Students holding only a baccalaureate will not be admitted to pursue the M.S. as a terminal degree. Students will be assigned to a research adviser on entry into the degree program. It is assumed that the equivalent of twelve months will be spent in full-time academic work, which will consist primarily of research, but will also involve advanced course work.

Course Requirements

A. Introductory Biomedical Sciences Courses

Students are expected to complete 12 credits of introductory Biomedical Sciences courses. The required introductory courses are as follows:

Phar	5801	General Pharmacology	2 cr.
Phar	5802-5	General Pharmacology	7 cr.
Bios	5823	Introductory Statistics I	3 cr.

plus 9 credits to be chosen from the courses given below:

BPhy	5500	Fundamentals of Computer Organization and Planning	3 cr.
Imm	5806	Basic Graduate Immunology	3 cr.

B. Advanced Courses in Pharmacology

Students will register for Phar 8840 Research in Pharmacology (6 credits) for a total of 4 quarters or 24 credits. During three of these quarters, they will also register for Phar 8800 Research Seminars in Pharmacology (1 credit). In addition, students must complete a minimum of 6 credits of course work from the following list:

Phar	8802	Pharmacology of Heart Muscle	3 cr.
Phar	8803	Biochemical Basis of Neuropharmacology	3 cr.
Phar	8804	Clinical Pharmacology	1 cr.
Phar	8805	Drug Metabolism	3 cr.
Phar	8806	Pharmacology of Receptors	3 cr.
Phar	8810	Toxicology	3 cr.

C. Course Work in Supporting Fields

Students are encouraged to undertake advanced didactic course work in other fields of basic Biomedical Science such as biostatistics, electronics and computer science, physiology, biochemistry, and immunology.

PHYSIOLOGY

R. A. Robb, Ph.D., *Graduate Education Coordinator*

K. An, M.D.
A. G. Andrews, D.M.V.
J. C. Burnett, M.D.
E. P. DiMagno, M.D.
T. P. Dousa, M.D.
J. M. Fernandez, Ph.D.
L. A. Fitzpatrick, M.D.
C. S. Frisk, D.V.M.
P. Gloviczki, M.D.
J. F. Greenleaf, Ph.D.
M. J. Joyner, M.D.
S. Khosla, M.D.
A. A. Khraibi, Ph.D.
D. W. Klass, M.D.
F. G. Knox, M.D., Ph.D.
V. M. Miller, Ph.D.
S. F. Phillips, M.D.
J. L. Rae, Ph.D.
E. L. Ritman, M.D., Ph.D.
M. G. Rock, M.D.
J. C. Romero, M.D.
H. V. Schaff, Ph.D.
G. C. Sieck, Ph.D.
S. M. Sine, Ph.D.
J. H. Szurszewski, Ph.D.

Master's Degree

General

The M.S. program is available only to Mayo fellows with an M.D. degree who hold appointments in the clinical or research programs of the Mayo Graduate School of Medicine. The program will generally consist of two years of academic and research work. During one of the years, students are expected to spend most of their efforts in the research laboratory while at the same time taking didactic course work. The other year of the program, which in the case of a resident, may coincide with the residency program, will consist of course work and/or preparation of the thesis. Defense of thesis will be held at the end of the program. To be admitted candidates must have achieved high academic standards as evidenced by performance on the GRE or MCAT or have two highly positive letters of recommendation from Mayo investigators who are in a position to evaluate the candidate's academic and research potential.

Course Requirements

Phys	8840	Research in Physiology (each quarter during research year)	24 cr.
Phys	8854	Readings in Physiology (each quarter during research year)	4 cr.

At least eight additional credits are required from the following advanced courses in Physiology.

Phys	5500	Research Animal Experimental Surgery and Methodology	3 cr.
Phys	5801	Principles of Biomechanics I	3 cr.
Phys	5802	Principles of Biomechanics II	3 cr.

Phys	8855	Cardiovascular Physiology	3 cr.
Phys	8856	Respiratory Physiology	2 cr.
Phys	8858	Physiology of Smooth Muscle	2 cr.
Phys	8859	Renal Physiology	2 cr.
Phys	8860	Endocrine Physiology	2 cr.
Phys	8862	Excitation-Contraction Coupling in Skeletal Muscle	3 cr.
Phys	8878	Physiology of Bone I	3 cr.
Phys	8879	Physiology of Bone II	2 cr.

Students will be expected to complete an additional minimum of 12 credits of course work in supporting fields in Biomedical Sciences. Courses in supporting fields are available in various departments at Mayo, such as Biochemistry, Biophysical Sciences, Immunology, Molecular Biology, Molecular Neuroscience and Pharmacology, or through other mechanisms such as the UNITE program which is affiliated with the University of Minnesota.

Description of Employee Master's Degree Program and Track Requirements

Master of Sciences Program in Biomedical Sciences for Mayo Employees

The Master's Degree in Biomedical Sciences is designed to develop the individual's information base in a basic science field and enable the individual to become competent in acquiring knowledge independently. This Master's program emphasizes course work and does not include a research thesis. A limited number of positions are available annually in each of the basic science tracks.

The Master's program provides the Mayo employee with an organized plan of study to enhance their professional development. The Master's degree is the culmination of this educational program and documents the acquisition of a high level of knowledge in a particular area of science. Although employees currently do not receive direct salary benefit from attaining a Master's degree, receipt of the degree may make the employee qualified for a job of a higher classification, should one become available.

Admissions Requirements and Procedures

Enrollment is restricted to permanent Mayo employees. Applicants must have received a bachelor's degree from an accredited college or university, must have taken appropriate undergraduate science courses to adequately prepare for the Master's program and must have an undergraduate grade point average that demonstrates a record of academic excellence. Scores on the verbal, analytical and quantitative aptitude tests of the Graduate Record Examination should be above the 70th percentile. The employee's supervisor must endorse in writing the application of the employee.

Applicants must fill out an application form, supplying transcripts from previous colleges, GRE scores, supervisor's endorsement and three letters of recommendation.

Tuition Expenses

Tuition for Mayo employees accepted into the Master's program will be provided by scholarship for courses taken to meet Master's degree requirements. Mayo will not provide a stipend or reimburse other costs that may be associated with the degree program.

Registration Requirement

At least 60% of the coursework for the Master's degree must be completed in Mayo Graduate School. Acceptance of transfer credits will follow the guidelines currently in place for the Ph.D. program.

Time Requirement

All requirements for the Master's degree must be completed within seven years. The seven year period begins on the date the letter of acceptance is sent.

Minimum Credit Requirements

Students must complete a minimum of 44 quarter credits. Twenty of the credits must be in the area of specialization and a minimum of 8 quarter credits in one or more related fields outside the area of specialization, including the course entitled, "Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research." The selection of the courses to be used to meet these requirements will be determined by the student and the student's graduate faculty committee. Individual basic science departments may have additional degree requirements for specific degree tracks. The student's graduate faculty committee will consist of at least three faculty members from the student's area of specialization and one member from outside the area of specialization. The composition of this committee will be determined by the Graduate School upon recommendation of the student and the student's departmental educational coordinator.

Official Degree Program

Students must submit their degree program form on or before completing 15 credits of coursework.

Minimum Grade Requirement

Students must maintain a grade point average of 3.0. Guidelines for probationary status resulting from academic or nonacademic deficiency will follow the guidelines established for the Mayo Ph.D. students.

Project

Master's degree tracks will specify the requirements for a nonresearch project to be completed as a required/optional component of the degree program.

Comprehensive Examination

At the completion of the required course work, students must take a comprehensive written examination. Departments will have the option of also requiring an oral examination. The examination(s) are designed to evaluate the

student's depth and breadth of knowledge in the student's area of specialization and related fields of study. A committee of at least three examiners from inside and one examiner from outside the student's area of study will be appointed by the Graduate School upon recommendation of the student and the student's department educational coordinator at the time of approval of the official degree program. A majority vote of the committee, all members present and voting, is required to pass the examination. In the case where the student fails the examination, the committee will recommend to the Graduate School remedial studies that should be undertaken by the student before the student retakes the examination. Students will be allowed to retake the examination only once.

GRADUATION

Students are graduated four times a year, the third Friday in February, August and November and mid-May. The latter involves a formal ceremony as part of the Mayo Foundation graduation exercises in conjunction with the Mayo Medical School. No ceremony is held in February, August and November, but students who do graduate at one of these times are encouraged to participate in the May ceremony.

To graduate in February, August or November students must have all requirements completed by the first working day of the month prior to the graduation month. To graduate in May, students must have all requirements completed by March 15.

BIOCHEMISTRY

F. M. Rusnak, Ph.D., *Graduate Education Coordinator*

Z. Bajzer, Ph.D.
M. E. Bolander, M.D.
R. E. Brown, Ph.D.
T. P. Burghardt, Ph.D.
G. W. Dewald, Ph.D.
N. L. Eberhardt, Ph.D.
D. N. Fass, Ph.D.
M. R. Federspiel, Ph.D.
L. A. Fitzpatrick, MD
S. J. Gendler, Ph.D.
M. J. Getz, Ph.D.
R. B. Jenkins, M.D.
J. D. Jones, Ph.D.
C. Kappen, Dr.rer.nat.
B. C. Kline, Ph.D.
R. Kumar, M.D.
J. J. Lee, Ph.D.
N. A. Lee, Ph.D.
E. B. Leof, Ph.D.
S. I. Macura, Ph.D.
N. J. Maihle, Ph.D.
D. J. McCormick, Ph.D.
J. A. McDonald, M.D., Ph.D.
C. T. McMurray, Ph.D.
M. A. McNiven, Ph.D
L. J. Miller, M.D.
S. Naylor, Ph.D.
W. G. Owen IV, Ph.D.
R. E. Pagano, Ph.D.
L. R. Pease, Ph.D.
J. T. Penniston, Ph.D.
J. F. Poduslo, Ph.D.
F. G. Prendergast, M.D., Ph.D.
J. R. Riordan, Ph.D.
J. L. Salisbury, Ph.D.
H.H.O. Schmid, Ph.D.
S. S. Sommer, M.D., Ph.D.
T. C. Spelsberg, Ph.D.
E. E. Strehler, Ph.D.
S. N. Thibodeau, Ph.D.
D. J. Tindall, Ph.D.
D. O. Toft, Ph.D.
R. T. Turner, Ph.D.
G. Vockley, M.D., Ph.D.
S. Vuk-Pavlovic, Ph.D.
Z. Vuk-Pavlovic, Ph.D.
E. D. Wieben, Ph.D.
C.Y.F. Young, Ph.D.

Employee Master's Degree

Area of Specialization (25 credit minimum)

Bioc	8000	General Biochemistry: Structure	3 cr.
Bioc	8001	General Biochemistry: Kinetics, Catalysis and Mechanisms	3 cr.
Bioc	8002	General Biochemistry: Energy Transduction and Signalling	3 cr.
Bioc	8005	Physical Biochemistry	1 cr.
Bioc	8010	Physical Biochemistry	1 cr.
Bioc	8015	Physical Biochemistry	1 cr.
Bioc	8050	Principles of Cell and Tissue Design	3 cr.
Bioc	8500	Biochemistry and Molecular Biology Journal Club (1 cr./yr.)	1 cr.
Bioc	8300	Master's Project	3 cr.
*MBio	8050	Principles of Cell and Tissue Design	3 cr.
*MBio	8101	Replication and Transcription Regulation	3 cr.
*MBio	8102	Regulation of Protein Synthesis	3 cr.

Outside Area of Specialization (8 credit minimum)

Ethic	5000	Maintenance of Scientific Integrity and Ethical Conduct in Scientific Research	1 cr.

Plus a minimum of 7 additional credits required in two areas not including

biochemistry. Courses noted with the asterisk (*) may be used to fulfill this requirement.

Elective Courses (15 credit minimum)
The balance of the 44 credits required for the degree may be distributed among biochemistry courses and courses in related fields, at the discretion of the student in consultation with the advisory committee.

Advisory Committee

Each student shall have an advisory committee consisting of three members of the graduate faculty. In addition to overseeing the student's educational program, this committee will be responsible for evaluating the scope and content of the Master's project. Selection of members of this committee should be discussed with the education coordinator.

One of these committee members should have graduate privileges outside the area of specialization. The student's employer may not sit on the advisory committee.

Biophysical Sciences Biomedical Imaging

R. A. Robb, Ph.D., *Graduate Education Coordinator*

U. Bite, M.D.
J. A. Bonner, M.D.
D. G. Bostwick, M.D.
D. E. Clapham, MD, PhD
R. L. Ehman, M.D.
J. P. Felmlee, Ph.D.
J. M. Fernandez, Ph.D.
B. K. Gilbert, Ph.D.
J. E. Gray, Ph.D.
J. F. Greenleaf, Ph.D.
C. R. Jack, M.D.
M. J. Joyner, M.D.
B. F. King, M.D.
R. W. Kline, Ph.D.
J. Lu, Ph.D.
A. Manduca, Ph.D.
C. H. McCollough, Ph.D.
E. C. McCullough, Ph.D.
R. L. Morin, Ph.D.
H. H. Ottesen, Ph.D.
W. Pavlicek, Ph.D.
J. L. Rae, Ph.D.
S. J. Riederer, Ph.D.
E. L. Ritman, M.D., Ph.D.
G. C. Sieck, Ph.D.
S. M. Sine, Ph.D.
J. H. Szurszewski, Ph.D.
S. R. Taylor, Ph.D.
R. J. Vetter, Ph.D.

Employee Master's Degree

I. Minimum Requirements

A minimum of 44 credits of course work are required for the Employee Master's Degree in Biophysical Sciences Biomedical Imaging Track. A minimum of 8 credits are taken outside the student's major area of concentration, as required by the Graduate School. A minimum of 20 credits are required in subjects within the major area, which includes a 3 credit course in advanced biomedical imaging. An additional 16 credits may be selected from the curriculum for a total of 44 credits.

II. Course Work

A program of course work for the Master's Degree program in the Biomedical Imaging Track may be selected from the following typical curriculum.

Outside Major Area (8 credit minimum)

Ethic	5000	Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research	1 cr.
HSR	5823	Introductory Statistics	3 cr.
HSR	5827	Introduction to Regression	1 cr.
Imm	5806	Basic Graduate Immunology	3 cr.
MBio	5000	Introduction to Molecular Biology	3 cr.
NSci	8300	Concepts in Neurophysiology	3 cr.
Phys	5801	Principles of Biomechanics	3 cr.

Within Major Area (20 credit minimum)

BPhy	5150	Introductory Radiation Biology	2 cr.
BPhy	5225	Introduction to Neural Networks	3 cr.
BPhy	5250	Anatomy for Biomedical Imagers	2 cr.
BPhy	5400	Molecular Electronics	3 cr.
BPHY	5450	Fundamental Concepts in Biomedical Imaging	3 cr.
BPhy	5500	Fundamentals of Computer Organization and Programming	3 cr.
BPhy	5610	Imaging and Computers	3 cr.
BPhy	5800	Physics and Technical Principles of Medical Imaging	3 cr.
BPhy	8740	Magnetic Resonance Imaging Systems	3 cr.
*BPhy	8450	Computer Image Processing	3 cr.

UNITE courses

CSci	5107	Computer Graphics I	3 cr.
CSci	5117	Computer Graphics II	3 cr.
CSci	5511	Artificial Intelligence I	4 cr.
CSci	8511	Computer Image Processing	4 cr.
Phy	5551, 5552, 5553	Topics in Physics for Biology and Medicine	15 cr.

* Required

III. Project

The students must complete a special project for 5 credits toward the Master's Degree in the Biomedical Imaging Track. Projects should not entail investigative research, but rather comprise written reports on established, state-of-the-art methods and procedures in the field of study.

IV. Examination

At the completion of the required coursework, each student must take a comprehensive written examination, followed by an oral examination. The examinations evaluate the student's depth and breadth of knowledge in the area of specialization and related fields of study. A committee of three examiners from the student's area of study and an examiner from outside the student's area of study conduct the examination.

IMMUNOLOGY

L. R. Pease, Ph.D., *Graduate Education Coordinator*

R. T. Abraham, Ph.D.
C. S. David, Ph.D.
G. J. Gleich, M.D.
J. J. Goronzy, M.D., Ph.D.
D. F. Jelinek, Ph.D.
P. J. Leibson, M.D., Ph.D.
V. A. Lennon, M.D., Ph.D.
D. J. McKean, Ph.D.
C. V. Paya, M.D.
D. H. Persing, M.D.
M. Rodriguez, M.D
P. J. Wettstein, Ph.D.
C. M. Weyand, M.D., Ph.D.

Employee Master's Degree

Courses in Area of Specialization (21 credit minimum)

A total of 9 credits from the following:

*Imm	5806	Basic Graduate Immunology	3 cr.
Imm	8863	Current Topics in Immunology	1 cr.
Imm	8865	Current Topics in Tumor Immunology	1 cr.
Imm	8867	Current Topics in Hypersensitivity	1 cr.

* Required

Students are required to take the following tutorial courses:

Imm	8876	Tutorial in T Cell Derived Lymphokines	2 cr.
Imm	8877	Tutorial in Molecular Basis of Immune Recognition	2 cr.
Imm	8878	Tutorial in Effector Mechanisms	2 cr.
Imm	8879	Tutorial in Cellular Activation	2 cr.
Imm	8880	Tutorial in Immunopathology	2 cr.
Imm	8882	Tutorial in Cellular Recognition and Development of the Immune Response	2 cr.

Outside Major Area of Specialization

Ethic	5000	Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research	1 cr.

An additional 7 credits in two different areas outside the Immunology track.

Electives (15 credits)

The remainder of the 44 credits can be selected from any field, with no more than 9 credits in seminar or journal club style courses.

Written Examination

The master's candidate must pass the written Immunology Qualifying Exam to complete the degree requirements.

Molecular Biology

F.M. Rusnak Ph.D., *Graduate Education Coordinator*

Z. Bajzer, Ph.D.
M. E. Bolander, M.D.
R. E. Brown, Ph.D.
T. P. Burghardt, Ph.D.
G. W. Dewald, Ph.D.
N. L. Eberhardt, Ph.D.
D. N. Fass, Ph.D.
M. R. Federspiel, Ph.D.
L. A. Fitzpatrick, M.D.
S. J. Gendler, Ph.D.
M. J. Getz, Ph.D.
R. B. Jenkins, M.D.
J. D. Jones, Ph.D.
C. Kappen, Dr.rer.nat.
B. C. Kline, Ph.D.
R. Kumar, M.D.
J. J. Lee, Ph.D.
N. A. Lee, Ph.D.
E. B. Leof, Ph.D.
S. I. Macura, Ph.D.
N. J. Maihle, Ph.D.
D. J. McCormick, Ph.D.
J. A. McDonald, M.D., Ph.D.
C. T. McMurray, Ph.D.
M. A. McNiven, Ph.D.
L. J. Miller, M.D.
S. Naylor, Ph.D.
W. G. Owen, IV, Ph.D.
R. E. Pagano, Ph.D.
L. R. Pease, Ph.D.
J. T. Penniston, Ph.D.
J. F. Poduslo, Ph.D.
F. G. Prendergast, M.D., Ph.D.
J. R. Riordan, Ph.D.
J. L. Salisbury, Ph.D.
H.H.O. Schmid, Ph.D.
S. S. Sommer, M.D., Ph.D.
T. C. Spelsberg, Ph.D.
E. E. Strehler, Ph.D.
S. N. Thibodeau, Ph.D.
D. J. Tindall, Ph.D.
D. O. Toft, Ph.D.
R. T. Turner, Ph.D.
G. Vockley, M.D., Ph.D.
S. Vuk-Pavlovic, Ph.D.
Z. Vuk-Pavlovic, Ph.D.
E. D. Wieben, Ph.D.
C.Y.F. Young, Ph.D.

Employee Master's Degree

Area of Specialization (20 credit minimum)

*Bioc	8000	General Biochemistry: Structure	3 cr.
*Bioc	8001	General Biochemistry: Kinetics, Cayalysis and Mechanisms	3 cr.
*Bioc	8002	General Biochemisty: Energy Transduction and Signalling	3 cr.
MBio	5500	Introduction to Cytogenetics (or any 8000 level Molecular Biology course except Journal Club)	2 cr.
MBio	8050	Principles of Cell and Tissue Design	3 cr.
MBio	8101	Replication and Transcription Regulation	3 cr.
MBio	8102	Regulation of Protein Synthesis	3 cr.
MBio	8500	Biochemistry and Molecular Biology Journal Club (1 cr/yr.)	1 cr.
MBio	8400	Master's Project	3 cr.

Three additional credits in Molecular Biology not including journal club credits.

Outside Area of Specialization (8 credit minimum)

Ethic	5000	Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research	1 cr.

An additional seven credits is required in two areas other than Molecular Biology. Courses with the asterisk (*) can be used to fulfill this requirement.

Elective Courses (16 credit minimum)

The balance of the 44 credits required for the degree may be distributed between Molecular Biology course and courses in related fields, at the discretion of the student in consultation with the advisory committee.

Advisory Committee

Each student shall have an advisory committee consisting of three members of the graduate faculty. In addition to overseeing the student's educational program, this committee will be responsible for evaluating the scope and content of the Master's project. Selection of members of this committee should be discussed with the education coordinator.

One of these committee members should have graduate privileges outside the area of specialization. The student's employer may not sit on the advisory committee.

PHARMACOLOGY

C. T. McMurray, Ph.D., *Graduate Education Coordinator*

R. T. Abraham, Ph.D.
M. M. Ames, Ph.D.
W. S. Brimijoin, Ph.D.
D. E. Clapham, M.D., Ph.D.
Z. Katusic, M.D.
S. H. Kaufmann, M.D., Ph.D.
J. J. Lipsky, M.D.
M. McKinney, Ph.D.
T. P. Moyer, Ph.D.
F. G. Prendergast, M.D., Ph.D.
E. Richelson, M.D.
C. Shin, M.D.
L. A. Stehno-Bittel, Ph.D.
J. H. Szurszewski, Ph.D.
S. R. Taylor, Ph.D.
R. M. Weinshilboum, M.D.

Employee Master's Degree

Core Courses (12 credits minimum)

Bioc	8000	General Biochemistry: Structure	3 cr.
Bioc	8001	General Biochemistry: Kinetics, Catalysis and Mechanisms	3 cr.
Bioc	8002	General Biochemistry: Energy Transduction and Signalling	3 cr.
Ethic	5000	Maintenance of Scientific Integrity and Ethical Conduct in Biomedical Research	1 cr.
Imm	5806	Basic Graduate Immunology	3 cr.
MBio	5000	Introduction to Molecular Biology	3 cr.

Track (19 credits)

Phar	5100	Pharmacology Seminar Series (1 cr./yr. - 4 yrs. req.)	4 cr.
Phar	5800	General Pharmacology	9 cr.
Phar	8800	Research Seminars in Pharmacology	1 cr.
Phar	8805	Drug Metabolism	3 cr.
Phar	8806	Pharmacology of Receptors	3 cr.
Phar	8808	Research Techniques in Pharmacology	3 cr.

Electives (11 credits)

Three credits each must be taken from at least 3 different categories A to D.

Category A

Phar	8803	Biochemical Basis of Neuropharmacology	3 cr.
N	8854	Basic Neurosciences	5 cr.

Category B

Phar	8802	Pharmacology of Heart Muscle	3 cr.
Phar	8850	Ionic Channels of Excited Membranes	3 cr.

Category C

Phar	8804	Clinical Pharmacology	1 cr.
Phar	8810	Toxicology	3 cr.
Phar	8879	Tutorial in Cellular Activation	2 cr.

Category D

HSR	5823	Introductory Statistics I	3 cr.
BPhy	5500	Fundamentals of Computer Organization and Programming	3 cr.

PHYSIOLOGY

R. A. Robb, Ph.D. *Graduate Education Coordinator*

K. An, M.D.
A. G. Andrews, D.M.V.
J. C. Burnett, M.D.
E. P. DiMagno, M.D.
T. P. Dousa, M.D.
J. M. Fernandez, Ph.D.
L. A. Fitzpatrick, M.D.
C. S. Frisk, D.V.M.
P. Gloviczki, M.D.
J. F. Greenleaf, Ph.D.
M. J. Joyner, M.D.
S. Khosla, M.D.
A. A. Khraibi, Ph.D.
D. W. Klass, M.D.
F. G. Knox, M.D., Ph.D.
V. M. Miller, Ph.D.
S. F. Phillips, M.D.
J. L. Rae, Ph.D.
E. L. Ritman, M.D., Ph.D.
M. G. Rock, M.D.
J. C. Romero, M.D.
H. V. Schaff, Ph.D.
G. C. Sieck, Ph.D.
S. M. Sine, Ph.D.
J. H. Szurszewski, Ph.D.

Employee Master's Degree

I. Minimum Requirements

A minimum of 44 credits of coursework is required for a Master's Degree in the Physiology Track. A minimum of eight credits are taken outside the student's major area of concentration, as required by the Graduate School. A minimum of 20 credits are required in subjects within the major area, which includes a three-credit course in physiology. An additional 16 credits may be selected from the curriculum for a total of 44 credits.

II. Course Work

A program of coursework for the Master's Degree program in the Physiology Track may be selected from the following typical curriculum.

Outside Major Area (8 credit minimum)

BPhy	5500	Fundamentals of Computer Organization and Programming	3 cr.
HSR	5823	Introductory Statistics I	3 cr.
HSR	5827	Introduction to Regression	1 cr.
Imm	5806	Basic Graduate Immunology	3 cr.
MBio	5000	Introduction to Molecular Biology	3 cr.
NSci	8300	Concepts in Neurophysiology	3 cr.

Within Major Area (20 credit minimum)

BPhy	5150	Introductory Radiation Biology	2 cr.
BPhy	5400	Molecular Electronics	2 cr.
Phar	8870	Ionic Channels of Excitable Membranes	3 cr.
Phys	5000	Laboratory Methods in Physiology	1 cr.
Phys	5500	Research Animal Experimental Surgery and Methodology	3 cr.
Phys	5801	Principles of Biomechanics I	3 cr.
Phys	5802	Principles of Biomechanics II	3 cr.
Phys	8855	Cardiovascular Physiology	3 cr.
Phys	8856	Respiratory Physiology	2 cr.
Phys	8858	Physiology of Smooth Muscle	2 cr.
Phys	8859	Renal Physiology	2 cr.
Phys	8860	Endocrine Physiology	2 cr.
Phys	8862	Excitation-Contraction Coupling in Skeletal Muscle	3 cr.
Phys	8878	Physiology of Bone I	3 cr.
Phys	8879	Physiology of Bone II	2 cr.

III. Project

The student must complete a special project for 5 credits toward the Master's Degree in the Physiology Track. Projects should not entail investigative research, but rather comprise written reports on established, state-of-the-art methods and procedures in the field of study.

IV. Examination

At the completion of the required coursework, each student must take a comprehensive written examination, followed by an oral examination. The examinations evaluate the student's depth and breadth of knowledge in the area of specialization and related fields of study. A committee of three examiners from the student's area of study and an examiner from outside the student's area of study conduct the examination.

Description of Master's Degree Program and Clinical Track Requirements

Master of Science Program in Biomedical Sciences
(Clinical Specialties)

The degree program requirements for a master's in a clinical field include a minimum of 20 credits in biomedical sciences and 15 credits in the area of specialization. Full-time registration for a minimum of one year is required. General program requirements and specialty track descriptions are outlined on the following pages. The equivalent of six months of full-time effort must be devoted to research.

Courses in basic biomedical sciences are required to provide the student with the knowledge to address a research problem, conduct the research and evaluate the results. Courses in the area of specialization are required in addition to provide special skills, techniques or knowledge related to the specialty track.

The primary purpose of the degree program is to enhance the scholarly dimension of the education of physicians who have an interest in academic medicine. Training in research is emphasized. The degree program provides a structure for development of a plan to address a research problem, an orderly approach to the project, assurance of the credentials of the adviser, appropriate supervision, and a suitable approach to the analysis and presentation of the results.

General Program Requirements

Eligibility: The program described below is designed chiefly for Mayo residents who hold appointments to the clinical programs of Mayo Graduate School of Medicine. Potential candidates for the degree must hold appointments of sufficient duration to complete degree program requirements.

Application: The candidate must complete a Statement of Intent to Pursue a Degree. This form, which requires departmental approval of the degree program and research project, is available in the Graduate School Office.

Time Requirement: All requirements must be satisfied within one year after completion of the fellowship.

Thesis Protocol: No later than two months after entering the laboratory, the candidate must submit a protocol to the Mayo Graduate School Education Committee. This protocol must clearly define the candidate's role in his/her project and must have sufficient detail to permit review by an advisory committee (guidelines are available in the Graduate School Office). If the protocol is not submitted during the first quarter in the laboratory, registration for research credits will not be allowed for the second quarter.

Official Program: Students are encouraged to submit their programs and thesis titles to the Graduate School before the end of the second year of registration. Students and advisers should include on the program forms: a) the minimum number of courses/credits necessary to fulfill degree requirements (credits may vary depending on the chosen area of specialization), b) the thesis title and c) the recommended thesis readers and final oral examining committee. The examining committee consists of a minimum of three individuals, one of whom is the student's adviser, who serves as chair of the committee. One member must be

from outside the department and no member other than the chair can be from among a student's research advisers. If the student has a clinical and research adviser, both will be put on the committee along with another examiner from the area of specialization and another from a basic science field. The recommended committee must be approved by the Graduate School.

Changes in Approved Program: Once approved, the program must be fulfilled in every detail to meet graduation requirements. Alterations in the program should be requested in writing and are subject to approval of the Mayo Graduate School Education Committee.

Minimum Grade Requirements: The minimum grade point average required by the Graduate School for courses included on the official program for the degree is 3.0 (on a 4.0 scale). Grades of A through C, and S are acceptable, but grades of S are not calculated in the grade point average. At least two-thirds of the credits taken and included on any degree program must be graded under the A through F system.

Minimum Credit Requirements: Students must complete a minimum of 20 credits in biomedical sciences and 15 additional credits in the area of specialization (see individual specialty track descriptions for specific course requirements). A maximum of 12 research credits can be applied towards the 20 biomedical science credits. One clinical rotation, to a maximum of 6 credits, can be used towards the 15 in the area of specialization. The remaining 9 must be didactic credits in the area of specialization. A minimum of six months or its equivalent in time and effort must be devoted to research. Students are not admitted to a specialty track unless there is reasonable assurance that course work required for completion of degree requirements is available.

Thesis: The thesis must be submitted to the final oral examining committee at least three weeks prior to the oral examination.

Written Examination: Must be taken no later than six months before completion of the training program.

Final Examination: Candidates for the M.S. degree must pass a final oral examination, which can be taken only after the written examination has been passed, courses on the official program completed, and the thesis reviewed. Successful completion of the final oral examination requires a unanimous decision by all of the members of the committee.

DENTISTRY - ORTHODONTICS

B. E. Larson, D.D.S., *Graduate Education Coordinator*

T. A. Guenthner, D.D.S. A. H. Sather, D.D.S.
A. J. Hill, Jr., D.D.S.

Master's Degree

Biomedical Sciences Courses

*Anat	8852	Surgical Anatomy of the Head and Neck	3 cr.
*HSR	5400	Introduction to Statistical Models	1 cr.
*HSR	5410	Design of Clinical Studies	1 cr.
*Odon	8857	Research in Selected Problems (1 cr./qtr. - 10 qtrs. required)	10 cr.
*Phys	5801	Principles of Biomechanics	3 cr.

*Required Courses

Three credits from the following courses required:
(Substitution permitted with prior approval)

HSR	5823	Introductory Statistics I	3 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
Path	8873	Oral Pathology (2 cr./yr. - 3 yrs. required)	6 cr.
Phys	8878	Physiology of Bone I (must audit if not taken for credit)	3 cr.
Pdon	8884	Pathology of Periodontal Disease	1 cr.

Orthodontic Didactic Courses (all required)

Odon	8806	Orthodontic Seminar: Technique (1 cr./qtr. - 11 qtrs. required)	11 cr.
Odon	8807	Orthodontic Seminar: Literature Review (1 cr./qtr. - 11 qtrs. required)	11 cr.
Odon	8808	Orthodontic Seminar: Case Presentation (1 cr./qtr. - 11 qtrs. required)	11 cr.
Odon	8809	Surgical Orthodontic Seminar (1 cr./qtr. - 9 qtrs. required)	9 cr.
Odon	8810	Clinical Oro-Facial Pathology and Developmental Disorders	1 cr.
Odon	8811	Facial Growth and Development	1 cr.

Orthodontic Clinical Courses (all required)

Odon	8800	Advanced Orthodontic Techniques	3 cr.
Odon	8802	Orthodontic Case Analysis	6 cr.
Odon	8803	Orthodontic Treatment Planning	6 cr.
Odon	8804	Clinical Orthodontics (6 cr./qtr. - 4 qtrs. required)	24 cr.
Odon	8805	Advanced Clinical Orthodontics (6 cr./qtr. - 4 qtrs. required)	24 cr.

Odon	8851	Dental Roentgenology	1 cr.
Odon	8852	Oral Diagnosis	5 cr.
OS	8850	Oral and Maxillofacial Surgery	3 cr.

DENTISTRY - PERIODONTICS

C. M. Reeve, D.D.S., *Graduate Education Coordinator*
P. J. Sheridan, D.D.S.

Master's Degree

Biomedical Sciences Courses

*Anat	8852	Surgical Anatomy of Head and Neck	3 cr.
Derm	8841	Diagnostic Dermatology	2 cr.
HSR	5400	Introduction to Statistical Models	1 cr.
HSR	5410	Design of Clinical Studies	1 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
*Pdon	8857	Research in Selected Problems (2 cr./qtr. - 6 qtrs. required)	12 cr.
*Path	8873	Oral Pathology (2 cr./yr. - 3 yrs. required).	6 cr.

*Required Courses

Periodontics Didactic Courses (all required)

Pdon	8883	Periodontal Seminar (1 cr./qtr. - 9 qtrs. required)	9 cr.
Pdon	8884	Pathology of Periodontal Disease	1 cr.

Periodontics Clinical Courses (all required)

Pdon	8880	Clinical Periodontics (6 cr./qtr. - 2 qtrs. required)	12 cr.
Pdon	8881	Advanced Clinical Periodontics (6 cr./qtr. - 2 qtrs. required)	12 cr.

DENTISTRY - PROSTHODONTICS

S. E. Eckert, D.D.S., *Graduate Education Coordinator*
R. P. Desjardins, D.M.D.

Master's Degree

Biomedical Sciences Courses

*Anat	8852	Surgical Anatomy of Head and Neck	3 cr.
*HSR	5400	Introduction to Statistical Models	1 cr.
*HSR	5410	Design of Clinical Studies	1 cr.
HSR	5827	Introduction to Regression	1 cr.

HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics Epidemiologic Studies	1 cr.
*Path	8873	Oral Pathology (2 cr./yr. 3 yrs. required)	6 cr.
*Pros	8857	Research in Selected Problems (2 cr./qtr. 6 qtrs. required)	12 cr.
*Phys	5801	Principles of Biomechanics I	3 cr.
Phys	8878	Physiology of Bone I	3 cr.

*Required Courses

Prosthodontic Didactic Courses (all required)

Pros	8841	Prosthodontic Seminar (Complete Dentures) (1 cr./qtr. -2 qtrs. required)	2 cr.
Pros	8843	Prosthodontic Seminar (Partial Dentures)	1 cr.
Pros	8845	Prosthodontic Seminar (Fixed)	1 cr.
Pros	8847	Seminar: Maxillofacial Prosthetics Advanced Prosthodontics (1 cr./qtr.-1 qtr. required)	1 cr.
Pros	8848	Seminar: Current Literature (1 cr./qtr. -9 qtrs. required)	9 cr.
Pros	8849	Seminar: Maxillofacial Prosthetics (Extraoral) and Advanced Prosthodontics	1 cr.
Pros	8850	Seminar: Implant Prosthodontics	1 cr.
Pros	8862	Dental Materials	1 cr.
Pros	8870	Occlusion	1 cr.
Pros	8871	Physiology, Pharmacology and Pre-Prosthetic Surgery	1 cr.
Pros	8872	Prosthodontic Practice Management	1 cr.
Pros	8873	Cranio-mandibular Disorders and Facial Pain	1 cr.
Pros	8874	Prosthodontic Management of the Geriatric Patient	1 cr.

Prosthodontic Clinical Courses (all required)

Pros	8840	Clinical Prosthodontics: Complete Dentures (6 cr./qtr. - 2 qtrs. required)	12 cr.
Pros	8842	Clinical Prosthodontics: Partial Dentures (6 cr./qtr. - 4 qtrs. required)	24 cr.
Pros	8844	Maxillofacial Prosthetics (Intraoral) Implant Prosthodontics - Advanced Prosthodontics (6 cr./qtr. - 3 1/2 qtrs. required)	21 cr.
Pros	8846	Maxillofacial Prosthetics (Extraoral) Advanced Prosthodontics	3 cr.
Pros	8851	Dental Roentgenology	1 cr.
Pros	8852	Oral Diagnosis and Treatment of Cranio-mandibular Disorders	2 cr.
Pros	8854	Implant Prosthodontics (6 cr./qtr. - 3 qtrs. required)	18 cr.
Pros	8876	Clinical Prosthodontics: Fixed Partial Dentures	6 cr.
Pros	8880	Dental Laboratory Technology	6 cr.
I	8866	Oncology (Special Clinical and Laboratory Techniques)	1 cr.

SpPa	8861	Speech Pathology	2 cr.
ENT	8851	Clinical Otolaryngology	6 cr.
R	8853	Radiation Oncology	2 cr.

Obstetrics and Gynecology

K. C. Podratz, M.D., Ph.D., *Graduate Education Coordinator*

L. D. Erickson, M.D.
R. H. Heise, M.D.
R. A. Lee, M.D.
J. Magrina, M.D.
P. L. Ogburn, Jr., M.D.
C. R. Stanhope, M.D.
M. J. Webb, M.D.
T. O. Wilson, M.D.

Master's Degree

Biomedical Sciences Courses

Didactic*

HSR	5823	Introductory Statistics	3 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
HSR	5840	Survival Analysis	1 cr.

*Six credits are required.

Research

**Bioc	8895	Research in Biochemistry	6 cr.
**MBio	8900	Research in Molecular Biology	6 cr.
**Imm	8840	Research in Immunology	6 cr.
**Phar	8840	Research in Pharmacology	6 cr.
**Phys	8840	Research in Physiology	6 cr.

**A minimum of two quarters of one of these is required.

A minimum of two additional credits of didactic course work is required in the area of research, with the approval of the adviser.

Obstetrics and Gynecology Didactic Courses (all required)

Anat	8000	Anatomy of the Pelvis-Perineum	2 cr.
ObG	5000	Basic Colposcopy	2 cr.
ObG	5801	Introduction to Obstetrics	3 cr.
ObG	5803	Introduction to Surgical Gynecology	3 cr.
ObG	8856	Reproductive Endocrinology	1 cr.

Obstetrics and Gynecology Clinical Courses

Satisfactory completion of a minimum of 3 years of clinical experience in Obstetrics and Gynecology.

ObG	8852	Clinical Obstetrics and Gynecology (6 cr./qtr. - 6 qtrs. required)	36 cr.
ObG	8853	Operative Surgery (6 cr./qtr. - 6 qtrs. required)	36 cr.

Obstetrics & Gynecology - Gynecologic Oncology

Master's Degree

Biomedical Sciences Didactic Courses

		Didactic*	
HSR	5823	Introductory Statistics	3 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
HSR	5840	Survival Analysis	1 cr.

*Six credits are required.

		Research	
**Bioc	8895	Research in Biochemistry	6 cr.
**MBio	8900	Research in Molecular Biology	6 cr.
**Imm	8840	Research in Immunology	6 cr.
**Phar	8840	Research in Pharmacology	6 cr.
**Phys	8840	Research in Physiology	6 cr.

**Four quarters of one of these is required.

A minimum of two additional credits of didactic course work is required in the area of research, with the approval of the adviser.

Gynecologic Oncology Didactic Courses

Anat	8000	Anatomy of the Pelvis-Perineum	2 cr.
ObG	5803	Introduction to Surgical Gynecology (1 cr./qtr. 8 qtrs. required)	8 cr.

Gynecologic Oncology Clinical Courses

ObG	8857	Gynecologic Oncology (6 cr./qtr. - 8 qtrs. required)	48 cr.

Obstetrics & Gynecology - Reproductive Endocrinology

Master's Degree

Biomedical Sciences Didactic Courses

		Didactic*	
HSR	5823	Introductory Statistics	3 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
HSR	5840	Survival Analysis	1 cr.

*Six credits are required.

Research

**Bioc	8895	Research in Biochemistry	6 cr.
**MBio	8900	Research in Molecular Biology	6 cr.
**Imm	8840	Research in Immunology	6 cr.
**Phar	8840	Research in Pharmacology	6 cr.
**Phys	8840	Research in Physiology	6 cr.

**Four quarters of one of these is required.

A minimum of two additional credits of didactic course work is required in the area of research, with the approval of the adviser.

Reproductive Endocrinology Didactic Courses

ObG	5803	Introduction to Surgical Gynecology	1 cr.
ObG	8854	Seminars in Gynecologic Endocrinology (1 cr./qtr. - 8 qtrs. required)	8 cr.
ObG	8856	Clinical Reproductive Endocrinology	1 cr.

Reproductive Endocrinology Clinical Courses

ObG	8858	Reproductive Endocrinology I	3 cr.
ObG	8859	Reproductive Endocrinology II	3 cr.
ObG	8860	Reproductive Endocrinology III	3 cr.

Obstetrics & Gynecology - Advanced Gynecologic Surgery

Master's Degree

Biomedical Sciences Didactic Courses

Didactic*

HSR	5823	Introductory Statistics I	3 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Statistical Methods for Epidemiologic Studies	2 cr.

*Six credits are required.

Research

**Bioc	8895	Research in Biochemistry	6 cr.
**MBio	8900	Research in Molecular Biology	6 cr.
**Imm	8840	Research in Immunology	6 cr.
**Phar	8840	Research in Pharmacology	6 cr.
**Phys	8840	Research in Physiology	6 cr.

**Four quarters of basic science research is required.

A minimum of two additional credits of didactic course work is required in the area of research, with the approval of the adviser.

Advanced Gynecologic Surgery Didactic Courses

Anat	8860	Special Topics in Anatomy	3-4 cr.

ObG	5803	Introduction to Surgical Gynecology (1 cr./qtr. - 4 qtrs. required)	4 cr.

Advanced Gynecologic Surgery Clinical Courses

ObG	8870	Advanced Gynecologic Operative Surgery (6 cr./qtr. - 4 qtrs. required)	24 cr.

OPHTHALMOLOGY

D. C. Herman, M.D., *Graduate Education Coordinator*

K. N. Baratz, M.D.
G. B. Bartley, M.D.
W. M. Bourne, M.D.
R. F. Brubaker, M.D.
H. Buettner, M.D.
R. J. Campbell, M.D.
J. C. Erie, M.D.
J. A. Garrity, M.D.
G. G. Hohberger, M.D.
D. H. Johnson, M.D.
J. A. Leavitt, M.D.
T. J. Liesegang, M.D.
L. J. Maguire, M.D.
T. J. McPhee, M.D.
J. M. Pach, M.D.
D. M. Robertson, M.D.
R. R. Waller, M.D.
B. R. Younge, M.D.

Master's Degree

Biomedical Sciences Courses

The candidate must complete a minimum of 20 quarter credits from the following biomedical sciences courses:

HSR	5823	Introductory Statistics I	3 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
Imm	5806	Basic Graduate Immunology	3 cr.
Phar	5801-5805	General Pharmacology	9 cr.
Phar	8803	Biochemical Basis of Neuropharmacology	3 cr.
Phar	8806	Pharmacology of Receptors	3 cr.
Phys	8300	Concepts in Neurophysiology	3 cr.
Phys	8855	Cardiovascular Physiology	3 cr.
Phys	8858	Physiology of Smooth Muscle and of its Innervation	2 cr.
Phys	8859	Renal Physiology	2 cr.
Phys	8860	Endocrine Physiology	2 cr.
Oph	8900	Research in Ophthalmology (6 cr./qtr. - 2 qtrs. required)	12 cr.

Ophthalmology Didactic Courses (all required)

Oph	8100	Fundamentals and Principles of Ophthalmology	4 cr.
Oph	8101	Optics, Refraction and Contact Lenses	4 cr.
Oph	8102	Ophthalmic Pathology, Ocular Tumors, Intraocular Inflammation, and Uveitis	4 cr.
Oph	8103	Retinal and Vitreous Diseases	4 cr.
Oph	8104	Neuro-ophthalmology and General Medical Ophthalmology	4 cr.

Oph	8015	Binocular Vision and Ocular Motility	4 cr.
Oph	8106	External and Corneal Diseases	4 cr.
Oph	8107	Glaucoma, Disorders of the Lens and Anterior Segment Trauma	4 cr.
Oph	8108	Orbital Diseases and Plastic and Reconstructive Surgery	4 cr.

Ophthalmology Clinical Courses

Oph	8851	Refraction and Strabismus	6 cr.
Oph	8852	Ocular Therapy	6 cr.
Oph	8853	Medical and Neurologic Ophthalmology	6 cr.
Oph	8854	Ophthalmic Surgery	6 cr.
Oph	8855	Ophthalmic Pathology, Anatomy, and Surgical Technique	6 cr.

ORTHOPEDICS

R. H. Cofield, M.D., *Graduate Education Coordinator*

P. C. Amadio, M.D.
K. An, Ph.D.
R. D. Beckenbaugh, M.D.
R. A. Berger, M.D., Ph.D.
A. T. Bishop, M.D.
M. E. Bolander, M.D.
M. E. Cabanela, M.D.
D. C. Campbell, II, M.D.
W. P. Cooney, M.D.
B. L. Currier, M.D.
A. D. Hanssen, M.D.
D. G. Lewallen, M.D.
B. F. Morrey, M.D.
S. W. O'Driscoll, M.D., Ph.D.
H. A. Peterson, M.D.
D. J. Pritchard, M.D.
M. G. Rock, M.D.
A. R. Schroeder
T. C. Shives, M.D.
F. H. Sim, M.D.
M. J. Stuart M.D.
R. T. Turner, Ph.D.
M. B. Wood, M.D.

Master's Degree

Biomedical Sciences Courses

*Phys	8878	Physiology of Bone I	3 cr.
*Phys	8879	Physiology of Bone II	2 cr.
*Phys	5801	Principles of Biomechanics I	3 cr.
*Phys	5802	Principles of Biomechanics II	3 cr.
*M	5805	Microbiology of Musculoskeletal System	1 cr.
*Anat	8855	Orthopedic Anatomy (1 cr./qtr. - 2 qtrs. required)	2 cr.
*Path	8872	Bone and Soft Tissue Pathology	3 cr.
*Phys	8840	Research in Physiology (6 cr./qtr. - 2 qtrs. required) or	12 cr.
*Bioc	8895	Research in Biochemistry (6 cr./qtr. - 2 qtrs. required)	12 cr.
Phys	8880	Principles of Solid Mechanics	3 cr.
Phys	8881	Mechanics of Deformable Materials	3 cr.

*Required Courses

Orthopedics Didactic Courses (all required)

Or	5803	Prosthetics for Orthopedics	1 cr.

Or	8500	Technique of Microvascular Anastomosis	2 cr.
Or	8860	Structure & Function of Bone	3 cr.
R	8854	Radiology of the Musculoskeletal System	1 cr.

Orthopedics Clinical Courses (all required)

Or	8851	Orthopedic Diagnosis	6 cr.
Or	8852	Adult Reconstruction	6 cr.
Or	8853	Surgery of the Hand	6 cr.
Or	8854	Pediatric Orthopedics	6 cr.
Or	8855	Orthopedic Oncology	6 cr.
Or	8856	Fractures	2 cr.

OTORHINOLARYNGOLOGY

C. W. Beatty, M.D., *Graduate Education Coordinator*

C. D. Bauch, Ph.D.
L. W. DeSanto, M.D.
D. A. Fabry, Ph.D.
G. W. Facer, M.D.
R. O. Gustafson, M. D.
S. G. Harner, M.D.
J. L. Kasperbauer, M.D.
E. B. Kern, M.D.
N.E. Maragos, M.D.
M. S. Marion, M.D.
T. V. McCaffrey, M.D., Ph.D.
T. J. McDonald, M.D.
H. B. Neel III, M.D., Ph.D.
K. D. Olsen, M.D.
W. O. Olsen, Ph.D.
B. W. Pearson, M.D.
M. S. Robinette, Ph.D.
J. R. Salassa, M.D.
D. A. Sherris, M.D.

Master's Degree

Biomedical Sciences Courses

*Anat	8852	Surgical Anatomy of Head and Neck	3 cr.
Anat	8860	Special Topics in Anatomy	1-4 cr.
*HSR	5823	Introductory Statistics I	3 cr.
HSR	5400	Introduction to Statistical Models	1 cr.
HSR	5410	Design of Clinical Studies	1 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
Phar	5801	General Pharmacology	2 cr.
Phar	5802-5	General Pharmacology	7 cr.
Phar	8803	Biochemical Basis of Neuropharmacology	3 cr.
Phar	8806	Pharmacology of Receptors	3 cr.
Phys	8859	Renal Physiology	2 cr.
Imm	5806	Basic Graduate Immunology	3 cr.
*ENT	8890	Graduate Research (6 cr./qtr. - 2 qtrs. required)	12 cr.

*Required courses, an additional six credits to be chosen from courses listed, for a total of at least 25 credits in the Biomedical Sciences area. Other biomedical sciences courses may be included as electives at the discretion of the staff adviser.

Otorhinolaryngology Didactic Courses (all required)

ENT	5150	Core Curriculum	2 cr.
ENT	5200	Maxillofacial Trauma	1 cr.
ENT	5300	Core Colloquium	1 cr.
ENT	8800	Seminar: Otorhinolaryngology	1 cr./yr.
ENT	8100	Problems in Clinical Diagnosis	4 cr.
ENT	8200	Clinical Testing Practicum	1 cr.
ENT	8300	Soft Tissue and Plastic Reconstruction	1 cr.
ENT	8500	Rhinology and Rhinologic Surgery Dissection	3 cr.
ENT	8857	Temporal Bone Anatomy and Surgery of the Temporal Bone	3 cr.

Otorhinolaryngology Clinical Courses (all required)

ENT	8851	Clinical Otorhinolaryngology	6 cr.
ENT	8852	Preoperative and Postoperative Care of Patients	6 cr.
ENT	8853	Operative Otorhinolaryngology	6 cr.
ENT	8854	Operative Otorhinolaryngology	6 cr.

Physical Medicine and Rehabilitation

K. A. Stolp-Smith, M.D., *Graduate Education Coordinator*
R. W. DePompolo, M.D.

Master's Degree

The basic residency program is designed to train residents to be competent in the field of physical medicine and rehabilitation and to meet the requirements of the American Board of Physical Medicine and Rehabilitation. Candidates for a Master's degree will require an additional year of training (authorized by the Graduate Education Committee for Medical and Laboratory Specialties of the Mayo Graduate School of Medicine).

***Biomedical Sciences Courses** (9 credits required in addition to 12 credits of research)

Anat	8855	Orthopedic Anatomy	2 cr.
HSR	5823	Introductory Statistics I	3 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in the Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
Phar	8803	Biochemical Basis of Neuropharmacology	3 cr.
Phys	5801	Principles of Biomechanics	3 cr.
**Phar	8862	Excitation-Contraction Coupling in Skeletal Muscle	3 cr.
PhM	8900	Research Work on Selected Problems (6 cr./qtr. - 2 qtrs. required)	12 cr.

***Electives**

Derm	8847	Cutaneous Photobiology	1 cr.
I	8861	Rheumatology (Special Clinical and Laboratory Techniques)	6 cr.

N	8859	Neurological Diseases in Children	6 cr.
R	8854	Radiology of the Musculoskeletal System	1 cr.

*The foregoing list includes courses relevant to the field of PM&R but is not intended to be all-inclusive.

**Requires permission of instructor

Physical Medicine & Rehabilitation Clinical Courses ***(all required)***

PhM	8851	Outpatient Clinical Physical Medicine and Rehabilitation (6 cr./qtr. - 1-2 qtrs. required)	6 cr.
PhM	8852	Physical Medicine and Rehabilitation Hospital Consulting Service (6 cr./qtr. - 2 qtrs. required)	12 cr.
PhM	8853	Hospital Rehabilitation Service (6 cr./qtr. - 3 qtrs. required)	18 cr.
N	8852	Neurologic Diseases in Adults	6 cr.
N	8860	Electromyography (6 cr./qtr. - 2 qtrs. required)	12 cr.
I	8853	Medical Diagnosis and Hospital Service	4 cr.
I	8858	Cardiovascular Diseases (Special Clinical and Laboratory Techniques) (6 cr./qtr. - .5 qtr. required)	3 cr.
Or	8852	Adult Reconstruction (6 cr./qtr. - .5 qtr. required)	3 cr.

Physical Medicine & Rehabilitation Didactic Courses ***(all required)***

Anat	5500	Functional Anatomy of Back and Extremities 1.5cr.	
PhM	8854	Basic and Applied Physiatry (2 cr./qtr. - 12 qtrs. required)	24 cr.
PhM	8855	Amputations and Prosthetics	3 cr.
PhM	8856	Seminars in Physical Medicine and Rehabilitation (1 cr./qtr. - 12 qtrs. required)	12 cr.
PhM	8857	Readings in Physical Medicine and Rehabilitation (1 cr./qtr. - 12 qtrs. required	12 cr.

PSYCHIATRY

J. A. Tinsley, M.D., *Graduate Education Coordinator*

Psychiatry

A. J. Cunnien, M.D.
R. E. Finlayson, M.D.
M. R. Hansen, M.D.
N. P. Hanson, M.D.
K. M. Logan, M.D.
A. R. Lucas, M.D.
M. J. Martin, M.D.
T. Maruta, M.D.
D. E. McAlpine, M.D.
G. L. Moore, M.D.
R. M. Morse, M.D.
D. C. Newman, M.D.
M. A. Palmen, M.D.
J. W. Richardson, M.D.
E. Richelson, M.D.
J. D. Rome, M.D.
L. A. Wells, M.D., Ph.D.

Psychology

R. C. Colligan, Ph.D.
L. J. Davis, Jr., Ph.D.
R. J. Ivnik, Ph.D.
D. Osborne, Ph.D.
M. S. Schwartz, Ph.D.

Master's Degree

Biomedical Science Courses

A minimum of 20 credits must be earned from the list below or equivalent course work approved by candidate's program adviser.

HSR	5823	Introductory Statistics I	3 cr.
HSR	5827	Introduction to Regression	1 cr.
HSR	5831	Introduction to Clinical Epidemiology	1 cr.
HSR	5833	Critical Appraisal of Statistical Methods in Medical Literature	1 cr.
HSR	5835	Logistic Regression and Related Topics	1 cr.
N	5801	Introduction to Neuroscience	6 cr.
Phar	8803	Biochemical Basis of Neuropharmacology	3 cr.
Phar	8806	Pharmacology of Receptors	3 cr.
P	8900	Research in Psychiatry (6 cr./qtr. - 2 qtrs. req.)	12 cr.

Psychiatry Didactic Courses - A minimum of 12 credits must be earned from those listed below.

*P	8501	Psychiatry Didactic Lecture Series I	2 cr.
*P	8502	Psychiatry Didactic Lecture Series II	2 cr.
*P	8503	Psychiatry Didactic Lecture Series III	2 cr.
*P	8504	Psychiatry Didactic Lecture Series IV	2 cr.

*Required Courses

P	8350	Individual Study in Psychiatry	2 cr.

Individual Study consists of directed readings in a specific area of the Behavioral Sciences, under the supervision of a consultant faculty member. At the end of this course, each candidate must present his or her chosen topic to the department in a one-hour lecture. Re-registration for the course is permitted, up to a maximum of 6 credits (a different topic must be studied each time).

P	8400	Behavioral Science Seminar	2 cr.

Specific quarter-long seminars in the Behavioral Sciences will be offered, depending on student interest and staff availability. These are intended to provide intensive, guided education in areas of interest and relevance to the students in the program at any given time. Topics may include Psychopharmacology, Neuropsychology, Specific Therapeutic Modalities, General Psychopathology, among others. Unlimited re-registration for this course is permitted (a different topic must be studied each time).

Psychiatry Clinical Courses

A minimum of 36 credits must be earned in this category.

P	8100	Hospital Psychiatry I: Second Assistant	4 cr.
P	8101	Hospital Psychiatry II: Second Assistant	4 cr.
P	8102	Hospital Psychiatry III: First Assistant	4 cr.
P	8103	Hospital Psychiatry IV: First Assistant	4 cr.
P	8150	ADDU: Adult Chemical Dependency	4 cr.
P	8160	ACDU: Adolescent Chemical Dependency	4 cr.
P	8170	IPC: Interpersonal Process	4 cr.
P	8180	Child Psychiatry	4 cr.
P	8200	OPS: Outpatient Psychiatry I	4 cr.

P	8201	OPS: Outpatient Psychiatry II	4 cr.
P	8250	Consultation/Liaison Psychiatry	4 cr.
P	8300	Theory and Practice of Psychology	4 cr.
P	8500	Zumbro Valley Mental Health Center	4 cr.
P	8550	Federal Medical Center: Prison Psychiatry	4 cr.

To earn degree credits, the following two criteria must be satisfied for each course attempted:

— Completion of the clinical rotation, with a passing grade being assigned by the clinical consultant supervisor.

— Passing a one-hour oral examination which will be administered by the "Examiner" indicated for each course, or another consultant in Psychiatry/Psychology so designated by the listed "Examiner." The person giving the oral examination may not have also functioned as a clinical consultant to the examinee during the clinical rotation.

Diagnostic Radiology

S. J. Swensen, M.D., *Graduate Education Coordinator*

J. W. Beabout, M.D.
B. J. Erickson, M.D., Ph.D.
J. J. Gisvold, M.D.
J. E. Gray, M.D.
R. R. Hattery, M.D.
M. A. Holbrook, M.D.
C. D. Johnson, M.D.
R. L. MacCarty, M.D.
E. C. McCullough, Ph.D.
W. E. Miller, M.D.
J. R. Muhm, M.D.
C. C. Reading, M.D.
P. F. Sheedy, M.D.
A. W. Stanson, M.D.
D. H. Stephens, M.D.
B. Williamson, M.D.

Master's Degree

Biomedical Sciences Courses

Select a minimum of 9 credits from the list below to meet the biomedical science requirement. Other courses may be approved with consultation and approval of the adviser.

BPhy	5601	Fundamental Concepts in Biomedical Imaging	3 cr.
BPhy	5225	Introduction to Neural Networks	3 cr.
BPhy	5400	Molecular Electronics	3 cr.
BPhy	5500	Fundamentals of Computer Organization and Programming	3 cr.
BPhy	5800	The Physics and Technical Principles of Medical Imaging	3 cr.
BPhy	8450	Computer Image Processing	3 cr.
BPhy	8470	Two-Dimensional Signal Processing	3 cr.
BPhy	8700	Digital Signal Processing I	3 cr.
BPhy	8705	Digital Signal Processing II	3 cr.
BPhy	8740	Magnetic Resonance Imaging Systems	3 cr.
BPhy	8857	Radiation Therapy Physics	3 cr.
CSci	5107	Computer Graphics I	3 cr.
CSci	5117	Computer Graphics II	3 cr.

CSci	5301	Numerical Analysis	4 cr.
CSci	5511	Artificial Intelligence I	4 cr.
CSci	8511	Concepts in Computer Vision	4 cr.
HSR	5823	Introductory Statistics I	3 cr.
R	8900	Research in Radiology (6 cr./qtr. - 2 qtrs. required)	12 cr.

Radiology Didactic Courses

A minimum of 9 credits must be selected from the following.

R	8833	Gastrointestinal Radiology	1 cr.
R	8834	Genitourinary Radiology	1 cr.
R	8835	Introduction to Diagnostic Radiology	3 cr.
R	8836	Musculoskeletal Radiology	1 cr.
R	8831	Chest Radiology	1 cr.
R	8830	Cardiac/Vascular Radiology	1 cr.
R	8832	Cross-sectional Imaging	1 cr.
R	8838	Nuclear Medicine	1 cr.
R	8839	Pediatric Radiology	1 cr.
R	8837	Neuroradiology	1 cr.

Radiology Clinical Courses

A minimum of 6 credits must be selected from the following:

R	8884	Pediatric Radiology	1 cr.
R	8887	Uroradiology	1 cr.
R	8885	Skeletal Radiology	1 cr.
R	8886	Ultrasound	1 cr.
R	8882	Hospital Radiology	1 cr.
R	8881	Gastrointestinal Radiology	1 cr.
R	8883	Neuroradiology	1 cr.
R	8880	Chest Radiology	1 cr.

Course Listing

Symbols and Explanations

The following symbols are used throughout the course descriptions in lieu of page footnotes:

* Mayo Medical School course, limited enrollment. Permission of course instructor required. Courses do not follow typical quarter schedule. Contact Graduate School Office to register and for the schedule.

\# Consent of the instructor is required prior to registration.

\+ Consent of the department or division offering the course is required prior to registration.

f,w,s,su Following course number indicates fall, winter, spring, or summer quarters.

A hyphen between course numbers (e.g., 5803-5804) indicates a sequence of courses that must be taken in the order listed.

A comma between course numbers (e.g., 8857,8858,8859) indicates a series of courses that may be entered any quarter.

Courses designated as "clinical" or "research" are open only to selected categories of students (usually residents or degree candidates enrolled in the training programs of the appropriate department).

Anatomy

*Anat 5001f. *HUMAN GROSS ANATOMY.* (8 cr; #) Cahill, Carmichael
A study of the entire human body by sequential dissection of body regions.

*Anat 5200s. *MICROSCOPIC ANATOMY.* (2 cr) Carmichael, Cahill
A lecture and laboratory course on the cell and tissue types.

Anat 5500su. *FUNCTIONAL ANATOMY OF BACK AND EXTREMITIES.* (1.5 cr) Carmichael, Christopherson
Dissection, demonstration, and discussion of the back and limbs with emphasis on applied anatomy of importance to physical medicine and rehabilitation.

Anat 8000s. *ANATOMY OF THE PELVIS-PERINEUM.* (2 cr) Cahill, Podratz
Six two hour dissection and demonstration periods on the female pelvis and perineum. Primarily intended for residents in ObGyn.

Anat 8851. *ANATOMY FOR GENERAL SURGEONS.* (3 cr) Cahill
Surgical anatomy of the thorax, abdomen, pelvis and neck, by dissection, demonstration and discussion. Also listed under S.

Anat 8852s. *SURGICAL ANATOMY OF HEAD AND NECK.* (3 cr; offered 1992 and alt yrs) Cahill, Carmichael, Kasperbauer
Cadaver dissection and lecture demonstration. Laboratory participation required for credits. Also listed under ENT.

Anat 8855f,w,s,su. *ORTHOPEDIC ANATOMY.* (2 cr) Carmichael and staff

Lectures, prosections and demonstrations of gross anatomy of the musculoskeletal system with special emphasis on relationships and surgical approaches. Also listed under Or.

Anat 8860f,w,s. *SPECIAL TOPICS IN ANATOMY.* (1-4 cr) Cahill
Dissection of cross-sections and/or regions of special interest.

BIOCHEMISTRY

Bioc 5200f,w,s. *MOLECULAR AND CELL BIOLOGY WORKSHOP.* (1 cr/yr) Strehler, Maher
Work-in-progress presentations on experimental research projects, given by graduate students and postdoctoral research fellows.

Bioc 5858f,w,s,su. *LABORATORY ROTATIONS IN BIOCHEMISTRY.* (2 cr/8 wks) Staff
Tutorial course involving methods of isolation, characterization, and assay of subcellular particles, proteins, nucleic acids, lipids, steroids, and carbohydrates. General techniques, instrumental analyses, and special procedures emphasized. A minimum of three rotations are required.

Bioc 8000f. *GENERAL BIOCHEMISTRY: STRUCTURE.* (3 cr; prereq calculus, organic chemistry, quantitative analytical chemistry or #) Owen
Structure in biological materials; structure in membranes, proteins and nucleic acids with emphasis on methods used to study macromolecular structure.

Bioc 8001w. *GENERAL BIOCHEMISTRY: KINETICS, CATALYSIS AND MECHANISMS.* (3 cr; prereq Bioc 8000) Rusnak
Enzyme mechanisms and kinetics, with emphasis on bioorganic chemistry and interpretation of rate data.

Bioc 8002s. *GENERAL BIOCHEMISTRY: ENERGY TRANSDUCTION AND SIGNALLING.* (3 cr; prereq Bioc 8001) Penniston
Mechanisms of energy transduction and signalling within cells.

Bioc 8005w. *PHYSICAL BIOCHEMISTRY.* (1 cr; prereq Bioc 8000 or equiv) Macura
Physical principles and measurement including spectroscopy, hydronamics, energetics.

Bioc 8010s. *PHYSICAL BIOCHEMISTRY.* (1 cr; prereq Bioc 8000 or equiv) Bajzer
Physical principles and measurement including spectroscopy, hydronamics, energetics.

Bioc 8015su. *PHYSICAL BIOCHEMISTRY.* (1 cr; prereq Bioc 8000 or eqiv) Owen
Physical principles and measurement including spectroscopy, hydronamics, energetics.

Bioc 8020f. *TUTORIAL IN QUANTUM MECHANICS.* (1 cr) Burghardt
The principles of quantum mechanics will be presented with emphasis on applications to problems in magnetic resonance and the interaction of light with matter.

Bioc 8030s. *DATA FITTING AND MODEL PARAMETER ESTIMATION.* (3 cr; prereq Linear Algebra, Calculus) Bajzer
An introduction to modeling and methods for data fitting with applications to biomedical sciences. Theoretical knowledge along with emphasis on data reduction practice are offered to provide sufficient skills in using data fitting procedures. Also listed under Molecular Biology.

Bioc 8050f. *PRINCIPLES OF CELL AND TISSUE DESIGN.* (3 cr; prereq MBio 5000 concurrent or equivalent) Salisbury, McNiven
This course covers general aspects of cell structure with particular emphasis on nuclear organization (exclusive of DNA!), membrane structure and dynamics, protein targeting and processing as they relate to cell structure, protein phosphorylation, calcium-binding proteins, the cytoskeleton (interphase and mitotic) and vesicular transport. Also listed under Molecular Biology.emphasis on data reduction practice are offered to provide sufficient skills in using data fitting procedures. Also listed under Molecular Biology.

Bioc 8101w. *REPLICATION AND TRANSCRIPTION REGULATION.* (3 cr; prereq undergraduate biochemistry) McMurray, Getz
This course will discuss the structure and function of replication and transcription complexes. Emphasis will be placed on control mechanisms and energetics of transcription/replication in prokaryotes and eukaryotes. Also listed under Molecular Biology.

Bioc 8102s. *REGULATION OF PROTEIN SYNTHESIS.* (3 cr; prereq general background in biochemistry or molecular biology) Toft
General and specialized aspects of protein synthesis and processing will be covered. Regulation of protein synthesis at several posttranscriptional levels will be included. Also listed under Molecular Biology.

Bioc 8290. *INDEPENDENT STUDY IN BIOCHEMISTRY.* (1-2 cr) Staff
Tutorials arranged on an individual basis in selected advanced topics in Biochemistry. Students will be expected to define a topic and specific reading list in consultation with a member of the faculty. Mastery of the subject matter will be assessed by examination or by submission of a formal review of the subject area.

Bioc 8300. *MASTER'S PROJECT IN BIOCHEMISTRY.* (3 cr) Staff
Readings in Biochemistry culminating in the submission of the Master's Thesis. Topics will be chosen by student in consultation with the advisor and the student's advisory committee. May be taken only once for credit.

Bioc 8500f,w,s. *BIOCHEMISTRY AND MOLECULAR BIOLOGY JOURNAL CLUB.* (1 cr) Rusnak, Wieben
Students of the Molecular Biology program will present current readings in the general areas of Cell and Molecular Biology.

Bioc 8501w. *FOCAL TOPICS IN GROWTH REGULATION.* (2 cr; prereq MBio 8005, Imm 8862 or #) Leof
Three areas of current study in growth regulation will be examined. This will permit an in-depth four week study of each. Potential topics will include ERKs/MAP kinases, tyrosine kinases, T cell antigen receptor signalling, cell cycle control, cyto-architecture, and tumor suppressors.

Bioc 8550f. *BIO-ORGANIC CHEMISTRY.* (3 cr; offered even yrs) Rusnak
A chemical approach to understanding enzyme catalysis. This course will cover extensively both theoretical and experimental methods aimed at elucidating the chemical details of enzyme action. Topics include radical reactions in biology, biometric catalysis, catalytic antibodies, catalytic RNA, enzyme mechanisms, and metalloprotein biochemistry.

Bioc 8700f,w,s. *SEMINAR IN PULMONARY CELLULAR BIOCHEMISTRY.* (1 cr) Vuk-Pavlovic, Z.
Review and criticism of the current literature concerning pulmonary cellular biochemistry.

Bioc 8705f. *CELLULAR MECHANISMS IN PULMONARY HOST-DEFENSE FUNCTION.* (2 cr; offered even yrs) Limper
This course will focus on defining the biochemical reactions that make up the signal transduction processes in stimulated lung cells. Alveolar macrophages will be the principle cells studied. Students will choose appropriate journal articles and present the material to the members of the class.

Bioc 8710w. *TOPICS IN MEMBRANE LIPIDS.* (2 cr; prereq Bioc 8000 or #) Pagano
The following will be covered: Lipid structures and properties; Liposomes: Organization of lipids in membranes; Cholesterol uptake and metabolism; Lipid traffic in eukaryotic cells; Lipid second messengers; and Lipid metabolic diseases.

Bioc 8715f,w,s. *MOLECULAR MECHANISMS OF SECRETION.* (1 cr) McNiven, Fernandez, Pagano
This course will review the rapidly expanding field of protein and lipid trafficking through the secretory pathway of eukaryotic cells. Papers reviewed will focus on the molecular mechanisms of membrane budding, transport, targeting, and fusion between endoplasmic reticulum, Golgi apparatus, and the plasma membrane. Special attention will be placed on the contributions of the small and trimeric GTP-binding proteins, molecular motor enzymes, COP proteins, and SNARE/SNAP complexes to secretory vesicle biogenesis and subsequent exocytic release. Also listed under Molecular Biology.

Bioc 8801f,w,s. *TUTORIAL: CONCEPTS OF VESICULAR TRAFFICKING.* (1 cr; prereq Bioc 8050) McNiven, Urrutia
Study of the basic mechanisms by which cells package, process, and transport synthesized and/or endocytosed proteins.

Bioc 8806s. *PHARMACOLOGY OF RECEPTORS.* (3 cr; offered odd yrs) Brimijoin and staff
Origin of concept of drug receptor interaction; molecular basis for drug macromolecule interactions; mathematical theories; isolation and physicochemical characterization useful in pharmacology. Also listed under Pharmacology.

Bioc 8860w. *BASIC METHODS IN BIOCHEMISTRY AND MOLECULAR BIOLOGY.* (2 cr; offered odd yrs; prereq #) Oursler
Lectures on the more general, routine methods in Biochemistry and Molecular Biology. The description and demonstration of the method, the

basic principles of and theory behind the methods, the interpretation of the results, the limitations of the method, and the artifacts to be avoided are included. The general operation and application of instruments are also described. Students participate in the presentation of topics.

Bioc 8863w. *MOLECULAR BIOLOGY: THEORY AND APPLICATION.* (3 cr; prereq MBio 5000; offered odd yrs) McMurray
Students will gain a thorough working knowledge of molecular biology. The course will deal with theoretical aspects of the techniques as a basis for their practical application. The course will use computer technology to aid in the design and application of all techniques.

Bioc 8905w. *PCR: THEORY, METHODS, AND APPLICATIONS.* (1 cr) Urrutia
This course is designed to analyze the basic principles of the most advanced PCR-based laboratory techniques. Emphasis will be given to the description of up-to-date PCR strategies. Protocols will be offered as a compilation of proven methods that can be easily repeated in the attendant's laboratory. Also listed under Molecular Biology and Molecular Neurosciences.

Bioc 8910f,w,s,su. *MOLECULAR CONTROL OF CELL DIFFERENTIATION.* (1 cr) Urrutia
Discussion of classic, as well as current, articles on the mechanisms underlying cell commitment, pattern formation, and phenotype acquisition. Emphasis will be given to articles on transcription factors and their target genes during embryogenesis, teratogenesis, and carcinogenesis. Also listed under Molecular Biology and Molecular Neurosciences.

Research

Bioc 8890. *RESEARCH IN BIOCHEMISTRY.* Staff
Graduate thesis research for Ph.D. students under supervision of staff.

Bioc 8895. *RESEARCH IN BIOCHEMISTRY.* (6 cr/qtr) Staff
Graduate thesis research for Master's students under supervision of staff.

Biophysical Sciences

BPhy 5001f,w,s,su. *LABORATORY ROTATIONS IN BIOPHYSICAL SCIENCES.* (1 cr) Staff
Laboratory rotation lasting four weeks. Familiarizes students with the techniques and procedures in the areas of expertise and research specialization of the investigators in the area of Biophysical Sciences. Specific laboratory methods of ultrasonic imaging, x-ray imaging, and radioisotope imaging will be studied as they are practiced in the laboratories of the investigators of Mayo Clinic.

BPhy 5002f,w,s,su. *LABORATORY ROTATIONS IN BIOPHYSICAL SCIENCES.* (2 cr) Staff
Laboratory rotation lasting eight weeks. Familiarizes students with the techniques and procedures in the areas of expertise and research specialization of the investigators in the area of Biophysical Sciences.

Specific laboratory methods of ultrasonic imaging, x-ray imaging, and radioisotope imaging will be studied as they are practiced in the laboratories of the investigators of Mayo Clinic.

BPhy 5003f,w,s,su. *LABORATORY ROTATIONS IN BIOPHYSICAL SCIENCES.* (3 cr) Staff
Laboratory rotation lasting twelve weeks. Familiarizes students with the techniques and procedures in the areas of expertise and research specialization of the investigators in the area of Biophysical Sciences. Specific laboratory methods of ultrasonic imaging, x-ray imaging, and radioisotope imaging will be studied as they are practiced in the laboratories of the investigators of Mayo Clinic.

BPhy 5100f. *RADIOLOGICAL HEALTH.* (2 cr; #) Vetter
Introduction to concepts of radiological health, philosophy and principles of radiation protection, interpretation of standards and regulations, and planning of facilities and activities.

BPhy 5150w. *INTRODUCTORY RADIATION BIOLOGY.* (2 cr) Bonner
Emphasis is on understanding the actions of radiation on living systems including physico-chemical interactions, effects at the molecular, cellular, tissue, and organismal levels, carcinogenesis, genetic effects, and embryo-fetus effects; mechanisms providing basis of radiation therapy are stressed.

BPhy 5160w. *INTRODUCTION TO RADIOLOGIC PHYSICS AND RADIATION DOSIMETRY.* (3 cr; prereq calculus, atomic or modern physics; offered even yrs) Felmlee
This is an introductory graduate course designed for those interested in the radiation sciences. It will rigorously cover ionizing radiation, interactions, cavity theory, and dosimetry fundamentals.

BPhy 5225f. *INTRODUCTION TO NEURAL NETORKS.* (3 cr; offered even yrs; prereq background of computer science, engineering or #) Manduca
This course will provide a theoretical and practical understanding of the most important artificial neural network models. The focus will be on practical applications of the technology.

BPhy 5250w. *ANATOMY FOR BIOMEDICAL IMAGERS.* (2 cr; offered odd yrs) Carmichael
This is a tutorial style course wherein each student dissects a region of interest and prepares a demonstration on that region for the other students. An overview of human anatomy will also be presented.

BPhy 5400w. *MOLECULAR ELECTRONICS.* (3 cr; offered odd yrs) Fernandez
This course will cover the theory of operation of the patch-clamp amplifier as it is used to study single ion channels and fusion pores. Students will be required to build a complete patch-clamp amplifier, demonstrate their performance and show a good understanding of the theory of operation. Prior knowledge of electronics is not required.

BPhy 5450f. *BIOMEDICAL IMAGING I - FUNDAMENTAL CONCEPTS.* (4 cr) Robb and staff
Provides an introduction to important concepts in applied biomedical imaging, including discussion of image composition, interactive display, image processing and segmentation, and quantitative analysis. Practical applications in basic science and medicine are discussed. Students will use

ANALYZE biomedical imaging software developed at Mayo to investigate these topics.

BPhy 5500w,s. *TUTORIAL IN COMPUTER ORGANIZATION AND PROGRAMMING.* (3 cr) Robb and staff
Provides an introduction to the architecture and functional organization of computers, and familiarity with the fundamental concepts and techniques for programming a computer, including learning the C programming language. for programming a computer, including learning the C programming language.

BPhy 5520s,su. *ALGORITHMS AND PROBLEM SOLVING.* (2 cr) Robb
A hands-on introduction to common software tools used in data analysis; matrix mathematics, statistical processing, image processing and analysis.

BPhy 5610s. *IMAGING AND COMPUTERS.* (3 cr; prereq BPhy 5450 or 5500 desirable) Robb and staff
This course will expose students to modern workstation computers and a variety of image processing computational techniques. Topics include serial and parallel processing, shared memory, kernal threading, remote procedure calls, vector and MPP systems. Theory will be coupled with working examples.

BPhy 5740f. *MAGNETIC RESONANCE IMAGING SYSTEMS.* (3 cr; prereq advanced calculus, Fourier analysis, and a course in modern physics) Riederer
Introduction to physics and engineering aspects of modern diagnostic magnetic resonance imaging (MRI).

BPhy 5800w. *PHYSICS AND TECHNICAL PRINCIPLES OF MEDICAL IMAGING.* (3 cr; prereq General and Modern Physics, Calculus, and Fourier analysis or #) McCollough
An in-depth study of the fundamental principles of medical image formation. Diagnostic imaging modalities to be covered include: Radiographic X-ray Imaging, X-ray Computed Tomography, Digital Radiography, Nuclear Medicine, Ultrasound, and Magnetic Resonance Imaging.

BPhy 5900f,w,s,su. *MASTER'S PROJECT IN BIOMEDICAL IMAGING.* (5 cr) Staff
This course is comprised of a special laboratory project in image acquisition, processing, and/or analysis in which the student uses tools and skills learned in coursework on solving a practical problem in biomedical imaging applications. The course is required for Employee Master's Degree candidates. The student must write a report on the project.

BPhy 8100f. *MEDICAL HEALTH PHYSICS.* (2 cr; prereq BPhy 5100 or equiv; #) Vetter
Radiation protection philosophy and principles as applied to the medical environment: protection of patients, public, and employees; procedures for obtaining Nuclear Regulatory Commission license.

BPhy 8150s. *RADIATION THERAPY PHYSICS.* (4 cr; prereq 5800 or equiv) Bourland
The physics of radiation therapy: radiation interactions, production,

quality, and measurement, dose functions and calculations, external beam treatment planning, calibration protocols, brachytherapy, radiation protection and special procedures.

BPhy 8300f,s. *TUTORIAL IN VISUAL PERCEPTION AND PSYCHOPHYSICS.* (2 cr; #) Gray
Effects of contrast and noise on visual detection. Emphasis will be placed on psychophysical aspects of imaging and techniques for psychophysical evaluation of image quality. Topics will include receiver operating characteristics (ROC) analysis as well as other appropriate techniques.

BPhy 8301su. *TUTORIAL IN HIGH--SPEED SIGNAL PROCESSING.* (2 cr; prereq Bioengineering) Gilbert
Very high-speed computer architecture and circuits.

BPhy 8302. *TUTORIAL IN ULTRASONIC IMAGING.* (2 cr; #) Greenleaf
Principles and methods of imaging tissue and related parameters.

BPhy 8304f,w,s. *TUTORIAL IN PHYSIOLOGICAL IMAGING.* (2 cr; prereq Physiology series) Ritman
X-ray imaging of physiological systems and analysis of resulting data.

BPhy 8420s. *WAVE PROPAGATIONS AND THEIR MEDICAL APPLICATIONS.* (2 cr; prereq college physics) Lu
Wave propagation is a fundamental phenomenon of acoustics, electromagnetics, and optics. This course will emphasize the wave propagation of ultrasound and their applications to medical imaging and tissue property identification. New beams such as limited diffraction beams and localized waves and their potential medical applications will be studied.

BPhy 8450w. *BIOMEDICAL IMAGE PROCESSING II - INTERMEDIATE ANALYSIS.* (3 cr; prereq BPhy 5450 or equivalent) Robb
Digital processing of images, image signal characteristics, histogram analysis, domain processing, digital filters, image compression, reconstruction from projections.

BPhy 8470s. *TWO-DIMENSIONAL DIGITAL SIGNAL PROCESSING.* (3 cr; prereq BPhy 8700 or working knowledge of linear system theory and one-dimensional digital signal processing) Ottesen
Fundamentals of 2-D digital signal processing, including Fourier and V-transforms, discrete cosine transforms, and finite impulse responses; foundation for image processing.

BPhy 8490s. *BIOMEDICAL IMAGE PROCESSING III - ADVANCED TOPICS.* (3 cr; prereq BPhy 5450, BPhy 8450 or equivalent experience/courswork) Manduca
An in-depth study of difficult problems in imaging science as they relate to biomedical images. Areas of study include image segmentation, image registration, texture analysis, shape description and matching, deconvolution, multispectral analysis, 3-D and 4-D image reconstruction and display (volume rendering).

BPhy 8500w,s. *TUTORIAL IN IMAGING SCIENCE.* (2 cr; prereq BPhy 8450, 8470 and 8490 or equivalent experience) Robb

Special topics in the imaging sciences; including 3-D imaging, volume rendering, image segmentation, image registration and correlations, shape description and analysis, multi-spectral imaging.

BPhy 8600f,w,s,su. *BIOPHYSICS/BIOENGINEERING SEMINARS.* (1 cr) Lu
Presentations of research topics, activities, and results from the Biodynamics Research Unit. Students are required to give a presentation, of a published article review or of their research project, during the course.

BPhy 8704f. *DIGITAL SIGNAL PROCESSING I.* (3 cr; prereq an introduction to complex variables and an exposure to linear systems theory for continuous time signals, including Laplace and Fourier transforms. No previous knowledge is required of discrete time signals, Z-transforms, or discrete Fourier transforms) Ottesen
First of a two-part series starts with discrete time signals and systems, and the effects of sampling. It moves into the areas of Discrete Fourier Transforms (DFT), Z-transforms, convultions, signal flow-graphs, and various methods for design of common digital filters of the Infinite Impulse Response (IIR) and Finite Impulse Response (FIR) types.

BPhy 8705w. *DIGITAL SIGNAL PROCESSING II.* (3 cr; prereq BPhy 8704 or #) Ottesen
Advanced designs of digital filters will be covered, followed by the effects of noise and introductions of the discrete Wiener and the steady-state Kalman filters. An introduction to adaptive digital signal processing and a discussion of the Fast Fourier Transform (FFT) will be given. The course concludes with two-dimensional Digital Signal Processing, its theory and approach for designing digital filters to be used in image processing.

BPhy 8740w. *MAGNETIC RESONANCE IMAGING SYSTEMS - ADVANCED TOPICS.* (3 cr; prereq BPhy 5740; offered even yrs) Riederer
A technical study of advanced topics in contemporary magnetic resonance imaging (MRI). Topics to be discussed include vascular imaging and flow assessment, motion effects and compensation, echo-planar imaging, cardiac imaging, and neuro-functional MRI.

BPhy 8750f,w,s. *MAGNETIC RESONANCE TECHNICAL SEMINAR.* (1 cr; #) Riederer
Seminar held weekly consisting of a presentation of some contemporary technical research topic in magnetic resonance.

BPhy 8770s. *FUZZY LOGIC THEORY AND APPLICATIONS.* (3 cr, prereq BPhy 8704 and an interest in intelligent systems and decision and control; offered odd yrs) Ottesen
Fuzzy logic theory and applications is intended for students and practicing scientists and engineers. It covers the applied concepts of fuzzy logic to several application areas. There will be homework, case studies, and class projects.

BPhy 8852f,w,s,su. *SEMINARS IN BIOPHYSICAL SPECIALTIES.* (1 cr) Staff
Specialized area of biophysical sciences reviewed in depth. Research papers presented by students and staff with active discussion.

BPhy 8853f,w,s,su. *READINGS IN BIOPHYSICAL SCIENCES.* (2 cr) Staff

Research

BPhy 8890. *RESEARCH IN BIOPHYSICAL SCIENCES.* Staff
Opportunities in research to be arranged with individual staff members.

UNITE courses from University of Minnesota

CSci 5107. *COMPUTER GRAPHICS I.* (4 cr; prereq CLA CSci major or IT CSci major upper div. or Grad; 3107 or 5101 and 5121 or #)
Introduction. Definition of interactive computer graphics, its goals and its problems. A model system. Data structures for computer graphics, picture structure and transformations. Structures of graphical programming languages. Interaction handling. Raster graphics.

CSci 5117. *COMPUTER GRAPHICS II.* (4 cr; prereq CLA CSci major or IT CSci major upper division or Grad; 3107 or 5101 and 5107 and 5121 or #)
Introduction to vector geometry. Three-dimensional modeling and viewing transformations. Perspective viewing generation and 3-D clipping. Introduction to curves and surfaces. Hidden line and hidden surface removal. Realistic image generation. Advanced display system architectures. Modeling of 3-D graphics programming.

CSci 5301. *NUMERICAL ANALYSIS.* (4 cr; prereq Math 3142 or equivalent or #...a knowledge of FORTRAN or PASCAL is assumed)
Floating point arithmetic and rounding errors. Iterative methods. Numerical solution of nonlinear equations. Newton's method. Direct methods for linear systems of equations. Gaussian elimination. Factorization methods. Interpolation and approximation. Numerical integration and differentiation. Introduction to numerical solution of ordinary differential equations.

CSci 5511. *ARTIFICIAL INTELLIGENCE I.* (4 cr; prereq CLA CSci major or IT CSci major upper div. or Grad, 5121 or #)
Introduction to the ideas and issues of Artificial Intelligence. Knowledge representation, problem solving, search, inference techniques, theorem proving. Expert systems. Introduction to applications of Artificial Intelligence. Artificial Intelligence programming languages.

CSci 8511. *ADVANCED CONCEPTS IN ARTIFICIAL INTELLIGENCE.*
(4 cr; prereq #)
In-depth coverage of selected areas of active research in artificial intelligence. Possible topics include machine perception, expert systems, robotics, natural language processing.

Phy 5551. *TOPICS IN PHYSICS FOR BIOLOGY AND MEDICINE* - Mechanics in Molecular Physics. (5 cr; prereq general physics and calculus; offered alt yrs)
Statics (forces in bones and joints). Graphical analysis. Statistical physics (entropy, reversibility, Boltzmann factor and Nernst equation, Browmian movement, free energy). Diffusion, bulk flow, and osmosis.

Phy 5552. *TOPICS IN PHYSICS FOR BIOLOGY AND MEDICINE* - Electricity and Signals. (5 cr; prereq general physics and calculus; offered alt yrs)
Electricity and circuits (electrocardiogram, networks, nerve conduction);

transducers, amplifiers, feedback and control; oscillators; signal analysis (Fourier analysis, correlation functions, power spectra).

Phy 5553. *TOPICS IN PHYSICS FOR BIOLOGY AND MEDICINE* - Lights Atoms and Nuclei. (5 cr; prereq general physics and calculus; offered alt yrs)
Atoms (dispersion, absorption, spectra, polarized light). X-rays (production, absorption, dosimetry). Nuclei (nuclear size, mass, decay).

DENTISTRY

Orthodontics

Didactic

Odon 8806f,w,s,su. *ORTHODONTIC SEMINAR: TECHNIQUE.* (1 cr) Staff
Seminar on technical orthodontic procedures.

Odon 8807f,w,s,su. *ORTHODONTIC SEMINAR: LITERATURE REVIEW.* (1 cr) Staff
Classical orthodontic literature as well as current literature review.

Odon 8808f,w,s,su. *ORTHODONTIC SEMINAR: CASE PRESENTATION.* (1 cr) Staff
Cases with complete records reviewed and new patient treatment plans discussed.

Odon 8809f,w,s. *SURGICAL ORTHODONTIC SEMINAR.* (1 cr) Lund, Sather
Case presentation, illustration, diagnostic and treatment procedures that encompass the various dental specialties.

Odon 8810 w. *CLINICAL ORO-FACIAL PATHOLOGY AND DEVELOPMENTAL DISORDERS.* (1 cr; offered every 3rd yr; prereq D.D.S., D.M.D., M.D. or equivalent required) Larson
A review of the clinical presentations of many congenital and acquired pathological disorders, developmental deficiencies, and malformations important to the dental specialist.

Odon 8811 w. *FACIAL GROWTH AND DEVELOPMENT.* (1 cr; offered every 3rd yr; prereq basic background in the anatomy and physiology of human facial growth and development) Guenthner
The one-quarter course will primarily consist of reviewing current knowledge of the growth and development of the human face from conception to adulthood. A course textbook will be utilized as well as classical and current literature which will be used to evaluate current state-of-the-art knowledge and discuss issues related to current clinical procedures and their effect on facial growth.

Research

Odon 8857f,w,s,su. *RESEARCH IN SELECTED PROBLEMS.* (2 cr) Staff
Arrangements for research in selected areas related to minor.

Clinical

Odon 8800f,w,s,su. *ADVANCED ORTHODONTIC TECHNIQUES.* (3 cr) Staff
Initial technical procedures in preparation for clinical patient care. Technical procedures on the typodont, model preparation, photography, metallurgy, and cephalometrics.

Odon 8802f,w,s,su. *ORTHODONTIC CASE ANALYSIS.* (6 cr) Staff
First phase involves complete review of previously treated cases. Second phase is application of basic analytic principles to clinical patients.

Odon 8803f,w,s,su. *ORTHODONTIC TREATMENT PLANNING.* (6 cr) Staff
Mechanical principles coordinated with case analyses to provide the treatment plan. Force analysis and biomechanics of tooth movement.

Odon 8804f,w,s,su. *CLINICAL ORTHODONTICS.* (6 cr) Staff
Individual treatment care and clinical observation. Treatment care coordinated with other services in selected instances in the hospital.

Odon 8805f,w,s,su. *ADVANCED CLINICAL ORTHODONTICS.* (6 cr) Staff
Final treatment care of individual patients.

Odon 8851f,w,s,su. *DENTAL ROENTGENOLOGY.* (1 cr) Staff
Includes x-ray diagnosis and techniques.

Odon 8852f,w,s,su. *ORAL DIAGNOSIS.* (5 cr) Staff
Clinical course in diagnosis related to dental problems.

Periodontics

Didactic

Pdon 8883f,w,s,su. *PERIODONTIC SEMINAR.* (1 cr) Reeve, Sheridan
Literature review and discussion.

Pdon 8884f,w,s,su. *PATHOLOGY OF PERIODONTAL DISEASE.* (1 cr) Reeve, Sheridan Histopathology of periodontal disease. Oral mucous membrane; calcified tissues. .

Research

Pdon 8857f,w,s,su. *RESEARCH IN SELECTED PROBLEMS.* (2 cr) Reeve, Sheridan and staff

Clinical

Pdon 8851f,w,s,su. *DENTAL ROENTGENOLOGY.* (1 cr) Reeve, Sheridan
X-ray diagnosis and technique.

Pdon 8852f,w,s,su. *ORAL DIAGNOSIS.* (5 cr) Reeve, Sheridan
Clinical diagnosis related to dental problems.

Pdon 8859f,w,s,su. *PERIODONTAL AND PROSTHODONTIC CONSIDERATIONS IN DENTISTRY.* (1 cr) Eckert, Reeve

Pdon 8880f,w,s,su. *CLINICAL PERIODONTICS.* (6 cr) Reeve, Sheridan
Etiology, diagnosis, and treatment of periodontal disease.

Pdon 8881f,w,s,su. *ADVANCED CLINICAL PERIODONTICS.* (6 cr) Reeve, Sheridan
Case presentation and treatment of difficult periodontal problems.

Prosthodontics

Didactic

Pros 8841. *PROSTHODONTIC SEMINAR.* (1 cr; offered f 1992, w 1993, every 3rd year) Desjardins, Eckert
Literature review and discussion of past and current concepts and practices of complete denture prosthesis.

Pros 8843w. *PROSTHODONTIC SEMINAR.* (1 cr; offered w 1994, every 3rd yr) Desjardins, Eckert
Literature review and discussion of past and current concepts and practices of removable partial denture prosthesis.

Pros 8845s. *FIXED PROSTHODONTIC SEMINAR.* (1 cr; offered s 1993, every 3rd yr) Eckert
Clinical and laboratory phases of prosthodontics; principles, practices, and concepts related to fixed prosthodontics.

Pros 8847w. *SEMINAR: MAXILLOFACIAL PROSTHETICS (INTRAORAL) ADVANCED PROSTHODONTICS.* (1 cr; offered w 1995, every 3rd yr) Desjardins, Eckert
Literature review and discussion of past and current concepts and practices of implant prosthodontics and maxillofacial prosthetics.

Pros 8848f,w,s. *SEMINAR: CURRENT LITERATURE.* (1 cr) Desjardins, Eckert
Review and discussion of practical, clinical, or laboratory applications of current literature in prosthodontics and related fields.

Pros 8849s. *SEMINAR: MAXILLOFACIAL PROSTHETICS (EXTRAORAL) ADVANCED PROSTHODONTICS* (1 cr; offered s 1992, every 3rd yr) Desjardins, Eckert
Lectures and discussions on clinical and laboratory procedures involved in fabrication of extraoral prostheses.

Pros 8850f. *IMPLANT PROSTHODONTICS.* (1 cr; offered f 1994, every 3rd yr) Desjardins, Eckert
Literature review and discussion of past and present concepts and practices of implant prosthodontics.

Pros 8859f,w,s. *PERIODONTAL AND PROSTHODONTIC CONSIDERATIONS IN DENTISTRY.* (1 cr) Eckert, Reeve
This course is designed to promote serious discussions of subjects of interest in the areas of periodontology and prosthodontics. The interrelationship of the two fields is stressed.

Pros 8862s. *DENTAL MATERIALS.* (1 cr; offered s 1994, every 3rd yr) Desjardins, Eckert
Discussion of physical properties, mechanical properties, and technical procedures related to dental materials most commonly used in prosthodontics.

Pros 8870f. *OCCLUSION.* (1 cr; offered f 1993, every 3rd yr) Eckert
A series of detailed discussions of the principles, practices, and concepts of occlusion.

Pros 8871f,w,s. *PHYSIOLOGY, PHARMACOLOGY AND PRE-PROSTHETIC SURGERY.* (1 cr; offered f 1996, and every 4th yr) Eckert, Desjardins
Discussion of physiology of major organ systems in conjunction with pharmacologic management of disorders of these systems. Pre-prosthetic surgery is discussed and reviewed through an evaluation of the literature.

Pros 8872su. *PROSTHODONTIC PRACTICE MANAGEMENT.* (1 cr/yr) Eckert, Desjardins
Discussion of topics related to the management of a prosthodontic practice.

Pros 8873f,w,s. *CARDIO-MANDIBULAR DISORDERS AND FACIAL PAIN.* (1 cr; prereq Pros 8870; offered f 1996 and every 4th yr) Eckert, Desjardins, Lund, Reeve
Literature review and discussion of past and current concepts and practices in the management of patients with cardio-mandibular disorders including myofascial pain dysfunction, temperomandibular disorders and atypical face pain.

Pros 8874f,w,s. *PROSTHODONTIC MANAGEMENT OF THE GERIATRIC PATIENT.* (1 cr; offered f 1996 and every 4th yr) Eckert, Desjardins
Literature review and discussion of medical complications found in the geriatric patient with emphasis placed on special considerations made during prosthodontic treatment.

Research

Pros 8857f,w,s,su. *RESEARCH IN SELECTED PROBLEMS.* (2 cr; offered 4 quarters of final year) Desjardins, Eckert

Clinical

Pros 8840f,w,s,su. *CLINICAL PROSTHODONTICS: COMPLETE DENTURES.* (6 cr) Desjardins, Eckert
Orientation and introduction to clinical and laboratory phases of prosthodontics in the medical center with emphasis on principles, concepts, and practices related to complete denture prosthesis.

Pros 8842f,w,s,su. *CLINICAL PROSTHODONTICS: PARTIAL DENTURES.* (6 cr) Desjardins, Eckert

Orientation and introduction to clinical and laboratory phases of prosthodontics in the medical center with emphasis on principles, concepts, and practices related to removable and fixed partial denture prosthesis.

Pros 8844f,w,s,su. *MAXILLOFACIAL PROSTHETICS (INTRAORAL)/IMPLANT PROSTHODONTICS ADVANCED PROSTHODONTICS.* (6 cr) Desjardins, Eckert
Clinical and laboratory procedures involved in management of patients with acquired, congenital, and developmental intraoral defects.

Pros 8846f,w,s,su. *MAXILLOFACIAL PROSTHETICS (EXTRAORAL) ADVANCED PROSTHODONTICS.* (6 cr) Desjardins, Eckert
Clinical and laboratory procedures involved in management of patients with acquired and congenital extraoral defects.

Pros 8851f,w,s,su. *DENTAL ROENTGENOLOGY.* (1 cr) Lund
Xray diagnosis and technique.

Pros 8852f,w,s,su. *ORAL DIAGNOSIS AND TREATMENT OF CRANIO-MANDIBULAR DISORDERS.* (2 cr) Lund
Clinical diagnosis related to dental problems.

Pros 8854f,w,s,su. *IMPLANT PROSTHODONTICS.* (6 cr) Eckert, Desjardins
Clinical and laboratory procedures involved in the management of patients who receive prostheses supported and retained by endosseous implants.

Pros 8876f,w,s,su. *CLINICAL PROSTHODONTICS: FIXED PARTIAL DENTURES.* (6 cr) Eckert
Presentation and introduction to clinical and laboratory phases of prosthodontics in the medical center with emphasis on principles, concepts and practices related to fixed partial denture prostheses.

Pros 8880f. *DENTAL LABORATORY TECHNOLOGY.* (6 cr) Desjardins, Eckert
A full-time clinical assignment to familiarize the resident with all aspects of laboratory technology used in the fabrication of fixed, removable and maxillofacial prostheses.

ETHICS

ETHIC 5000su. *MAINTENANCE OF SCIENTIFIC INTEGRITY AND ETHICAL CONDUCT IN BIOMEDICAL RESEARCH.* (1 cr) Staff
A series of presentations on various aspects of biomedical ethics.

HEALTH SCIENCES RESEARCH

HSR 5000s. *INTRODUCTION TO HEALTH SERVICES RESEARCH.* (1 cr) Evans
This course will present basic concepts, theory, and methods associated with health services research. This multidisciplinary field will be critically appraised from both a sociological and an economic perspective. The limitations of a clinical perspective will be delineated. The following topics will be covered during the course: health care economics, technology assessment, health care financing, outcome measurement and analysis, medical appropriateness evaluation, risk adjustment, severity measurement, economic determination analysis (includingt cost-effectiveness analysis), quality of care measurement, and continuous quality improvement. This course will focus on the foregoing topics as they relate to the organization and delivery of health care services. An

essential distinction will be made between the goals of research and the dogma sometimes associated with continuous quality improvement. Finally, the relationship between health services research and the coverage and reimbursement policies of third party payers will be explored. This course will be presented in the form of lectures by several instructors.

HSR 5200su. DESIGN OF CLINICAL RESEARCH. (1 cr) Gray
This course will present the principles and methodologic concepts relevant to the design of clinical research. The focus of this course will be on translation of research questions into study designs that allow hypotheses to be tested. Topics that will be addressed include: conception of a testable hypothesis, specification of a research design, development of measurement instruments, sample size and power considerations, and planning data analysis. This course will consist of lectures by the instructor. The students participating in the course will develop their own clinical research proposal for review by the instructors and peers and present it for critique by the class.

HSR 5300s. *PHILOSOPHY OF INFERENCE.* (1 cr; prereq HSR 5823) Bailey
The two main schools of inference, Bayesian and frequentist, will be compared and contrasted, using actual data sets and inference problems. The role of each approach will be examined, as well as strengths and weaknesses of each. The difference between a confidence interval and a posterior probability interval, and between a P-value and the posterior probability of a hypothesis, will be delineated. Specific inference problems will be used to compare the approaches, including sequential monitoring and inference, multiple comparisons, model selection and prediction, and nuisance parameter problems. The empirical Bayes approach, and the likelihood principle, will also be touched on.

HSR 5400su. *INTRODUCTION TO STATISTICAL MODELS.* (1 cr) Wollan
A survey of families of statistical models most often used in clinical research, emphasizing consequences of the choice of model, interpretation of the model, and interpretation of statistical conclusions about the model. Choice of model based on type of data, choice based on goodness-of-fit, and choice based on tradition. Interpretation of coefficients and confidence intervals for coefficients. Interpretation of hypothesis tests for individual coefficients and hypothesis tests for groups of coefficients. Checking assumptions of a model, and alternatives if they are violated, such as transformations and non-parametric methods. Sample sizes and power. Examples chosen from recent medical research.

HSR 5410su. *DESIGN OF CLINICAL STUDIES.* (1 cr; prereq HSR 5400 or equiv) Wollan
Introduction to types of designs frequently used in clinical studies. Discussion of structure of clinical studies, factorial studies, matched observations and surveys. Examples will be chosen from recent medical research, with discussion of the reasons for choosing the design, sample sizes needed, difficulties, and alternatives.

HSR 5823f. *INTRODUCTORY STATISTICS I.* (3 cr) Staff
This course describes the role of statistics in evaluating data based on experimental designs and random sampling. Starting with elementary probability theory, basic techniques of summarizing and analyzing data are discussed including: measures of central tendency and variability,

tabulating and graphing, point and interval estimation, and hypothesis testing. Parametric and non-parametric methods for continuous and discrete data will be presented. Applications to medical research will be emphasized using illustrations from actual research studies.

HSR 5827w. *INTRODUCTION TO REGRESSION.* (1 cr; prereq HRS 5823) Staff
This course considers the evaluation of the relationship between a continuous dependent variable (e.g. serum cholesterol) and a continuous or discrete independent variable (e.g. age or gender). Topics include the method of least squares, prediction, correlation, analysis-of-variance approach to regression, analysis of residuals, design considerations, and an introduction to basic multiple regression.

HSR 5831su. *INTRODUCTION TO CLINICAL EPIDEMIOLOGY* (1 cr) Melton
This course will present basic terminology and methodologic concepts in epidemiology from a clinical perspective. Topics which will be covered will include clinical measurement (reliability, validity, abnormality), diagnosis sensitivity, specificity, predictive value, receiver operator curves, screening vs. case finding), measures of disease frequency (prevalence, incidence, cumulative incidence), prognosis (cohort studies, selection bias, follow-up bias), etiology (causation, relative risk, case-control studies, odds ratios), and therapy (randomized clinical trials, generalizability). This course will be presented in the form of lectures by the instructor, which will emphasize the application of these epidemiologic concepts to interpretation of the clinical literature.

HSR 5833s. *CRITICAL APPRAISAL OF STATISTICAL METHODS IN THE MEDICAL LITERATURE* (1 cr; prereqs HSR 5823, HSR 5827, HSR 5835, HSR 5840) O'Brien
This module will be concerned with reading papers in the medical literature with a view towards understanding the statistical aspects. There will be 12 one-hour sessions, each involving the review of one paper. All students will be required to prepare a written review of each paper prior to the start of each class. These will be reviewed, with comments added, and returned. They will not be graded. All students will participate in the discussion of each paper.

HSR 5835w. *LOGISTIC REGRESSION AND RELATED TOPICS.* (1 cr; prereq HRS 5823, HRS 5827) Schaid
Logistic regression is often used as an analytic tool for medical studies with binary outcomes, such as case-control studies. The goals of this course are: 1) to demonstrate how logistic regression may be used to estimate the magnitude of association between a risk variable and disease, in terms of an odds ratio (OR), to estimate a confidence interval for this OR, and to test hypotheses regarding the OR; 2) to demonstrate how the OR may be influenced by confounding variables and/or interactions among variables, and how logistic regression may be used to adjust for the presence of confounders and to test for the presence of interactions; 3) to illustrate how stepwise logistic regression may be used to select a model when several risk variables are of interest; 4) to demonstrate the analysis of matched case-control studies by logistic regression. Additional topics which are similar to logistic regression and which will be covered are Poisson regression for analysis of rates and discriminant analysis (i.e. classification of subjects into groups based on patient characteristics).

Since the theme of this course is appropriate analysis and interpretation of clinical data, computer printouts of analyses of medical research data are reviewed, and results published in the medical literature are discussed. An understanding of basic statistics and linear regression is required.

HSR 5837s. *CLINICAL TRIALS DESIGN AND CONDUCT.* (1 cr; prereq HRS 5823 or equivalent) O'Fallon, J.
This course will focus on the theoretical considerations and practical implementation issues involved in designing and conducting clinical trials. There are four major units: study design, protocol development, protocol implementation and study conduct. The study design unit includes designs for all types of clinical trials together with consideration of the rationale for randomization, stratification, blinding of treatment arms, early stopping rules. The protocol development unit addresses protocol content issues, including consideration of procedures needed to implement protocol requirements in the areas of patient entry, patient management, and data collection, along with efficient methods to present them. The protocol implementation unit addresses the practical aspects of developing quality controlled systems and procedures at the local center, operations office, and statistical center for carrying out protocol requirements and generating routine reports. The study conduct unit focuses issues involved in the proper analysis of clinical trials data, namely, evaluability of problem cases, characteristics of a thorough analysis, and consideration of the effects of multiple tests, interim analysis, stopping rules, and use of biased statistics.

HSR 5839s. *QUESTIONNAIRE AND SURVEY DESIGN - PRACTICAL ASPECTS OF SURVEY RESEARCH.* (1 cr; offered even yrs) Offord
Presented will be techniques useful in conducting mailed self-administered surveys, telephone interviews, and personal interviews. Components of a survey, including writing of goals, objectives, sample design, question construction, logistics, and analysis will be discussed. In addition, there will be a brief section on validity of questionnaires.

HSR 5840w. *SURVIVAL ANALYSIS.* (1 cr; prereq HRS 5823, HRS 5827) Suman
Topics will include estimation of survival functions, methods of comparing survival for several groups of patients, methods of identifying and adjusting for important covariates, tests for interaction, and use of time-dependent covariates. Specific methods to be discussed include the Kaplan-Meier estimator, the actuarial life-table estimator, the log-rank (Mantel-Haenszel) statistic, the Wilcoxon-Gehan statistic, and the Cox proportional hazards model.

IMMUNOLOGY

Imm 5500f,w,s,su. *LABORATORY METHODS IN IMMUNOLOGY.* (2 cr/8 wks; open only to Immunology Ph.D. Track Students) Staff
A minimum of three rotations are required. Immunology graduate students must take all three in immunology laboratories.

*Imm 5806f. *BASIC GRADUATE IMMUNOLOGY.* (3 cr) McKean and staff

Structure, genetics, and function of immunoglobulins; biosynthesis of antibody; cellular regulation of immune response; tumor and transplantation immunology; immune response to infectious agents; autoimmunity and immune deficiencies.

Imm 8862f,w,s. *CURRENT TOPICS IN CELLULAR REGULATION.* (1 cr) Abraham
Weekly discussions of recent scientific literature on topics related to receptors, transmembrane signalling mechanisms, and gene expression.

Imm 8863f,w,s. *CURRENT TOPICS IN IMMUNOLOGY.* (1 cr; prereq Imm 5806 or equivalent) Jelinek, Wettstein
Current literature on important areas of immunology. Critical review of methods, results and findings.

Imm 8867f,w,s. *CURRENT TOPICS IN HYPERSENSITIVITY REACTIONS.* (1 cr; #) Gleich
This is a series of seminars on hypersensitivity with particular emphasis on immediate-type reactions, vasoactive amine-containing cells, eosinophils and helminths. Students are evaluated by their performance of a seminar during the course.

Imm 8876w. *TUTORIAL IN T CELL DERIVED LYMPHOKINES.* (2 cr; prereq basic immunology; offered even yrs) McKean
The course will use primary literature citations to explore the biological and biochemical basis of T lymphocyte-derived lymphokine responses. fundamental principles of immunology, animal models and clinical observations.

Imm 8877w. *TUTORIAL IN MOLECULAR BASIS OF IMMUNE RECOGNITION* (2 cr; prereq Imm 5806 or equivalent; offered odd yrs) Pease
Regulation and structure of genes and proteins that function in specific immune recognition. Genes of the MHC, T cell receptors, and immunoglobulins will be featured.

Imm 8878s. *TUTORIAL IN EFFECTOR MECHANISMS.* (2 cr; prereq Imm 5806; offered even yrs) Leibson
Current concepts on effector mechanisms employed during cell-mediated and antibody-mediated immune responses, with major focus on cytotoxic T lymphocytes, natural killer cells, eosinophils, basophils and mast cells.

Imm 8879w. *TUTORIAL IN CELLULAR ACTIVATION.* (2 cr; prereq Imm 5806 or equivalent, basic knowledge of receptor pharmacology is desirable but not a requisite; offered even yrs) Abraham
This course focuses on the intracellular signaling pathways which regulate the activation, growth, and differentiation of lymphoid cells. Additional emphasis is placed on molecular mechanism of immunosuppression by cyclosporine, FK506, and related compounds.

Imm 8880s. *TUTORIAL IN IMMUNOPATHOLOGY.* (2 cr; offered odd yrs) Rodriguez
Concepts in the immunopathology of virus and bacterial infection, autoimmunity, tumor immunology, and transplantation. Emphasis will be on immune mechanisms that the host uses to respond to against pathologic agents, how disregulation of these responses lead to autoimmunity, and adaptative strategies infectious agents use to evade immunity.

Imm 8882w. *TUTORIAL IN CELLULAR RECOGNITION AND DEVELOPMENT OF THE IMMUNE RESPONSE.* (2 cr; prereq Imm 5806; offered odd yrs) Goronzy, Weyand
The course will review the biology of T cells and B cells as the two major cellular components of the immune system. The current concept of the formation of a functional T and B cell repertoire will be discussed. In particular, positive and negative selection mechanisms and the induction of tolerance will be reviewed. The basic understanding of the molecular and functional structures of MHC molecules, T cell receptors, and immunoglobulins is required to understand the different selection mechanisms. Finally, the role of the immune repertoires and the regulatory events in the generation of functional T and B cell immune responses will be discussed. This course will review studies of the mechanisms of graft rejection and the induction of self tolerance. Topics will include transplantation antigens, tumor-specific antigens, relationship between in vivo and in vitro assays of T-cell immunity, and self-tolerance.

Research

Imm 8840f,w,s,su. *RESEARCH IN IMMUNOLOGY.* (6 cr/qtr) Staff
Graduate thesis research for Master's students under supervision of staff.

Imm 8852f,w,s,su. *RESEARCH IN IMMUNOLOGY.* Staff
Graduate thesis research for Ph.D. students under supervision of staff.

M.D.-PH.D.

MDPD 5000f,w,s,s. *LABORATORY ROTATIONS FOR M.D.-PH.D. STUDENTS.* (1 cr) Staff
Three one-month rotations required.

MEDICINE

Didactic

*I 5801s. *ENDOCRINE SYSTEM.* (6 cr; prereq 1 yr organic and inorganic chemistry) Abboud
Lecture and discussion course emphasizing normal and abnormal endocrine physiology and biochemistry. Graduate students required to complete a paper.

*I 5804s. *RENAL SYSTEM.* (4 cr) Erickson
Lectures and discussion regarding basic renal pathophysiology. Examination required for credit.

*I 5805s. *DIGESTIVE SYSTEM.* (4 cr; prereq 1 yr general physiology or equiv or #) Wang
Lecture and discussion emphasizing normal and abnormal gastrointestinal physiology. Graduate students required to complete a paper.

*I 5806s. *RESPIRATORY SYSTEM.* (6 cr) Peters
Introduction to the respiratory system structure and function, with emphasis on normal physiology and concepts of pathophysiology.

*I 5807w. *HEMATOPOIETIC SYSTEM.* (4 cr) Tefferi
Designed to give students background in pre-clinical sciences necessary to solve problems presented by patients with disorders of hemostasis and of blood forming and lymphoreticular systems.

*I 5809su. *ALLERGY.* (1 cr; prereq I 5806) Maddox
Discussion of immunologic hypersensitivity, hypersensitivity disorders, pathophysiology of asthma, allergic rhinitis and drug allergy. Included are case discussions and demonstrations of skin testing and spirometry.

*I 5810w. *CARDIOVASCULAR SYSTEM.* (5 cr) Bresnahan
Lectures, seminars, and laboratories on the fundamentals of cardiovascular anatomy, physiology, and biochemistry.

I 5900f,w,s,su. *PRACTICAL ASPECTS OF PATIENT-ORIENTED RESEARCH SEMINAR.* (1 cr/yr) Poland and staff
A seminar series designed to allow an initial examination of the practical issues and concerns related to patient-oriented research. The course is designed for those entering research careers or desiring further skills in patient-oriented research.

MOLECULAR BIOLOGY

MBio 5000w. *INTRODUCTION TO MOLECULAR BIOLOGY.* (3 cr; prereq #) Kline
Basic principles of cell organization and function, with emphasis on the use of molecular biology to increase the understanding of cellular physiology at the molecular level.

MBio 5200f,w,s. *MOLECUALAR AND CELL BIOLOGY WORKSHOP.* (1 cr/yr) Strehler, Maher
Work-in-progress presentations on experimental research projects, given by graduate students and postdoctoral research fellows.

MBio 5500w. *HUMAN CYTOGENETICS.* (2 cr; offered even yrs) Dewald
Emphasizes structure and function of chromosomes and how cytogenetics relates to human clinical problems. Topics include karyotype evolution, aneuploidy, polyploidy, structural anomalies, nomenclature, and principles of banding. A review of chromosomal syndromes, chromosome breakage syndromes, cell division, and genomic imprinting will be included. Some clinical areas to be discussed include prenatal diagnosis, malignant hematologic disorders, and pediatric and obstetrical problems with chromosome anomalies. Research topics will include the chromosomal and molecular basis of cancer and molecular cytogenetics.

MBio 5858f,w,s,su. *LABORATORY ROTATIONS IN MOLECULAR BIOLOGY.* (2 cr/8 wks) Staff
A minimum of three rotations are required.

MBio 8000w. *TUMOR BIOLOGY II: ORIGINS OF HUMAN CANCER.* (3 cr; prereq TBio 5000) Maihle

Topics to be covered include: basic tumor biology, oncogenes, tumor viruses, anti-oncogenes (tumor suppressors), tumor immunity, cancer chemotherapy, and biological response modifiers. Also listed under Tumor Biology.

MBio 8005f. *TUMOR BIOLOGY III: GROWTH FACTORS AND ONCOGENES* (3 cr; prereq TBio 5000, TBio 8000) Maihle, Tindall
This course will focus on the mechanisms by which growth factors and oncogenes influence cell growth and division. Topics include: transmembrane signal transduction; cell cycle and regulation of cell division; ontogeny of oncogenes; mechanisms of oncogene activation; the insulin receptor family; PDGF/sis and PDGF receptor; EGF receptor/c-erb B 1 and 2 (neu); introduction to hematopoietic growth factors/receptors; receptors which lack intrinsic kinase activity, ras family of oncogenes; introduction to nuclear signal transduction; chromosome/DNA-binding proteins; development and differentiation; wound-healing and angiogenesis; carcinogenesis in humans; and anti-oncogenes. Also listed under Tumor Biology.

MBio 8030s. *DATA FITTING AND MODEL PARAMETER ESTIMATION.* (3 cr; prereq Linear Algebra, Calculus) Bajzer
An introduction to modeling and methods for data fitting with applications to biomedical sciences. Theoretical knowledge along with emphasis on data reduction practice are offered to provide sufficient skills in using data fitting procedures. Also listed under Biochemistry

MBio 8050f. *PRINCIPLES OF CELL AND TISSUE DESIGN.* (3 cr; prereq MBio 5000 concurrent or equivalent) Salisbury, McNiven
This course covers general aspects of cell structure with particular emphasis on nuclear organization (exclusive of DNA!), membrane structure and dynamics, protein targeting and processing as they relate to cell structure, protein phosphorylation, calcium-binding proteins, the cytoskeleton (interphase and mitotic) and vesicular transport. Also listed under Biochemistry.

MBio 8101w. *REPLICATION AND TRANSCRIPTION REGULATION.* (3 cr; prereq undergraduate biochemistry) McMurray, Getz
This course will discuss the structure and function of replication and transcription complexes. Emphasis will be placed on control mechanisms and energetics of transcription/replication in prokaryotes and eukaryotes. Also listed under Biochemistry.

MBio 8102s. *REGULATION OF PROTEIN SYNTHESIS.* (3 cr; prereq general background in biochemistry or molecular biology) Toft
General and specialized aspects of protein synthesis and processing will be covered. Regulation of protein synthesis at several posttranscriptional levels will be included. Also listed under Biochemistry.

MBio 8390. *INDEPENDENT STUDY IN MOLECULAR BIOLOGY.* (1-2 cr) Staff
Tutorials arranged on an individual basis in selected advanced topics in Molecular Biology. Students will be expected to define a topic and specific reading list in consultation with a member of the faculty. Mastery of the subject matter will be assessed by examination or by submission of a formal review of the subject area.

MBio 8400. *MASTER'S PROJECT IN MOLECULAR BIOLOGY.* (3 cr) Rusnak

Readings in Molecular Biology culminating in the submission of the Master's Thesis. Topics will be chosen by the student in consultation with the advisor and the student's advisory committee. May be taken only once for credit.

MBio 8500f,w,s. *BIOCHEMISTRY AND MOLECULAR BIOLOGY JOURNAL CLUB.* (1 cr) Rusnak, Wieben
Students of the Molecular Biology program will present current readings in the general areas of Cell and Molecular Biology.

MBio 8501w. *FOCAL TOPICS IN GROWTH REGULATION.* (2 cr; prereq MBio 8005, Imm 8862 or #) Leof
Three areas of current study in growth regulation will be examined. This will permit an in-depth four week study of each. Potential topics will include ERKs/MAP kinases, tyrosine kinases, T cell antigen receptor signalling, cell cycle control, cyto-architecture, and tumor suppressors.

MBio 8600w. *TOPICS IN HUMAN MOLECULAR GENETICS.* (2 cr; prereq introductory courses in genetics and molecular biology) Jenkins, Vockley
Concepts, approaches and techniques of human genetics are presented by way of detailed discussion of original articles.

MBio 8710w. *TOPICS IN MEMBRANE LIPIDS.* (2 cr; prereq Bioc 8000 or #) Pagano
The following will be covered: Lipid structures and properties; Liposomes: Organization of lipids in membranes; Cholesterol uptake and metabolism; Lipid traffic in eukaryotic cells; Lipid second messengers; and Lipid metabolic diseases. Concepts, approaches and techniques of human genetics are presented by way of detailed discussion of original articles.

MBio 8715f,w,s. *MOLECULAR MECHANISMS OF SECRETION.* (1 cr) McNiven, Fernandez, Pagano
This course will review the rapidly expanding field of protein and lipid trafficking through the secretory pathway of eukaryotic cells. Papers reviewed will focus on the molecular mechanisms of membrane budding, transport, targeting, and fusion between endoplasmic reticulum, Golgi apparatus, and the plasma membrane. Special attention will be placed on the contributions of the small and trimeric GTP-binding proteins, molecular motor enzymes, COP proteins, and SNARE/SNAP complexes to secretory vesicle biogenesis and subsequent exocytic release. Also listed under Biochemistry.

MBio 8801f,w,s. *CONCEPTS OF VESICULAR TRAFFICKING.* (1 cr; prereq MBio 8050) McNiven, Urrutia
Study of the basic mechanisms by which cells package, process, and transport synthesized and/or endocytosed proteins.

MBio 8863w. *MOLECULAR BIOLOGY: THEORY AND APPLICATION.* (3 cr; prereq MBio 5000; offered odd yrs) McMurray
Students will gain a thorough working knowledge of molecular biology. The course will deal with theoretical aspects of the techniques as a basis for their practical application. The course will use computer technology to aid in the design and application of all techniques.

MBio 8877w. *TUTORIAL IN MOLECULAR BASIS OF IMMUNE RECOGNITION.* (2 cr; prereq Imm 5806 or equivalent; offered odd yrs) Pease

Current concepts in immunology addressed at the level of the gene with primary focus on the MHC, immunoglobulin, and T-cell receptor gene complexes. Also listed under Immunology.

MBio 8905w. *PCR: THEORY, METHODS, AND APPLICATIONS.* (1 cr) Urrutia
This course is designed to analyze the basic principles of the most advanced PCR-based laboratory techniques. Emphasis will be given to the description of up-to-date PCR strategies. Protocols will be offered as a compilation of proven methods that can be easily repeated in the attendant's laboratory. Also listed under Biochemistry and Molecular Neuroscience.

MBio 8910f,w,s,su. *MOLECULAR CONTROL OF CELL DIFFERENTIATION.* (1 cr) Urrutia
Discussion of classic, as well as current, articles on the mechanisms underlying cell commitment, pattern formation, and phenotype acquisition. Emphasis will be given to articles on transcription factors and their target genes during embryogenesis, teratogenesis, and carcinogenesis. Also listed under Biochemistry and Molecular Neuroscience.

Research

MBio 8900f,w,s,su. *RESEARCH IN MOLECULAR BIOLOGY.* Staff
Graduate thesis research under supervision of staff.

Molecular Neuroscience

NSci 5001f,w,s,su. *LABORATORY ROTATIONS IN MOLECULAR NEUROSCIENCE.* (1 cr) Staff
Laboratory rotation lasting four weeks.

NSci 5002f,w,s,su. *LABORATORY ROTATIONS IN MOLECULAR NEUROSCIENCE.* (2 cr) Staff
Laboratory rotation lasting eight weeks.

NSci 5003f,w,s,su. *LABORATORY ROTATIONS IN MOLECULAR NEUROSCIENCE.* (3 cr) Staff
Laboratory rotation lasting twelve weeks.

NSci 8300w. *CONCEPTS IN NEUROPHYSIOLOGY.* (3 cr) Windebank
Essential physiology of excitable membranes, channels, cell signalling, mechanisms, and electromechanical coupling. Also listed under Physiology.

NSci 8400f. *NEUROANATOMY.* (3 cr) Caselli
Structure and functional anatomy of the nervous system. The human system will be used as the most complex model of the nervous system available.

NSci 8500f,w,s. *NEUROSCIENCE SEMINAR.* (1 cr/yr) Windebank
Seminar series by Mayo faculty and visiting faculty covering advanced topics in Molecular Neuroscience research.

NSci 8600f,w,s. *NEUROSCIENCE JOURNAL CLUB.* (1 cr) Windebank
A journal club for graduate students covering advanced topics in molecular neuroscience.

NSci 8650su. *MOLECULAR NEUROSCIENCE WORKS IN PROGRESS.* (1 cr) Windebank
Presentation of ongoing research projects by graduate students in Molecular Neuroscience Ph.D. Program.

NSci 8854w. *BASIC NEUROSCIENCE.* (5 cr) Benarroch
Lectures dealing with basic topics in CNS structure function and pharmacology.

NSci 8905w. *PCR: THEORY, METHODS, AND APPLICATIONS.* (1 cr) Urrutia
This course is designed to analyze the basic principles of the most advanced PCR-based laboratory techniques. Emphasis will be given to the description of up-to-date PCR strategies. Protocols will be offered as a compilation of proven methods that can be easily repeated in the attendant's laboratory. Also listed under Biochemistry and Molecular Biology.

NSci 8910f,w,s,su. *MOLECULAR CONTROL OF CELL DIFFERENTIATION.* (1 cr) Urrutia
Discussion of classic, as well as current, articles on the mechanisms underlying cell commitment, pattern formation, and phenotype acquisition. Emphasis will be given to articles on transcription factors and their target genes during embryogenesis, teratogenesis, and carcinogenesis. Also listed under Biochemistry and Molecular Biology.

Research

NSci 8840 *RESEARCH IN MOLECULAR NEUROSCIENCE.* (6 cr / qtr) Staff
Graduate thesis research for Master's students under supervision of staff.

NSci 8900. *RESEARCH IN MOLECULAR NEUROSCIENCE.* Staff
Graduate thesis research under supervision of staff.

Obstetrics and Gynecology

Didactic

ObG 5000su. *BASIC COLPOSCOPY.* (2 cr; offered odd yrs) Kastner and staff
Introduction to the pathology and clinical features of intraepithelial neoplasia of the low female genital tract through lectures, demonstrations, and historical case material. Algorithms for the appropriate use of the methodology of colposcopy will be present. At the completion of the didactic portion of the course, the student will be prepared to begin utilizing this technique clinically.

ObG 5801f,w,s,su. *INTRODUCTION TO OBSTETRICS.* (1 cr) Ogburn and staff
Didactic sessions presented weekly. Student preparation and participation required.

ObG 5802f,w,s. *INTRODUCTION TO MEDICAL GYNECOLOGY.* (1 cr) Fish and staff
Selected topics in gynecology presented weekly. Student preparation and participation required.

ObG 5803f,w,s. *INTRODUCTION TO SURGICAL GYNECOLOGY.* (1 cr) Wilson
Theoretical and practical basis of gynecologic surgery.

ObG 8100s. *INTRODUCTORY REPRODUCTIVE ENDOCRINOLOGY.* (1 cr) Staff
Introduction to management of reproductive endocrinology and infertility patients. During a six-week rotation, residents will perform the initial evaluation for a variety of infertility and reproductive endocrine problems and will participate in subsequent evaluations and care. They will gain expertise in performing all relative infertility tests and participate in the management of patients undergoing ovulation induction therapy with clomiphene, human menopausal gonadotropins, and bromocriptine. They will be involved in the preoperative evaluation, surgical treatment, and postop care of these patients and they will participate in bi-weekly Reproductive Endocrinology conferences. Relevant physiology and pathophysiology will be reviewed.

ObG 8854f,w,s,su. *SEMINARS IN GYNECOLOGIC ENDOCRINOLOGY.* (1 cr) Staff
Weekly seminar(s), case presentations and didactic sessions.

ObG 8856w. *CLINICAL REPRODUCTIVE ENDOCRINOLOGY.* (1 cr; offered even yrs) Staff
Clinical aspects of reproductive endocrinology and infertility reviewed in didactic sessions.

Research

ObG 8890. *RESEARCH IN OBSTETRICS-GYNECOLOGY.* (6 cr; +) Staff
Graduate thesis research under supervision of staff.

Clinical

ObG 8852f,w,s,su. *CLINICAL OBSTETRICS AND GYNECOLOGY.* (6 cr) Ogburn and staff
This course consists of two equal emphases: 1) Clinical training in the management of problems and diseases involving the reproductive system of women as well as health maintenance for women overall, and 2) the clinical care of pregnant women and their labor and delivery including diseases affecting pregnant women and their fetuses, management of complications and strategies to optimize the outcome for women and their children.

ObG 8853f,w,s,su. *OPERATIVE SURGERY.* (6 cr) Lee, Podratz, Stanhope, Webb, Wilson

ObG 8857f. *GYNECOLOGIC ONCOLOGY.* (6 cr; prereq satisfactory completion of an obstetrical and gynecologic residency training program at an accredited institution and maintenance of satisfctory status within the Gynecologic Oncology Fellowship Program) Podratz

Preoperative evaluation, surgical treatment, and postoperative management of benign and malignant gynecologic disease processes and the complications thereof arising within the female genitalia. In addition, the acquisition of theoretical and practical knowledge regarding the natural history, the diagnosis, alternatives to surgical management, prognosis, and the postoperative immediate and long-term disposition for each of the disease processes requiring surgery will be anticipated.

ObG 8858f. *REPRODUCTIVE ENDOCRINOLOGY.* (3 cr; prereq satisfactory completion of a residency in obstetrics and gynecology and maintenance of satisfactory status within the Reproductive Endocrinology Fellowship Program) Staff
Outpatient and surgical management of patients presenting with reproductive endocrinology disorders and infertility. Also will encompass the relevant physiology and pathophysiology.

ObG 8859w. *REPRODUCTIVE ENDOCRINOLOGY II.* (3 cr; prereq ObG 8858) Staff
Outpatient and surgical management of patients presenting with reproductive endocrinology disorders and infertility. Also will encompass the relevant physiology and pathophysiology.

ObG 8860s. REPRODUCTIVE ENDOCRINOLOGY III. (3 cr; prereq ObG 8859) Staff
Outpatient and surgical management of patients presenting with reproductive endocrinology disorders and infertility. Also will encompass the relevant physiology and pathophysiology.the relevant physiology and pathophysiology.

ObG 8861. *REPRODUCTIVE ENDOCRINOLOGY.* (6 cr) Staff
Experience is obtained in the outpatient setting with regard to reproductive endocrinology including exposure to in vitro fertilization as well as with operating room experience. Experience is also obtained in transvaginal ultrasound.

ObG 8870f,w,s,su. *ADVANCED GYNECOLOGIC OPERATIVE SURGERY.* (6 cr; prereq completion of Ob-Gyn residency training program) Webb, Magrina and staff
The preoperative, intra operative and postoperative management of gynecological patients.

ObG 8880f,w,s,su. *SURGICAL GYNECOLOGY AND REPRODUCTIVE ENDOCRINOLOGY - CHIEF RESIDENT ASSOCIATE.* (6 cr) Webb and staff

ObG 8885f,w,s,su. *OBSTETRICS AND MEDICAL GYNECOLOGY - CHIEF RESIDENT ASSOCIATE.* (6 cr) Ogburn

ObG 8891. *ELECTIVE ROTATION.* (6 cr) Wilson and staff
Typical rotations would include gynecologic surgery, high-risk obstetrics, reproductive endocrinology and infertility, research or off-campus rotations.

ObG 8900f,w,s,su. *FAMILY MEDICINE RESIDENT OBSTETRICAL ROTATION.* (1 cr; prereq previous obstetrical rotation, no MMS III or obstetrical residents serving OB out-patient rotations) Heise

The Family Medicine resident will be based on Charlton 4 Obstetrical outpatient care clinic and be exposed to prenatal care as administered by obstetrical staff coordinators, level 1 and level 2 ultrasound, indications for and observations of amniocentesis, cordocentesis, and chorionic villi sampling. He/she will learn indications for and participate with routine antepartum testing. The resident will also attending obstetrical morning high-risk rounds, weekly OB grand rounds, and receive didactic presentations by obstetrical staff coordinators.

ObG 8905f,w,s,su. *FAMILY MEDICINE GYNECOLOGY ELECTIVE ROTATIONS.* (1-2 cr; prereq second and third year family medicine residents) Heise
The Family Medicine resident will enhance his/her skills in gynecologic history taking and gynecologic examination performance. The resident will observe colposcopy, office laser surgery, and become familiar with various screening techniques for maintaining gynecologic health. The resident will become familiar with various contraceptive techniques and heir specific indications, as well as being introduced to common gynecologic disorders emphasizing menstrual irregularities, vaginitis, pelvic inflammatory disease, fibroids, pelvic pain, urinary incontinence, postmenopausal estrogen replacement therapy, and breast disease. He/she will have daily reading assignments with didactic presentations and clinic al rotational exposures with a number of staff medical gynecologists.

OPHTHALMOLOGY

Didactic

Oph 8100. *FUNDAMENTALS AND PRINCIPLES OF OPHTHALMOLOGY.* (4 cr) Staff
Anatomy, biochemistry, physiology, and pathology.

Oph 8101. *OPTICS, REFRACTIONS AND CONTACT LENSES.* (4 cr) Staff

Oph 8102. *OPHTHALMIC PATHOLOGY, OCULAR TUMORS, INTRAOCULAR INFLAMMATION, AND UVEITIS.* (4 cr) Staff

Oph 8103. *RETINAL AND VITREOUS DISEASES.* (4 cr) Staff

Oph 8104. *NEUROOPHTHALMOLOGY AND GENERAL MEDICAL OPHTHALMOLOGY.* (4 cr) Staff

Oph 8105. *BINOCULAR VISION AND OCULAR MOTILITY.* (4 cr) Staff

Oph 8106. *EXTERNAL AND CORNEAL DISEASES.* (4 cr) Staff

Oph 8107. *GLAUCOMA, DISORDERS OF THE LENS AND ANTERIOR SEGMENT TRAUMA.* (4 cr) Staff

Oph 8108. *EYELID, LACRIMAL, AND ORBITAL DISORDERS.* (4 cr) Staff

Research

Oph 8900f,w,s,su. *OPHTHALMOLOGY RESEARCH.* (6 cr) Brubaker, Bourne, Johnson
Thesis research under supervision of staff.

Clinical

Oph 8851f,w,s,su. *REFRACTION AND STRABISMUS.* (6 cr) Baratz, Dyer, Erie, Hardwig, Hohberger
Theory of refraction, retinoscopy, diagnosis of refractive errors of the eye, prescribing of lenses, disturbances of motility of the eyes, orthoptics and strabismus surgery. Prescribing and fitting contact lenses.

Oph 8852f,w,s,su. *OCULAR THERAPY.* (6 cr) Bartley, Bourne, Brubaker, Buettner, Herman, Garrity, Johnson, Maguire, Pach, Robertson
Diagnosis and treatment of diseases of the eye and its adnexa.

Oph 8853f,w,s,su. *MEDICAL AND NEUROLOGIC OPHTHALMOLOGY.* (6 cr) Garrity, Leavitt, Younge
Ophthalmology and ophthalmoscopy as they pertain to the fields of internal medicine and neurology.

Oph 8854f,w,s,su. *OPHTHALMIC SURGERY.* (6 cr) Baratz, Bartley, Bourne, Brubaker, Buettner, Erie, Garrity, Hardwig, Herman, Hohberger, Johnson, Maguire, Pach, Robertson

Oph 8855f,w,s,su. *OPHTHALMIC PATHOLOGY, ANATOMY, AND SURGICAL TECHNIQUE.* (6 cr; prereq resident in ophthalmology) Bartley, Campbell, Herman

Oph 8860f,w,s,su. *OPHTHALMOLOGY - CHIEF RESIDENT ASSOCIATE.* (6 cr; prereq must have completed PGY-1, 2, and 3 years and must be in good academic standing as determined by the Education Committee of the Department of Ophthalmology.) Staff

ORTHOPEDICS

Didactic

Or 5803f,s. *PROSTHETICS FOR ORTHOPEDICS.* (1 cr) Shives
Lectures and discussions regarding upper and lower extremity prosthetics for amputations at various levels - includes class participation in the application of immediate-type pylons.

See Anat 8855. *ORTHOPEDIC ANATOMY.* (2 cr) Carmichael and staff
Lectures, prosections and demonstrations of gross anatomy of the musculoskeletal system with special emphasis on relationships and surgical approaches.

Or 8500su. *TECHNIQUE OF MICROVASCULAR ANASTOMOSIS.* (2 cr) Wood
This course offers supervised instruction in the techniques of microvascular anastomosis, care and use of microsurgical instruments, and

proper application of the operating microscope. It will familiarize the candidate with the techniques of small vessel repair as well as nerve repair. Techniques of nerve and vascular dissection will also be emphasized. At the completion of the course the student will have repaired lacerations in synthetic material, conducted vascular repairs of blood vessels 1 mm in size, and carried out end-to-end nerve repair in the rat.

Or 8550f,w,s,su. *NONSTRUCTURED MICROVASCULAR ANASTOMOSIS.* (2 cr; prereq student must be involved in or have completed a training program in an approved surgical specialty or subspecialty or be involved as a research fellow, technician, etc.) Schroeder
Forty hours of instruction and practice which includes the care and adjustment of the operating microscope, the basic techniques of microsurgical suture placement, and microvascular anastomosis of a rat femoral artery and rat femoral vein. Following successful completion of the above measures, the students will extend their application to end-to-side microvascular anastomosis as well as epineural and fascicular nerve repair using the rat sciatic nerve model.

Or 8860f,w,s,su. *BASIC KNOWLEDGE AND MOTOR SKILLS OF ORTHOPEDIC SPECIALTIES.* (3 cr; #) Rock
This course will cover pertinent basic knowledge and motor skills as it applies to the subspecialties of Orthopedics, including adult reconstruction/trauma, hand and upper extremity, pediatrics, spine, and sports medicine.

Clinical

Or 8851f,w,s,su. *ORTHOPEDIC DIAGNOSIS.* (6 cr) Morrey and staff
Instruction in patient assessment by history, physical examination, imaging modes, laboratory tests and other adjunctive special evaluation techniques in the investigation of the musculoskeletal system and its disease processes. Included are experiences in outpatient, inpatient and operating room settings. The didactic program includes clinical conferences, lectures and journal clubs.

Or 8852f,w,s,su. *ADULT RECONSTRUCTION.* (6 cr) Cabanela and staff
This course covers all areas of Adult Reconstructive Surgery, including spine, hip, knee, shoulder, elbow, ankle and foot. Course will include personal teaching on patient assessment, surgical technique, pre and postoperative care, as well as follow-up care.

Or 8853f,w,s,su. *SURGERY OF THE HAND.* (6 cr) Cooney and staff
Supervised exposure to clinical hand surgery with weekly teaching conference and monthly journal club.

Or 8854f,w,s,su. *PEDIATRIC ORTHOPEDICS.* (6 cr) Peterson
Incidence, etiology, evaluation and treatment of congenital developmental, metabolic, and post-traumatic orthopedic conditions from birth to physiologic maturity.

Or 8855f,w,s,su. *ORTHOPEDIC ONCOLOGY.* (6 cr) Pritchard and staff
Orthopedic oncology residents participate in evaluation and management of patients with various musculoskeletal neoplasms. The surgical experience includes modern limb salvage procedures.

Or 8856f,w,s,su. *FRACTURES AND RELATED INJURIES.* (6 cr) Lewallen and staff
Instruction in patient assessment by history, physical examination, imaging modes, laboratory tests and other adjunctive special evaluation techniques in the investigation of the musculoskeletal system and its fractures and related injuries. Included are experiences in outpatient, inpatient and operating room settings. The didactic program includes clinical conferences, lectures and journal clubs.

Or 8858f,w,s,su. *FOOT FELLOWSHIP.* (6 cr) Johnson
One-year experience in diagnosis and treatment of foot and ankle problems.

Or 8870f,w,s,su. *ORTHOPEDICS - CHIEF RESIDENT ASSOCIATE.* (6 cr; prereq appointment is recommended by the Department of Orthopedics Education Committee and then undergoes institutional review.) Staff

OTORHINOLARYNGOLOGY

Didactic

ENT 5150f,w,s,su. *CORE CURRICULUM.* (2 cr) Staff
This series of Saturday morning lectures rotates systematically every two years through basic and advanced discussions of topics in the various aspects of the field of otorhinolaryngology. The lectures are presented by the staff and are divided into eight-week segments covering otology/audiology, rhinology, head and neck, general ENT, and plastic/reconstructive.

ENT 5200s. *MAXILLOFACIAL TRAUMA COURSE.* (1 cr) McCaffrey
Principles of diagnosis and management of maxillofacial trauma are discussed.
Treatment techniques covered are: interosseous wiring, intermaxillary fixation, external fixation, and rigid internal fixation with dynamic compression plating techniques.

ENT 5300f,w,s,su. *CORE COLLOQUIUM.* (1 cr) Olsen, McCaffrey Course is designed for open discussion among staff and participants regarding surgical indications and management and prevention of complications in patients with medical and surgical problems in otorhinolaryngology-head and neck surgery.

ENT 8100f,w,s,su. *PROBLEMS IN CLINICAL DIAGNOSIS.* (4 cr) Beatty and staff
Presentations by resident and consulting staff of representative diagnostic and management problems in otorhinolaryngology.

ENT 8200f,w,s,su. *CLINICAL TESTING PRACTICUM.* (1 cr) Beatty and staff
The purpose of this study is to acquaint the resident with the principles of audiologic testing, electronystagmography and rhinomanometry.

ENT 8300s. *SOFT TISSUE AND PLASTIC RECONSTRUCTION.* (1 cr; offered even years) Olsen
The purpose of this course is to acquaint the resident with the basic principles of soft tissue surgery. Local skin flaps including advancement, rotation, transposition and island flaps will be discussed. The techniques of scar revision will be demonstrated.

ENT 8500f. *RHINOLOGY AND RHINOLOGIC SURGERY DISSECTION.* (3 cr; offered odd yrs) Kern
This rhinology dissection course is given with fresh frozen cadavers. The basic purpose of this course is to acquaint the resident with the surgical anatomy and basic operative procedures of the nasal septal and external nose, including nasal septal reconstruction, sinus surgery, and rhinoplasty. There are dissections assigned and didactic material presented.

ENT 8800f,w,s,su. *SEMINAR: OTORHINOLARYNGOLOGY.* (1 cr per year) Neel

See Anat 8852s. *SURGICAL ANATOMY OF HEAD AND NECK.* (3 cr) Kasperbauer
Cadaver dissection and lecture demonstration. Laboratory participation required for credits.

ENT 8857w. *TEMPORAL BONE ANATOMY AND SURGERY OF THE TEMPORAL BONE.* (3 cr) Beatty, Facer, Harner, McDonald
This course is designed to present the basic anatomy of the temporal bone, surgical landmarks, and to familiarize the resident with the surgical techniques of temporal bone surgery and the appropriate anatomy.

Research

ENT 8890f,w,s,su. *GRADUATE RESEARCH.* (6 cr; #) McCaffrey
Graduate thesis research under staff supervision.

Clinical

ENT 8851f,w,s,su. *CLINICAL OTORHINOLARYNGOLOGY.* (6 cr) Staff
Theory and practice with differential diagnosis and treatment of diseases of the ear, nose, paranasal sinuses, pharynx, larynx, head, and neck; their relation to general diagnosis.

ENT 8852f,w,s,su. *PREOPERATIVE AND POSTOPERATIVE CARE OF PATIENTS.* (6 cr) Staff
Junior residency service. Care of the pre- and postoperative in-hospital management of patients with diseases associated with the ears, nose and throat. Initial assessment of trauma involving head and neck as well as emergency room management of those patients.

ENT 8853f,w,s,su. *OPERATIVE OTORHINOLARYNGOLOGY.* (6 cr) Staff
Senior residency service. Senior surgical residency with the teaching staff. Management of the patient during entire hospital stay. Surgery performed under direction of faculty by the resident when properly qualified.

ENT 8854f,w,s,su. *OPERATIVE OTORHINOLARYNGOLOGY - CHIEF RESIDENT ASSOCIATE.* (6 cr) Staff
The chief resident manages the pre-operative, surgical and postoperative care of the patient. Faculty are available for supervision and consultation.

PATHOLOGY

Didactic

Path 8854f,w,s,su. *DISEASES OF THE LIVER.* (2 cr) Bjornsson
Diagnostic exercise on the multiheaded microscope, using current liver biopsy specimens. Intended for morphologists, but also suitable for physicians with special interest in hepatology.

Path 8872w,su. *BONE AND SOFT TISSUE PATHOLOGY.* (3 cr) Unni
Discussion of the gross and microscopic appearances of tumors and tumor-like conditions of bone and joints.

Path 8873f,w,s,su. *ORAL PATHOLOGY.* (2 cr) Unni

Research

Path 8890f,w,s,su. *GRADUATE RESEARCH.* (6 cr; #) Staff

PHARMACOLOGY

Phar 5001f,w,s,su. *LABORATORY ROTATIONS IN PHARMACOLOGY.* (1 cr) Staff
Four-week laboratory rotation to gain experience with a broad spectrum of research techniques useful in pharmacology.

Phar 5002f,w,s,su. *LABORATORY ROTATIONS IN PHARMACOLOGY.* (2 cr) Staff
Eight-week laboratory rotation to gain experience with a broad spectrum of research techniques useful in pharmacology.

Phar 5003f,w,s,su. *LABORATORY ROTATIONS IN PHARMACOLOGY.* (3 cr) Staff
Twelve-week laboratory rotation to gain experience with a broad spectrum of research techniques useful in pharmacology.

Phar 5100f,w,s. *PHARMACOLOGY SEMINAR SERIES.* (1 cr/yr) Brimijoin
Attendance at weekly pharmacology seminars. Attendance at lectures is required.

*Phar 5800f,w,s. *PHARMACOLOGY AND THERAPEUTICS.* (9 cr for series; Pharmacology graduate students must use this registration; prereq a good background in vertebrate physiology and general biochemistry at the college or graduate level) Weinshilboum and staff

Survey course for medical and graduate students with no previous training

in pharmacology. Covers the basic principles of drug uptake distribution and metabolism, receptor-activation, and pharmacology of specific organ systems.

*Phar 5801f. *GENERAL PHARMACOLOGY I.* (2 cr) Weinshilboum

*Phar 5802f. *GENERAL PHARMACOLOGY II.* (2 cr; prereq Phar 5801) Weinshilboum

*Phar 5803w. *GENERAL PHARMACOLOGY III.* (2 cr; prereq Phar 5801, Phar 5802) Weinshilboum

*Phar 5804w. *GENERAL PHARMACOLOGY IV.* (2 cr; prereq Phar 5801, Phar 5802) Weinshilboum

*Phar 5805w. *GENERAL PHARMACOLOGY V.* (2 cr; prereq Phar 5801, Phar 5802) Weinshilboum

*Phar 5806s. *GENERAL PHARMACOLOGY VI.* (2 cr; prereq Phar 5801, Phar 5802) Weinshilboum

Phar 8000f. *TUTORIAL IN PATCH CLAMP TECHNIQUE.* (2 cr) Clapham
An introduction to patch clamp electronics and ion channel measurements. A limited number of students pursuing research with patch clamp techniques will be accepted.

Phar 8800f,w,s. *RESEARCH SEMINARS IN PHARMACOLOGY.* (1 cr) Taylor
The purpose of this course is to provide a forum for development of graduate speaking skills in a seminar setting. Students prepare talks presented to students, faculty, fellows, and research technicians.

Phar 8802w. *PHARMACOLOGY OF HEART MUSCLE.* (3 cr; #; offered odd yrs) Staff
Lectures, discussions, and demonstrations on the cellular basis of action of drugs on heart muscle. Origin of concept of drug-receptor interaction; molecular basis for ligand-protein building; classical analysis of dose-response curves; isolation and characterization of receptor; current progress in amine, peptide, and steroid receptors.

Phar 8803s. *BIOCHEMICAL BASIS OF NEUROPHARMACOLOGY.* (3 cr; offered odd yrs; #) Brimijoin and staff
Lectures and discussions on the cellular and biochemical basis of drug actions in the nervous system. In-depth review of classical papers on mechanisms of neurotransmission, exocytosis transmitter inactivation, neurotoxicity, and cellular pathophysiology of the nervous system. Regular student presentations are expected.

Phar 8804f. *CLINICAL PHARMACOLOGY.* (1 cr; prereq Phar 5800; offered 1996 and every 3rd yr) Lipsky and staff
Rational pharmacologic basis of therapy with major categories of drugs used in clinical practice of medicine. Emphasis on pharmacokinetics, drug metabolism, pharmacogenetics, and mechanism of action of drugs.

Phar 8805s. *DRUG METABOLISM.* (3 cr; offered odd yrs) Ames, Weinshilboum
Principles of disposition of drugs in biological systems. Lectures on absorption, distribution, excretion, and metabolic transformation of drugs; descriptions of enzyme systems and factors affecting them.

Phar 8806s. *PHARMACOLOGY OF RECEPTORS.* (3 cr; offered odd yrs;#) Brimijoin and staff
Origin of concept of drug-receptor interaction; molecular basis for ligand-protein building; classical analysis of dose-response curves; isolation and characterization of receptor; current progress in amine, peptide, and steroid receptors.

Phar 8810s. *TOXICOLOGY.* (3 cr; offered even yrs) Moyer
Lectures and discussion on the principles of intoxication by drugs and other foreign substances. Includes mechanisms of intoxication, detoxication, and a review of specific organic and inorganic intoxicants.

Phar 8811s. *CELLULAR PHARMACOLOGY: THE MOLECULAR BASIS OF DRUG ACTION.* (3 cr; offered even yrs) Kaufmann
Using recent literature articles, this course will examine the mechanisms of action of selected pharmaceutical agents at the cellular and subcellular level. Drug targets to be examined during the quarter include the bacterial cell wall, plasma membrane receptors, ion channels, ras farnesyl transferase, glycosylation pathways, the vesicular flow pathway, microtubules, DNA, DNA topoisomerases, and HIV transcriptase.

Phar 8862w. *EXCITATION-CONTRACTION COUPLING IN SKELETAL MUSCLE.* (3 cr; offered odd yrs; prereq courses in electronics, computer science and mathematics) Taylor and staff
Areas covered include cell-specific features of excitation, excitation-contraction coupling, and molecular mechanisms in force generation. Also listed under Physiology.

Phar 8863w. *MOLECULAR BIOLOGY: THEORY AND APPLICATION.* (3 cr; prereq MBio 5000; offered odd yrs) McMurray
Students will gain a thorough working knowledge of molecular biology. The course will deal with theoretical aspects of the techniques as a basis for their practical application. The course will use computer technology to aid in the design and application of appropriate techniques.

Phar 8879w. *TUTORIAL IN CELLULAR ACTIVATION.* (2 cr; prereq Imm 5806 or equivalent, basic knowledge of receptor pharmacology is desirable but not a requisite; offered even yrs) Abraham
This course will focus on current topics related to receptors and transmembrane signaling events involved in the activation and growth of hematopoietic cells. Also listed under Immunology.

Research

Phar 8801. *RESEARCH IN PHARMACOLOGY.* Staff
Directed research projects for Ph.D. students under the supervision of a faculty adviser.

Phar 8840. *RESEARCH IN PHARMACOLOGY.* (6 cr/qtr) Staff
Directed research projects for Master's students under the supervision of a faculty adviser.

Physical Medicine and Rehabilitation

Didactic

PhM 8850su. *INTRODUCTION AND ORIENTATION TO PHYSICAL MEDICINE AND REHABILITATION.* (2 cr) Staff
Introduction to the functions of the Department of Physical Medicine and Rehabilitation and the roles of physicians and other health professionals in the department.

PhM 8854f,w,s. *BASIC AND APPLIED PHYSIATRY.* (2 cr) Staff
Study, presentation, and discussion of selected relevant subjects.

PhM 8856f,w,s. *SEMINARS IN PHYSICAL MEDICINE AND REHABILITATION.* (1 cr) Staff
Selected readings, seminars, and research papers presented by staff and residents.

PhM 8857f,w,s,su. *READINGS IN PHYSICAL MEDICINE AND REHABILITATION.* (1 cr) Staff
Presentation by students and staff of selected readings devoted to a single subject area at each session.

Research

PhM 8900f,w,s,su. *RESEARCH WORK ON SELECTED PROBLEMS.* (6 cr) Staff
The resident will conduct a research project with prior approval of the Physical Medicine and Rehabilitation Research Committee and faculty adviser.

Clinical

PhM 8100f,w,s,su. *PEDIATRIC REHABILITATION.* (6 cr) Schutt and staff
The resident (2nd or 3rd year) works only with pediatric cases for one quarter. The duties are generally in St. Marys Hospital in the morning and in the outpatient department in the afternoon.

PhM 8851f,w,s,su. *OUTPATIENT CLINICAL PHYSICAL MEDICINE AND REHABILITATION.* (6 cr) Staff

PhM 8852f,w,s,su. *PHYSICAL MEDICINE AND REHABILITATION HOSPITAL CONSULTING SERVICE.* (6 cr) Staff
Physical medicine and rehabilitation as related to rheumatology, orthopedic surgery, neurology, and various other medical and surgical specialties.

PhM 8853f,w,s,su. *HOSPITAL REHABILITATION SERVICE.* (6 cr) Staff

PhM 8855f,w. *AMPUTATIONS AND PROSTHETICS.* (3 cr) Staff
Surgical, medical, and rehabilitative aspects of amputee management. Lectures, laboratories, experience, and attendance at the Amputee Clinic.

PhM 8860 w,s,su,f. *FELLOWSHIP IN SPORTS MEDICINE.* (6 cr; prereq Board eligible or Board certified physician in Physical Medicine and Rehabilitation) Rizzo

The program will consist of a supervised clinical experience in Sports Medicine of not less than six months and an additional 0.2 to 0.5 FTE of research time. The fellow will be directly supervised by a member of the Department of Physical Medicine and Rehabilitation and will work closely with orthopedists and physical therapists as well as counselors with expertise in the area of Sports Medicine.

PhM 8880f,w,s,su. *PHYSICAL MEDICINE AND REHABILITATION - SENIOR RESIDENT ASSOCIATE.* (6 cr) Staff
The Physical Medicine and Rehabilitation Senior Resident Associate rotation is offered to PM&R residents during their final year of training who have successfully completed their inpatient PM&R rotations. The SRA rotation is designed to offer an independent clinical practice opportunity in inpatient primary care and consultative rehabilitation. The clinical experience is complemented by Department Grand Rounds, clinical conferences, basic science lecture series, discussion groups, and Journal Club.

PHYSIOLOGY

Phys 5001f,w,s,su. *LABORATORY ROTATIONS IN PHYSIOLOGY.* (1 cr) Staff
Laboratory rotation lasting four weeks. Students rotate through laboratories of several senior investigators to get exposure to areas of research, state-of-the-art methods, and senior faculty programs. The student will write a summary of laboratory projects and methods at completion of rotation.

Phys 5002f,w,s,su. *LABORATORY ROTATIONS IN PHYSIOLOGY.* (2 cr) Staff
Laboratory rotation lasting eight weeks. Students rotate through laboratories of several senior investigators to get exposure to areas of research, state-of-the-art methods, and senior faculty programs. The student will write a summary of laboratory projects and methods at completion of rotation.

Phys 5003f,w,s,su. *LABORATORY ROTATIONS IN PHYSIOLOGY.* (3 cr) Staff
Laboratory rotation lasting twelve weeks. Students rotate through laboratories of several senior investigators to get exposure to areas of research, state-of-the-art methods, and senior faculty programs. The student will write a summary of laboratory projects and methods at completion of rotation.

Phys 5500w. *RESEARCH ANIMAL EXPERIMENTAL SURGERY AND METHODOLOGY.* (3 cr) Frisk, Andrews
Presentation of information on the humane use of laboratory animals in biomedical research. Material covered will include the biology and experimental techniques of the majority of species used and regulations and ethics involving animal experimentation. Sessions on experimental surgery will include veterinary anesthesia, aseptic technique, post-operative care and experimental surgical techniques. A laboratory will be included.

Phys 5801w,su. *PRINCIPLES OF BIOMECHANICS I.* (3 cr) An and staff
Basic concepts of orthopedic biomechanics.

Phys 5802f,s. *PRINCIPLES OF BIOMECHANICS II.* (3 cr; prereq Phys 5801) An and staff
Advanced concepts of orthopedic biomechanics.

Phys 5900f,w,s,su. *MASTER'S DEGREE PROJECT IN PHYSIOLOGY.* (5 cr) Staff
This course is comprised of a special laboratory project in physiology in which the student uses tools and skills learned in coursework. The course is required for Employee Master's Degree candidates. The student must write a report on the project.

Phys 8300w. *CONCEPTS IN NEUROPHYSIOLOGY.* (3 cr) Windebank
Essential physiology of excitable membranes, channels, cell signalling, mechanisms, and electromechanical coupling. Also listed under Molecular Neuroscience.

Phys 8851f,w,s. *PHYSIOLOGY SEMINARS.* (1 cr; prereq Phys 8854 or, with other listed courses, +) Staff
Weekly seminars in which whole department participates. Research papers presented by students, staff or invited lecturers.

Phys 8854f,w,s,su. *READINGS IN PHYSIOLOGY.* (2 cr) Staff
Assigned readings and reports on current topics and issues in Physiology. Areas covered include cell-specific features of excitation, excitation-contraction coupling, and molecular mechanisms in force generation. Also listed under Pharmacology.

Phys 8855f. *CARDIOVASCULAR PHYSIOLOGY HYPERTENSION.* (3 cr; offered odd yrs; prereq human anatomy and principles of biophysics) Romero
Hemodynamics, neural, and renal regulatory mechanisms: their participation in the development of hypertension.

Phys 8856w. *RESPIRATORY PHYSIOLOGY.* (3 cr; offered odd yrs) Sieck
The goal of this course is to provide an in-depth account of the functional components of the respiratory system and their integration in health and disease.

Phys 8858w. *PHYSIOLOGY OF SMOOTH MUSCLE AND OF ITS INNERVATION* (2 cr; offered even yrs) Szurszewski, Miller and staff
Lectures and discussions on electrical behavior of smooth muscle, ionic basis of electrical behavior; innervation of various types of smooth muscle and neuromuscular transmission in smooth muscle. Regular student presentations will be expected.

Phys 8859w. *RENAL PHYSIOLOGY.* (2 cr; offered odd yrs) Khraibi
Renal hemodynamics, glomerular function, mechanisms and regulation of electrolyte transport. Two laboratory sessions demonstrating basic renal function and the effects of diuretics.

Phys 8860s. *ENDOCRINE PHYSIOLOGY.* (2 cr; offered odd yrs) Khosla
This course focuses on several aspects of endocrine physiology, including mechanisms of hormone action, calcium homeostasis, glucose, and fatty acid metabolism, pituitary, thyroid and adrenal physiology, and immunologic aspects of endocrinology.

Phys 8862w. *EXCITATION-CONTRACTION COUPLING IN SKELETAL MUSCLE.* (3 cr; offered odd yrs; prereq courses in electronics, computer science and mathematics) Taylor and staff
Areas covered include cell-specific features of excitation, excitation-contraction coupling, and molecular mechanisms in force generation. Also listed under Pharmacology.

Phys 8878w,su. *PHYSIOLOGY OF BONE* I. (3 cr; #) Turner and staff
Lectures in physiology of both normal and abnormal bone; renal, respiratory, and endocrine physiology and function as related to bone.

Phys 8879f,s. *PHYSIOLOGY OF BONE II.* (2 cr; #) Turner and staff
Studies include structure and mineralization of bone both normal and abnormal, ion transport, mineral and hormonal metabolism as related to bone.

Phys 8880. *PRINCIPLES OF SOLID MECHANICS.* (3 cr; prereq physics and calculus; offered on request) An
Application of vector mechanics to musculoskeletal systems; experimental methodology in obtaining anatomic kinematic data.

Phys 8881. *MECHANICS OF DEFORMABLE MATERIALS.* (3 cr; prereq Phys 8880; offered on request) An
Stress and strain concepts and method of calculation for biological and implantable materials. Methodology and instrumentation for measuring stress, strain, fracture, and wear.

Research

Phys 8840f,w,s,su. *RESEARCH IN PHYSIOLOGY.* (6 cr/qtr) Staff
Opportunities in research for master's students to be arranged with individual staff members.

Phys 8853f,w,s,su. *RESEARCH IN PHYSIOLOGY.* (+) Staff
Opportunities in research for Ph.D. students to be arranged with individual staff members.

PSYCHIATRY

Didactic

P 8301w. *ELECTIVE: TEACHING MEDICAL STUDENTS.* (3 cr) Hansen
This course is an elective for senior residents. It is a half-time course. The resident serves as a teaching assistant for the first-tear medical school course in Human Growth and Development from Conception to Death. The resident attends lectures, acts as discussion leader with a group of students approximately once each week, advises students for their special projects, runs the medical student group, and works with the adolescent project. This course provides the resident an opportunity to interact with medical students in a major academic, pre-clinical course, to learn teaching techniques, and to review material.

P 8350. *INDIVIDUAL STUDY IN PSYCHIATRY.* (2 cr) Staff
A tutorial/individualized study program intended for fellows in the Department of Psychiatry and Psychology as a one-to-one learning experience under the direction and supervision of an appropriate faculty member. This experience encourages the fellow to intensively examine a specific issue in Psychiatry under the tutelage of a faculty member who is an expert on that issue. Re-registration is permitted, up to a maximum of three completed individual study courses.

P 8400. *BEHAVIORAL SCIENCE SEMINAR.* (2 cr) Staff
A group learning experience employing didactic presentations and group discussion of specialized issues in the Behavioral Sciences, intended as an advanced learning experience for fellows in the Department of Psychiatry and Psychology. Content of each seminar will be determined by the interests and needs of the fellows in conjunction with the availability of faculty expertise. Reregistration is permitted with no limit.

P 8501. *PSYCHIATRY DIDACTIC LECTURE SERIES I.* (2 cr) Staff
The first of four six-month lecture series in the major theoretical and clinical areas of Psychiatry. Topics include an introduction to the medical and behavioral sciences of Psychiatry and Psychology, the history of Psychiatry and Psychology, theories of personality development, and issues relevant to the initial evaluation, assessment and disposition of the acute psychiatric patient.

P 8502. *PSYCHIATRY DIDACTIC LECTURE SERIES II.* (2 cr) Staff
The second of four six-month lecture series in the major theoretical and clinical areas of Psychiatry. Topics include the detailed study of the primary diagnostic entities in Psychiatry (e.g. psychotic illnesses, personality disorders, neurotic disorders, organic brain syndromes) and the study of related neurosciences (e.g. seizure disorders, neurodiagnostic procedures, learning disabilities).

P 8503. *PSYCHIATRY DIDACTIC LECTURE SERIES III.* (2 cr) Staff
The third of four six-month lecture series in the major theoretical and clinical areas of Psychiatry. Lectures and readings in this sequence focus upon the primary interventions used in the fields of Psychiatry and Psychology (e.g. pharmacotherapies and psychotherapies) as well as the contribution made to other medical specialties (e.g. coronary care, dialysis, Physical Medicine and Rehabilitation) through liaison psychiatric consultations.

P 8504. *PSYCHIATRY DIDACTIC LECTURE SERIES IV.* (2 cr) Staff
The last of four six-month lecture series in the major theoretical and clinical areas of Psychiatry. Topics include major areas of subspecialty interest in Psychiatry (e.g. Child and Adolescent Psychiatry, Chemical Dependencies, Forensic Psychiatry), the professional interface of Psychiatry with Clinical Psychology, and selected topics of special interest to psychiatrists (e.g. Ethical Issues in Psychiatry).

Research

P 900. *RESEARCH IN PSYCHIATRY.* (6 cr) Staff
Graduate thesis research.

Clinical

P 8100. *HOSPITAL PSYCHIATRY I: SECOND ASSISTANT.* (4 cr) Staff
Entry-level clinical experience in hospital psychiatry emphasizing major forms of psychopathology and standard hospital based psychiatry therapies.

P 8101. *HOSPITAL PSYCHIATRY II: SECOND ASSISTANT.* (4 cr) Staff
Intermediate-level clinical experience in inpatient psychiatry.

P 8102. *HOSPITAL PSYCHIATRY III: FIRST ASSISTANT.* (4 cr) Staff
Advanced inpatient hospital psychiatry with greater emphasis on independent clinical decision processes and the supervision/teaching of second assistants.

P 8103. *HOSPITAL PSYCHIATRY IV: FIRST ASSISTANT.* (4 cr) Staff
Most advanced inpatient hospital psychiatry with greatest emphasis on independent clinical decision processes and the supervision/teaching of second assistants.

P 8140f,w,s,su. *PAIN MANAGEMENT CENTER.* (2-4 cr) Staff
Intermediate level clinical experience in outpatient/inpatient pain rehabilitation program.

P 8150. *ADDU: ADULT CHEMICAL DEPENDENCY.* (4 cr) Staff
Clinical experience in the adult aspects of chemical dependency diagnosis and treatment emphasizing the medical, psychological, and social parameters of chemical addictions.

P 8160. *ACDU: ADOLESCENT CHEMICAL DEPENDENCY.* (4 cr) Staff
Clinical experience in the adolescent aspects of chemical dependency diagnosis and treatment emphasizing the medical, psychological, and social parameters of chemical addictions.

P 8170. *IPC: INTERPERSONAL PROCESS.* (4 cr) Staff
Clinical experience with intensive group, milieu and individual psychotherapies provided to nonpsychotic patients in a day-hospital setting with emphasis on interpersonal processes and theories.

P 8180. *CHILD PSYCHIATRY.* (6 cr) Staff
Clinical experience in child and adolescent psychopathology and treatment, both inpatient and outpatient.

P 8200. *OPS: OUTPATIENT PSYCHIATRY I.* (4 cr) Staff
Elementary-level clinical experience in the outpatient practice of psychiatry.

P 8201. *OPS: OUTPATIENT PSYCHIATRY II.* (4 cr) Staff
Advanced-level clinical experience in the outpatient practice of psychiatry.

P 8250. *CONSULTATION/LIAISON PSYCHIATRY.* (4 cr) Staff
Advanced clinical experience in psychiatric consultation to other medical subspecialties.

P 8270f,w,s,su. *FELLOWSHIP IN SUBSTANCE ABUSE.* (6 cr) Morse
This is a one-year clinical fellowship in addictive disorders designed primarily for graduates of psychiatric residencies. With the institution of

subspecialty examination in addiction psychiatry offered by the ABPN beginning in 1993, a basic one-year fellowship in addictions will be a prerequisite for this certification. The fellow will have clinical experience and supervision in both inpatient and outpatient assessment and treatment of addiction in adults and the outpatient assessment and treatment of drug abuse in adolescents. In addition, the fellow will design and carry out a clinical research project and will participate in educational seminars as well as teach psychiatric residents and Mayo medical students.

P 8271f,w,s,su. *FELLOWSHIP IN CONSULTATION-LIAISON PSYCHIATRY.* (6 cr) O'Connor
This is a one-year long experience in consultation-liaison psychiatry at the post-graduate year 5 level. The fellowship consists of six months of a core experience and six months of electives. The core experience entails performing inpatient and outpatient consultations under the supervision of a staff psychiatrist and serving as a senior resident on a medical psychiatry unit. A wide range of elective activities is available--the only requirement being the choice be consistent with the fellow's career goals.
ample time is provided for research.

P 8300. *THEORY AND PRACTICE OF PSYCHOLOGY.* (4 cr) Staff
Clinical experience and exposure to the interface between Psychiatry and Psychology.

P 8500. *ZUMBRO VALLEY MENTAL HEALTH CENTER.* (4 cr) Staff
Clinical experience in the evaluation and treatment of patients at a community mental health center. Coordination of services with community agencies is emphasized.

P 8550. *FEDERAL MEDICAL CENTER: PRISON PSYCHIATRY.* (4 cr) Staff
Clinical experience in the evaluation and management of mentall ill inmates at this major correctional treatment facility. Issues in forensic psychiatry will be considered.

P 8890f,w,s,su. *FELLOWSHIP IN SLEEP DISORDERS.* (6 cr; prereq finished residency in Pulmonology, Neurology or Psychiatry) Hauri
The main emphasis of this fellowship is on the clinical treatment of all sleep disorders. Fellows rotate through Psychiatry, Pulmonology, and ENT, and they take a two-month course in clinical neurophysiology.
ample time is provided for research.

RADIOLOGY

Didactic

R 8830f,w,s,su. *CARDIAC/VASCULAR RADIOLOGY.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of cardiac/vascular radiology. Course is intended for Diagnostic Radiology residents.

R 8831f,w,s,su. *CHEST RADIOLOGY.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of chest radiology. Course is intended for Diagnostic Radiology residents.

R 8832f,w,s,su. *CROSS-SECTIONAL IMAGING.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of cross-sectional imaging radiology. Course is intended for Diagnostic Radiology residents.

R 8833f,w,s,su. *GASTROINTESTINAL RADIOLOGY.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of gastrointestinal radiology. Course is intended for Diagnostic Radiology residents.

R 8834f,w,s,su. *GENITOURINARY RADIOLOGY.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of genitourinary radiology. Course is intended for Diagnostic Radiology residents.

R 8835su. *INTRODUCTION TO DIAGNOSTIC RADIOLOGY.* (3 cr) Reading and staff
Introduction to all aspects of Diagnostic Radiology including bone, chest, GI, GU, neuro, nuclear medicine, ultrasound, MRI, pediatrics, vascular, radiologic physics, and radiation protection.

R 8836f,w,s,su. *MUSCULOSKELETAL RADIOLOGY.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of musculoskeletal radiology. Course is intended for Diagnostic Radiology residents.

R 8837f,w,s,su. *NEURORADIOLOGY.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of neuroradiology. Course is intended for Diagnostic Radiology residents.

R 8838f,w,s,su. *NUCLEAR MEDICINE.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of nuclear medicine. Course is intended for Diagnostic Radiology residents.

R 8839f,w,s,su. *PEDIATRIC RADIOLOGY.* (1 cr; offered 2 quarters per year--quarters vary each year) Reading and staff
Case-based presentation, didactic lectures, and group discussion about all aspects of pediatric radiology. Course is intended for Diagnostic Radiology residents.

R 8854w,su. *RADIOLOGY OF THE MUSCULOSKELETAL SYSTEM.* (1 cr) Staff
Radiological principles in evaluation of bone pathology and skeletal disorders.

Research

R 8900 f,w,s,su. *RESEARCH IN RADIOLOGY.* (1 cr) Reading and staff
Instruction in research techniques combined with practical research experience. Much of this research experience will occur in the MRI Research Laboratory setting, but other areas of imaging research experience, outside of MRI, may be pursued as well. Course is intended for Diagnostic Radiology residents.

Clinical

R 8807f,w,s,su. *NUCLEAR MEDICINE.* (6 cr) Staff
Twelve months of Nuclear Medicine training as part of a complete residency program to meet the requirements of Diagnostic Radiology with special competence in Nuclear Radiology, or 12 months following an approved Diagnostic Radiology residency program. This training is to prepare candidates for a career in Diagnostic Radiology with special training in Nuclear Medicine, and to prepare them for the oral examinations and special competency of the American Board of Radiology.

R 8852f,w,s,su. *DIAGNOSTIC RADIOLOGY.* (6 cr) Staff
Forty-eight months of Diagnostic Radiology as a resident to meet the requirements of the Residency Review Committee in Diagnostic Radiology of the ACGME. This training is to prepare candidates for a career in Diagnostic Radiology and to prepare them to take the written and oral exams of the American Board of Radiology.

R 8862f,w,s,su. DIAGNOSTIC RADIOLOGY ELECTIVE. (13 cr) Staff
Two-six weeks in diagnostic radiology observing the role of the radiologist in the evaluation and treatment of patients in all areas of radiology including: chest radiology, uroradiology, skeletal radiology, pediatric radiology, gastrointestinal radiology, computed tomography, ultrasonography, neuroradiology, nuclear medicine, and hospital radiology. For those residents with a particular area of interest, time may be spent in one or more specific areas: pediatric residents in pediatric radiology, neurology or neurosurgical residents in neuroradiology, urology residents in uroradiology, G.I. residents in gastrointestinal radiology, etc.

R 8870f,w,s,su. *ABDOMINAL IMAGING FELLOWSHIP.* (6 cr; prereq Board eligible in Diagnostic Radiology) Reading
GI Core includes gastrointestinal fluoroscopy/double contrast exam-outpatient, inpatient (to include exposure to interventional procedures), body CT, ultrasound, elective. GU Core includes adult urography, GU CT, GU ultrasound, digital/angio, MRI, and elective.

R 8871f,w,s,su. *ANGIO-INTERVENTIONAL IMAGING FELLOWSHIP.* (6 cr; prereq Board eligible or certified in Diagnostic Radiology) Reading
The program includes angiography, vascular computed tomography, MRI, ultrasound, interventional, and electives.

R 8872f,w,s,su. *CARDIAC IMAGING FELLOWSHIP.* (6 cr; prereq Board eligible, having completed a four-year radiology training program or equivalent if foreign applicant) Reading

The program includes cardiac catheterization laboratory, echocardiology, cardiac CT/cine CT, cardiac MRI, research, cardiac pathology.

R 8873f,w,s,su. *CROSS-SECTIONAL IMAGING FELLOWSHIP.* (6 cr; prereq Board eligible in Diagnostic Radiology) Reading
Program includes ultrasonography, computed tomography, and MRI.

R 8874f,w,s,su. *MUSCULOSKELETAL IMAGING FELLOWSHIP.* (6 cr; prereq Board eligible in Diagnostic Radiology) Reading
The program includes musculoskeletal radiography and arthrography, musculoskeletal CT, musculoskeletal MRI, musculoskeletal nuclear medicine, musculoskeletal elective, and bone reading.

R 8875f,w,s,su. *NEURORADIOLOGY FELLOWSHIP.* (6 cr; prereq Board eligible, having completed a four-year radiology training program) Reading
The program includes neuropathology, cerebral antiography, myelography, head/spine CT, head/spine MRI.

R 8876f,w,s,su. *RADIOLOGY RESEARCH FELLOWSHIP.* (6 cr; prereq Board certified or eligible in Diagnostic Radiology) Reading
This program is designed to provide an opportunity for medical imaging research training at the fellowship level. The fellow will progress from participation in existing research programs within the department to formulation of an original program of investigation. Individual research projects will require advocacy and supervision by a staff member of the Department of Radiology. These projects will be considered for presentation at scientific meetings and for publication in the peer review literature.

R 8877f,w,s,su. *THORACIC IMAGING FELLOWSHIP.* (6 cr; prereq Board eligible or certified in Diagnostic Radiology) Reading
The program includes outpatient chest radiology, thoracic computed tomography, hospital/inpatient chest radiography, pulmonary medicine hospital rounds, thoracic surgery, and elective.

R 8878f,w,s,su. *CLINICAL MEDICAL PHYSICS.* (6 cr) Gray
This program provides comprehensive training and experience for candidates with doctoral degrees in the relevant physics sciences and who are interested in careers as clinical medical physicists in diagnostic imaging. Medical physics residents will learn the principles and procedures involved in the production of clinical diagnostic images, methods of image evaluation applicable in the clinical environment, techniques for optimization of radiation exposure for diagnostic examinations, radiation protection, methods of calculating specific organ doses and risk estimates, and principles, terminology, and applications of anatomical and physiological imaging techniques.

R 8880f,w,s,su. *CHEST RADIOLOGY.* (1 cr) Reading and staff
Instruction in clinical chest radiology film interpretation and procedural skills. Course is intended for Diagnostic Radiology residents.

R 8881f,w,s,su. *GASTROINTESTINAL RADIOLOGY.* (1 cr) Reading and staff
Instruction in clinical gastrointestinal radiology film interpretation and procedural skills. Course is intended for Diagnostic Radiology residents.

R 8882f,w,s,su. *HOSPITAL RADIOLOGY.* (1 cr) Reading and staff
Instruction in clinical hospital radiology film interpretation and procedural skills. Course is intended for Diagnostic Radiology residents.

R 8883f,w,s,su. *NEURORADIOLOGY.* (1 cr) Reading and staff
Instruction in clinical neuroradiology film interpretation and procedural skills. Course is intended for Diagnostic Radiology residents.

R 8884f,w,s,su. *PEDIATRIC RADIOLOGY.* (1 cr) Reading and staff
Instruction in clinical pediatric radiology film interpretation and procedural skills. Course is intended for Diagnostic Radiology residents.

R 8885f,w,s,su. *SKELETAL RADIOLOGY.* (1 cr) Reading and staff
Instruction in clinical skeletal radiology film interpretation and procedural skills. Course is intended for Diagnostic Radiology residents.

R 8886f,w,s,su. *ULTRASOUND.* (1 cr) Reading and staff
Instruction in clinical ultrasound radiology film interpretation and procedural skills. Course is intended for Diagnostic Radiology residents.

R 8887f,w,s,su. *URORADIOLOGY.* (1 cr) Reading and staff
Instruction in clinical uroradiology film interpretation and procedural skills. Course is intended for Diagnostic Radiology residents.

Technical Writing

Tech 5000su. *WRITING SCIENTIFIC PAPERS FOR PUBLICATION.* (1 cr) Staff
This course will include the following topics: Choosing the Journal; Identifying the Audience; Choosing the Title; Writing the Introduction; Tone and Style; Writing the Methods and Results; Writing the Discussion and Abstract.

Tumor Biology

TBio 5000f. *TUMOR BIOLOGY I: INTRODUCTION TO TUMOR BIOLOGY.* (3 cr) Maihle, Tindall
Material to be covered includes fundamental concepts and methods in tumor biology, as well as normal tissue histology and tumor pathobiology.

TBio 5100f,w,s,su. *RESEARCH SEMINARS IN TUMOR BIOLOGY.* (1 cr/yr) Maihle, Salisbury
Informal presentation of intramural research findings from the laboratories involved in relevant research investigations. Discussions will be based on chalk-talk format with the open research notebook. In addition, speakers from outside the institution will present throughout the year. All Tumor Biology trainees will be expected to present their research plans/findings in this forum annually and will be encouraged to actively participate in this highly multidisciplinary exchange of ideas and information.

TBio 5150f,s. *CURRENT TOPICS IN TUMOR BIOLOGY.* (1 cr) Salisbury, Maihle

This journal club will discuss current primary literature covering all aspects of tumor biology with an emphasis on women's cancers. The journal club will meet once per week and be conducted under the open discussion format with directed student and faculty presentations. During the fall quarter, journal articles of fundamental and historic interest in the area of tumor biology will be read and discussed. Topics to be covered include: cell cycle, oncogenes, tumor suppressors, growth factors, signal transduction, metastasis, DNA tumor viruses, retroviruses.

TBio 5200w. *PRINCIPLES OF PANCREATIC CANCER.* (1 cr) Urrutia
Anatomy, fine structure, and embryology of the pancreas. Basic cell biology and regulation of pancreatic gene expression. Cellular and animal models for the study of normal and neoplastic pancreatic cell differentiation. Epidemiology, etiology, diagnosis and management of pancreatic cancer.

TBio 5250w. *GENE THERAPY AND CANCER.* (1 cr) Federspiel, Salisbury
Current papers in the area of gene therapy and cancer will be reviewed and discussed in the journal club format. Students in the Tumor Biology program will participate in all sessions and will present a paper during the quarters that they are enrolled in this journal club.

TBio 5300su. *THE BUSINESS OF SCIENCE AND THE SCIENCE OF BUSINESS.* (1 cr; offered even years) Bennet, Maihle
This course reviews concepts fundamental to the commercial potential of biotechnology. Topics include current patent issues in biotechnology, regulatory issues in biotechnology and research funding mechanisms, as well as the grant review process.

TBio 5858f,w,s,su. *LABORATORY ROTATIONS IN TUMOR BIOLOGY* (2 cr) Staff
Tutorial course involving general techniques, instrumental analysis, and special procedures undertaken in the laboratory of choice. In addition, the student will assimilate the general research area of the laboratory through readings, lab meetings, and discussion. Students and faculty shall use these rotations to determine the degree of general mutual interest in research topics for potential thesis projects.

TBio 8000w. *TUMOR BIOLOGY II: ORIGINS OF HUMAN CANCER.* (3 cr; prereq TBio 5000) Maihle, Tindall
Topics to be covered include: basic tumor biology, oncogenes, tumor viruses, anti-oncogenes (tumor suppressors), tumor immunity, cancer chemotherapy, and biological response modifiers. Also listed under Molecular Biology.

TBio 8005f. *TUMOR BIOLOGY III: GROWTH FACTORS AND ONCOGENES.* (3 cr; prereq TBio 5000, TBio 8000) Maihle, Tindall
This course will focus on the mechanisms by which growth factors and oncogenes influence cell growth and division. Topics include: transmembrane signal transduction; cell cycle and regulation of cell division; ontogeny of oncogenes; mechanisms of oncogene activation; the insulin receptor family; PDGF/sis and PDGF receptor; EGF receptor/c-erb B 1 and 2 (neu); introduction to hematopoietic growth factors/receptors; receptors which lack intrinsic kinase activity, ras family of oncogenes;

introduction to nuclear signal transduction; chromosome/DNA-binding proteins; development and differentiation; wound-healing and angiogenesis; carcinogenesis in humans; and anti-oncogenes. Also listed under Molecular Biology.

TBio 8200w. *CELL BIOLOGY OF CANCER.* (3 cr) Salisbury, Gendler, Lingle
This advanced graduate level course will cover cell biology topics relevant to cancer using the tissue paradigm of breast cancer as a model. The format of the course will be didactic lecture, group discussions, and problem sets covering the following topics: Normal Breast Anatomy, Development, and Histology; Development and Differentiation; Epithelial-Stromal Interactions; Extracellular Matrix; Metastasis; Wound Healing; Angiogenesis; Hormones and Cancer; Targets for Therapeutic Intervention - Cell Cycle Control Points, Cell Signalling Pathways.

Research

TBio 8900f,w,s,su. *RESEARCH IN TUMOR BIOLOGY.* Staff
Graduate thesis research under supervision of staff.

Graduate Faculty Listing

FACULTY OF THE GRADUATE SCHOOL

The following are Full Members (FM) of the Graduate School faculty and are available as thesis advisers for doctoral candidates in the indicated areas of specialization within the Biomedical Sciences Ph.D. program.

Abraham, Robert T., Ph.D., University of Pittsburgh, 1981, FM-Immunology, Pharmacology & Tumor Biology. Biochemistry and molecular biology of T-lymphocyte activation and proliferation. Cytokine receptor signal transduction. Molecular mechanisms of action of immunosuppressant drugs.

Representative articles: Interleuken-2 triggers a novel phosphatidylinositol 3-kinase-dependent MEK activation pathway. *Molec. Cell. Biol.* 15:3049-3057, 1995 (with Karnitz, Burns, Sutor and Blenis).

Immunopharmacology of rapamycin. *Annual Review of Immunology,* in press, 1996 (with Wiederrecht).

Ames, Matthew M., Ph.D., California, San Francisco, 1976, FM-Molecular Neuroscience, Pharmacology & Tumor Biology. Design, synthesis and evaluation of novel anticancer agents; mechanism of action of anticancer agents; preclinical and clinical pharmacology (metabolism, disposition, pharmacokinetics) of anticancer agents in adult and pediatric cancer patients.

Representative projects: the role of serine proteases in tumor cell growth and mechanism-based serine protease inhibitors as potential antitumor agents; biology and biochemistry of carcinoid tumors, a neuroendocrine malignancy.

Representative articles: Comparative resistance of idarubicin, doxorubicin and their C-13 alcohol metabolites in human MDR1-transfected NIH-3T3 cells. *Cancer Chemother. Pharmacol.* 36, 223-226, 1995 (with Kuffel).

Kinetic properties of tryptophan hydroxylase and aromatic-L-amino acid decarboxylase in human carcinoid tumors. *Biochem. Pharmacol.,* 50(6), 845-850, 1995 (with Gilbert and Bates).

Brimijoin, W. Stephen, Ph.D., Harvard, 1969, FM-Pharmacology & Molecular Neuroscience. Neurobiology of cholinesterases. Development of cholinergic systems in the brain.

Representative articles: Using antibodies to unwire the sympathetic nervous system. *News in Physiol. Sci.* 10:101-106, 1995.

Transient Expression of Acetylcholinesterase mRNA and Enzyme Activity in Developing Rat Thalamus Studied by Quantitative Histochemistry and In Situ Hybridization. *Neurosci.* 71:555-556, 1996 (with Hammond).

Burnett, Jr., John C., M.D., Loyola University, 1974, FM-Physiology. Regulation of cardiovascular-renal homeostatis, natriuretic peptides, endothelial-derived vasoactive factors, endocrinology of congestive heart failure and hypertension.

Representative articles: Angiotensin converting enzyme inhibition modulates endogenous endothelin in chronic canine thoracic inferior vena caval construction. *J. Clin. Invest.* 97:1286-1292, 1996 (with Clavell, Mattingly, Stevens, Nir, Wright, Aarhus and Heublein).

A functional role for endogenous atrial natriuretic peptide in a canine model of

early left ventricular dysfunction. *J. Clin. Invest.* 95:1101-1108, 1995 (with Stevens, Kinoshita, Matsuda and Redfield).

Clapham, David E., M.D., Ph.D., Emory University, 1981, FM-Biophysical Sciences, Pharmacology & Molecular Neuroscience & Tumor Biology. Cell signalling mechanisms and the control of ion channels; regulation of intracellular calcium; role of G proteins.

Representative articles: The G-protein-gated atrial K+ channel I_{KACh} is a heteromultimer of two inwardly rectifying K+ channel proteins. *Nature* 374:135-141, 1995 (with Krapivinsky, Gordon, Wickman, Velimirovic, and Krapivinsky).

Nuclear Ca^{2+} store regulates diffusion across the nuclear envelope. *Science* 270:1835-1838, 1995 (with Stehno-Bittel and Perez).

David, Chella S., Ph.D., Iowa State University, 1966, FM-Immunology & Tumor Biology. Research centers on immunogenetic aspects of immune response, with emphasis on the major histocompatibiltiy complex (MHC) class II Ia genes and T-cell receptor gene (TCR). This group has generated several transgenic mice expressing human MHC genes, which are used in structure/function analysis, disease correlation, and thymic regulation of T-cell development. Two major ongoing studies on disease models are (1) using collagen-induced arthritis to study the role of MHC, TCR, and other parameters in arthritis and to evaluate different immunotherapeutic protocols; and (2) studying the role of enterobacteria in HLA-B27-linked spondyloarthropathies.

Representative articles: Immune response of HLA-DQ8 transgenic mice to HLA-DRB1 HV3 peptides correlates with predisposition to rheumatoid arthritis. *Proc. Natl. Acad. Sci.* 93:2824-2829, 1996 (with Zanelli, Krco, Baisch, and Cheng).

Spontaneous inflammatory arthritis in HLA-B27 transgenic mice lacking ß-microglobulin: A model of human spondyloarthropathies. *J. Exp. Med.* 182:1153-1158, 1995 (with Khare and Luthra)

Dewald, Gordon W., Ph.D., University of North Dakota, 1972, FM-Biochemistry and Molecular Biology & Tumor Biology. Human Cytogenetics: Structure, function and behavior of chromosome abnormalities in congenital disorders and malignant neoplasms.

Representative articles: The application of fluorescent in situ hybridization to detect Mbcr/abl fusion in variant Ph chromosomes in CML and ALL. *Cancer Genetics and Cytogenetics* 71:7-14, 1993 (with Schad, Christensen, Tiede, Zinsmeister, Spurbeck, Thibodeau and Jalal).

Cytogenetic guidelines for fragile X studies tested in routine practice. *American Journal of Medical Genetics* 44:816-821, 1992 (with Buckley, Sprubeck and Jalal).

Dousa, Thomas P., M.D., Charles University, Prague, 1962, Ph.D., Academy of Sciences, Prague, 1968, FM-Medicine & Physiology. Mechanism of hormone action on kidney; role of cyclic 3',5'-nucleotides and phosphorylations in regulation in normal kidney and in kidney in disease; role of cyclic 3',5'-nucleotide phosphodiesterases in renal cell injury. Regulatory role of cyclic ADP-ribose on Na+/Pi cotransporter in the kidney cells.

Representative articles: Formation of reactive oxygen metabolism in glomeruli is suppressed by inhibition of cAMP phosphodiesterase isozyme type IV. *Kidney Int.* 46:28-36, 1994 (with Chini, Chini, Williams and Matousovic).

Nicotinate Adenine Dinucleotide Phosphate (NAADP) triggers a specific calcium release system in sea urchin eggs. *J. Biol. Chem.* 270:3216-3223, 1995 (with Chini and Beers).

Dyck, Peter J., M.D., University of Toronto, 1955, FM-Molecular Neuroscience. Neurobiology of nerve; neuropathological alterations and morphormetric changes in experimental and human neuropathies; assessment of vibratory cold and warm sensation thresholds; corollation of neuropathologic and clinical abnormalities.

Representative articles: Ultrastructural morphometric abnormalities of sural nerve endoneurial microvessels in diabetes mellitus. *Ann. Neurol.* 36:408-415, 1994 (with Giannini).

A plasma exchange versus immune globulin infusion trail in chronic inflammatory demyelinating polyradiculoneuropathy. *Ann. Neurol.* 36:838-845, 1994 (with Litchy, Kratz, Suarez, Low, Pineda, Windebank, Karnes and O'Brien).

Ehman, Richard L., M.D., University of Saskatchewan, 1979, FM-Biophysical Sciences. Basic development of MR imaging techniques, vascular, cardiac, and flow imaging with MRI, functional imaging with MRI.

Engel, Andrew G., M.D., McGill University, 1955, FM-Molecular Neuroscience & Neurology. Disorders of neuromuscular transmission; immunology of muscle diseases.

Representative articles: Congenital myasthenic syndrome caused by prolonged acetylcholine receptor channel openings due to a mutation in the M2 domain of the E subunit. *Proc. Natl. Acad. Sci. USA* 92:758-762, 1995 (with Ohno, Hutchinson, Milone, Brengman, Bouzat and Sine).

Patch-clamp analysis of the properties of acetylcholine receptor channels at the normal human end-plate. *Muscle Nerve* 17:1364-1369, 1994 (with Milone and Hutchinson).

Fass, David N., Ph.D., Florida State University, 1969, FM-Biochemistry and Molecular Biology. Hemostasis and regulation of clotting factor levels and activities; genetics and gene expression in von Willebrand's disease; regulation of cell proliferation.

Representative articles: Molecular cloning of cDNA encoding human antihaemophilic factor. *Nature* 312:342-347, 1984 (with Toole, Knopf, Wozney, Sultzman, Buecker, Pittman, Kaufman, Brown, Shoemaker, Orr, Amphlett, Foster, Coe, Knutson, and Newick).

Molecular genetic analysis of porcine von Willebrand disease: Tight linkage to the von Willebrand factor locus. *Blood* 72:308-318, 1988 (with Bahou, Bowie, and Ginsburg).

Fernandez, Julio M., Ph.D., University of California, Los Angeles, FM-Biophysical Sciences, Physiology & Molecular Neuroscience. Mechanisms of secretion.

Representative articles: The exocytotic fusion pore and neurotransmitter. *Neuron,* in press (with Monck).

Release of secretory products during transient vesicle fusion. *Nature* 363:554-557 (with Alvarez de Toledo and Fernandez-Chacon).

Fitzpatrick, Lorraine A., M.D., University of Chicago, 1980, FM-Tumor Biology & AM-Biochemistry and Molecular Biology & Physiology. Bone disease, metastasis, and cancer.

Representative articles: Antithetic effects of ryanodine and ruthenium red on osteoclast-mediated bone resorption and intracellular calcium concentration. *J. Cell Biochem.* 59:281-289, 1995 (with Ritchie, Strei and Maercklein).

Diffuse calcification in human artherosclerotic coronary arteries: Association of osteopontin with atherosclerosis. *J. Clin. Invest.* 94:1597-1604, 1994 (with Severson, Edwards and Ingram).

Gendler, Sandra J., Ph.D., University of Southern California, 1984, FM-Biochemistry and Molecular Biology & Tumor Biology. Mucins in cancer, cystic fibrosis, and development; transgenic mouse studies of breast and colon cancer; protein targeting.

Representative publications: Delayed Mammary Tumor Progression in Muc-1 Null Mice. *J. Biol. Chem.* 270:30093-30101, 1995 (with Spicer, Rowse and Lidner).

The epithelial mucin MUC1 contains at least two discrete signals specifying membrane localization in cells. *J. Biol. Chem.* 271:2332-2340, 1996 (with Pemberton, Rughetti, and Taylor-Papadimitriou).

Getz, Michael J., Ph.D., Texas at Houston, 1972, FM- Biochemistry and Molecular Biology & Tumor Biology. Molecular and cellular biology of peptide growth factors; regulation of specific gene transcription; pathobiology of cancer.

Representative articles: Negative regulation of the vascular smooth muscle α-actin gene in fibroblasts and myoblasts: Disruption of enhancer function by sequence-specific single-stranded-DNA-binding proteins. *Mol. Cell. Biol.* 15:2429-2436, 1995 (with Sun et al.)

Tissue factor gene transcription in serum-stimulated fibroblasts is mediated by recruitment of c-Fos into specific AP-1 DNA-binding complexes. *Biochemistry* 34:12355-12362, 1995 (with Felts et al.).

Gilbert, Barry K., Ph.D., Mayo Graduate School (University of Minnesota), 1972, FM-Biophysical Sciences. Design of computer hardware; development of computer aided design (CAD) software; development of Gallium Arsenide digital integrated circuit and high performance, compact electronic packaging technologies for high-performance digital signal processors; studies of mathematical algorithms for biomedical signal and image processing and analysis; computation-bound problems in biomedical research.

Representative articles: Frequency-Domain Analysis of Coupled Nonuniform Transmission Lines Using Chebyshev Pseudo-Spatial Techniques. *IEEE Transactions on Microwave Theory and Techniques* 40(11):2025-2033, November 1992.

Design Guidelines for Digital Multichip Modules Operating at High System Clock Rates. *The International Journal of Microcircuits and Electronic Packaging* 15(4):171-182, Fourth Quarter 1992.

Gleich, Gerald J., M.D., University of Michigan, 1956, FM- Immunology & Medicine. Allergic inflammation with particular reference to the role of the eosinophilic leukocyte; analysis of eosinophil granules to define biologic activities associated with the eosinophil; the mechanism of eosinophilia in clinical syndromes and, in particular, the importance of cytokines such as interleukin 5 in

the causation of clinical eosinophilia; and the cause of the eosinophilia-myalgia syndrome.

Representative articles: Eosinophil granule proteins increase microvascular macromolecular transport in the hamster cheek pouch. *J Immunol* 153:2664-2670, 1994 (with Minnicozzi, Durán and Egan).

Expression, purification, and characterization of the recombinant proform of eosinophil granule major basic protein. *J Immunol* 155:1472-1480, 1995 (with Popken-Harris, McGrogan, Loegering, Checkel, Kubo, Thomas, Moy, Sottrup-Jensen, Snable, and Kikuchi).

Goronzy, Jorg J., M.D., University of Aachen, West Germany, 1979, **Ph.D.,** Heidelberg University, West Germany, 1988, FM- Immunology. Chronic inflammatory immune responses. Research is focused on elucidating the role of T cells in the initiation and perpetuation of chronic inflammatory response.

Representative articles: Dominant clonotypes in the repertoire of peripheral $CD4^+$ T cells in rheumatoid arthritis. *J Clin Invest* 94:2068-2076, 1994 (with Bartz-Bazzanella, Hu, Jendro, Walser-Kuntz, and Weyand).

Mechanisms underlying the formation of the T cell receptor repertoire in rheumatoid arthritis. *Immunity* 2:597-605, 1995.

Gray, Joel E., Ph.D., University of Toronto, 1977, FM-Biophysical Sciences & AM-Radiology. Diagnostic imaging, psychophysics and perception, radiation risk.

Representative articles: Evaluation of resolution and sensitometric characteristics of an asymmetric screen-film imaging system. *Radiology* 188:537-539, 1993 (with Stears, Swensen, and Bunch).

Acceptance and use of the SMPTE medical diagnostic imaging test pattern for television and hard-copy recording cameras. *SMPTE Journal* 99(12):1001-1007, 1990 (with Lisk, Anderson, Harshbarger, Schwenker and Uzenoff).

Greenleaf, James F., Ph.D., Purdue, 1970, FM-Biophysical Sciences & AM-Physiology. Computer methods of biological data acquisition, analysis, and display; algebraic reconstruction; ultrasonic imaging; mathematical signal processing, ultrasonic therapy.

Representative articles: The effect of concave and convex weight adjustments on self-organizing maps. *IEEE Trans. Neural Networks* 7(1):87-96, January, 1996 (with Zheng).

Ultrasound: Physics and instrumentation. *Acacemic Radiology* 2:S115-S117, 1995.

Jelinek, Diane F., Ph.D., Southwestern Graduate School in Biomedical Sciences, 1985, FM-Immunology & AM-Tumor Biology. Molecular biology of cytokine regulation of normal and malignant B cell growth and differentiation.

Representative articles: CD40 expression in malignant plasma cells: Role in stimulation of autocrine IL-6 secretion by a human myeloma cell line. *J. Immunol.* 152:117-128, 1994 (with Westendorf, Ahmann, Armitage, Spriggs, Lust, Greipp and Katzmann).

Differentiation activation of a calcium-dependent endonuclease in human B lymphocytes: Role in ionomycin-induced apoptosis. *J. Immunol.* 155:3297-3307, 1995 (with Aagaard-Tillery).

Kaufmann, Scott H., M.D., Ph.D., Johns Hopkins University, 1981, FM-Pharmacology & AM-Tumor Biology. Resistance to cancer chemotherapy agents. Mechanisms of drug-induced apoptosis.

Representative articles: Cleavage of Poly (ADP-ribose) Polymerase by a Proteinase with Properties like ICE. *Nature* 371:346-347, 1994 (with Lazebnik, Desnoyers, Poirier, and Earnshaw).

Increased expression of the multidrug resistance-associated protein gene in relapsed acute leukemia. *Blood* 85:186-193, 1995 (with Schneider, Cowan, Bader, Toomey, Schwartz, Karp, and Burke).

Knox, Franklyn G., M.D., Ph.D., SUNY, Buffalo, 1965, FM-Physiology & Medicine. Renal physiology; the study of the intrarenal regulation of electrolyte transport.

Representative articles: Renal Regulation of Phosphate Excretion. IN: *The Kidney*, Seldin and Giebisch, eds., Chapter 71, pp 2511-2532, 1992 (with Berndt).

Control of Sodium Excretion: An Integrative Approach. IN: *Handbook of Physiology*, Section 8, Renal Physiology, E. Windhager, ed., Chapter 21, pp 927-968, 1992 (with Granger).

Kumar, Rajiv, M.D., Delhi University, 1972, FM-Biochemistry and Molecular Biology & AM-Medicine. Calcium and phosphorus metabolism; the mechanism of action of sterol (vitamin D) and steroid hormone, clinical research involving mineral metabolism; mechanism of vasopressin action.

Representative articles: A factor derived from human sclerosing hemangioma cells inhibits sodium-dependent phosphate transport in cultured renal epithelia. *New Engl. J. Med.* 330:1645-1649, 1994 (with Cai, Hodgson, Kao, Lenno, Klee, Zinsmiester, and Kumar)

Identification of metal binding sites in rat brain calcium-binding protein. *J. Biol. Chem.* 270:30353-30358, 1995 (with Veenstra, Gross, Hunziker and Kumar).

Lee, James J., Ph.D., California Institute of Technology, 1986, FM-Biochemistry and Molecular Biology. Transgenic mouse models of immune mediated inflammation: recruitment and activation of eosinophils.

Leibson, Paul J., M.D., Ph.D., University of Chicago, 1979, 1981, FM-Immunology & Tumor Biology. Exploring human cell-mediated antiviral and anti-tumor immunity, with a special interest in natural killer (NK) cell activity.

Representative articles: Inhibition of selective signaling events in natural killer cells recognizing major histocompatibility complex class I. *Proc. Natl. Acad. Sci. USA* 92:6484-6488, 1995 (with Kaufman, Schoon, and Robertson).

Interaction between lck and syk family tyrosine kinases in Fcγ receptor-initiated activation of natural killer cells. *J. Biol. Chem.* 270:16415-16421, 1995 (with Ting, Dick, Schoon, Karnitz and Abraham).

Lennon, Vanda A., M.B.,B.S. (M.D.), University of Sydney, 1966, **Ph.D.**, University of Melbourne, 1973, FM-Immunology, Molecular Neuroscience & Tumor Biology & T/E-Neurology. Organ-specific autoimmunity directed against the nervous system is often a manifestation of a patient's immune responses against a remote and occult carcinoma of lung, ovary, or breast, or thymic

epithelial neoplasm. Our molecular and immunobiological studies of ionic channels, neurotransmitter receptors and other neuron-related molecules expressed in these human tumors are yielding novel and clinically important insights into the nature of tumor molecules that are spontaneously immunogenic in man, and the immunologic mechanisms responsible for by-passing self-tolerance.

Representative articles: Calcium channel antibodies in Lambert-Eaton myasthenic syndrome and other paraneoplastic syndromes. *New Engl. J. Med.* 332:1467-1474, 1995.

ß subunit heterogeneity in N-type Ca^{2+} channels. *J. Biol. Chem.* 271:3207-3215, 1996.

Leof, Edward B., Ph.D., University of North Carolina, 1982, FM - Biochemistry and Molecular Biology & Tumor Biology. Cellular signalling and the mechanism of action of growth factors.

Representative articles: Conditional binding to and cell cycle-regulated inhibition of cyclin-dependent kinase complexes by $p27^{Kip1}$. *Cell Growth Diff.* 6, 915-925, 1995 (with Eblen, Fautsch and Anders).

Chimeric GM-CSF/TGFß receptors define a model system for investigating the role of homomeric and heteromeric receptors in TGFß signaling. Submitted.

Lipsky, James J. M.D., Johns Hopkins, 1972, FM-Pharmacology. Clinical pharmacology, sulfur drug metabolism, metabolic activation, vitamin K metabolism, enzymology.

Representative articles: S-Methyl N,N-Diethylthiocarbamate Sulfone, a Potential Metabolite of Disulfiram and Potent Inhibitor of Low Km Mitochondrial Aldehyde Dehydrogenase. *Biochem. Pharmacol.* 49:693-700, 1995 (with Mays, Nelson, Fauq, Shriver, Veverka, and Naylor).

Simultaneous Structure-Activity Determination of Disulfiram Photolysis Products by On-line Continuous Flow-Liquid Secondary Ion Mass Spectrometry (CF-LSIMS) and Enzyme Inhibition Assay. *J. Chromatogr.* 693:102-106, 1995 (with Benson, Veverka, Mays, Nelson, Shriver, and Naylor).

Low, Phillip A., MBBS, University of Sydney, 1966, **M.D.,** (Research), 1977; FM-Molecular Neuroscience. Neurophysiology of peripheral nerve microenvironment. Human autonomic physiology.

Representative articles: Low PA (Ed), *Clinical Autonomic Disorders: Evaluation and Management.* Boston: Little, Brown and Company, 1993.

Hypoxic effect of exogenous insulin on normal and diabetic peripheral nerve. *Am J Physiol* 226:E980-E985, 1994 (with Kihara, Zollman, Smithson, and Lagerlund).

Macura, Slobodan, Ph.D., University of Belgrade, 1978, FM-Biochemistry and Molecular Biology. The solution structure of macromolecules using NMR.

Representative articles: Somatostatin Analogue Octreotide Modulates Metabolism and Effects of 5-Fluorouracil and 5-Fluorouridine in Human Colon Cancer Spheroids. Cancer Letter 86:41-51, 1994 (with Chen, Huzak, and Vuk-Pavolovic).

Hydrogen Bonding Networks in Proteins as Revealed by Amide $^{1}J_{NC'}$ Coupling Constant. *J. Am. Chem. Soc.* 117:405-410, 1995 (with Juranic and Ilich).

Maher, L. James, III, Ph.D., University of Wisconsin, 1988, FM-Biochemistry and Molecular Biology & Tumor Biology. Nucleic acid biochemistry, triple helix DNA.

Representative articles: Inhibition of DNA binding Proteins by Oligonucleotide-Directed Triple Helic Formation. *Science* 245:725-730, 1989 (with Wold and Dervan).

DNA Binding by Asymmetric Phosphate Neutralization. *Science* 266:1829-1834, 1994 (with Strauss).

Maihle, Nita J., Ph.D., Albert Einstein College of Medicine, 1983, FM-Biochemistry and Molecular Biology & Tumor Biology & AM-Molecular Neuroscience. Molecular basis of carcinogenesis: oncogenes, tumor suppressors, tumor virus. Human cancers: breast, ovarian and prostate carcinomas, gliomas.

Representative articles: A 1.8 kb alternative transcript from the human epidermal growth factor receptor gene encodes a soluble, truncated form of the receptor. *Genomics*, submitted, 1996 (with Reiter).

Ligand-independent dimerization of oncogenic v-*erbB* products involves covalent interactions. *J. Virology* 70:2533-2544, 1996 (with Adelsman and Huntley).

McCullough, Edwin C., Ph.D., University of Wisconsin, 1971, FM-Biophysical Sciences & AM-Radiology. Radiation therapy physics including treatment planning, quality assurance of simulators and linear accelerators, and intraoperative electron beam therapy and stereotactic radiotherapy.

Representative articles: Doses to radiation sensitive organs and structures located outside the radiotherapeutic target volume for four treatment situations. *International Journal of Radiation Oncology, Biology and Physics* 26:483-489, 1993.

An analysis of photon beam buildup region dosage with regard to treatment energy preference. *Medical Dosimetry* 19:5-14, 1994.

McDonald, John A., Ph.D., Rice University, 1970, **M.D.,** Duke University, 1973, FM-Biochemistry and Molecular Biology. Cell biology of extracellular matrix, including integrins, fibronectin, and hyaluronan, during embryogenesis, cancer, and tissue repair.

Representative articles: Integrin activation and cytoskeletal interaction are essential for the assembly of fibronectin matrix cell. *Cell* 83:715-724, 1995 (with Wu, Keivens, Otoole, and Ginsberg).

Identification of a new biological function for the inegrein avb3: Initiation of matrix assembly. *Cell Adhesion and Communication,* in press, 1996 (with Wu, Hughes and Ginsberg).

McKean, David J., Ph.D., Johns Hopkins, 1973, FM-Immunology & Tumor Biology. Characterization of molecular intracellular signaling mechanisms regulating lymphokine gene transcription and T lymphocytes activated by antigen, CD28 and IL-1 receptors. Structure-function analysis of murine major histocompatibility complex class II molecules: regulation of class II complex assembly and intracellular transport.

Representative articles: *International Immunology* 7:9-20, 1995. *J. Exper. Med.* 180:1321-1328, 1995.

McKinney, Michael, Ph.D., Johns Hopkins, 1982, FM-Molecular Neuroscience & AM-Pharmacology. Neuropharmacology, central cholinergic neurotransmission, molecular neurobiology of cholinergic neurons, Alzheimer's Disease.

Representative articles: Differential expression of GAP-43 mRNA in central cholinergic neuronal populations. *Mol. Brain Res.* 23:213-220, 1994 (with Kent).

Differntial expression of mRNA for the calmodulin-dependent nitric oxide synthase within cholinergic neuronal populations. *Mol. Brain Res.* 23:111-125, 1994 (with Sugaya).

McMurray, Cynthia T., Ph.D., Oregon State University, 1987, FM-Pharmacology, AM-Biochemistry and Molecular Biology & Molecular Neuroscience. Mechansims of nuclear signalling via membrane receptors: second-messengers, phosphorylation, gene expression, protein/DNA structure function; chromatin packaging; neurodegenerative disease; mutation.

Representative publications: Trinucleotides associated with expansion in human disease from hairpin structures in vitro. *Cell* (in press), 1995 (with Gacy, Goellner, Juranic, and Macura).

Induction of rat prodynorphin gene through G-coupled receptors may involve phosphorylation-dependent derepression and activation. *Mol. Cell. Biol.* 14(5):2837-2848, 1994 (with Collins-Hicok, Lin, Spiro, Laybourn, Tschumper, and Rapacz).

McNiven, Mark A., Ph.D., University of Maryland, 1987, FM-Molecular Neuroscience & AM-Biochemistry and Molecular Biology. Molecular mechanisms of vesicular transport, cytoskeleton, secretion and endocytosis in mammalian cells.

Representative articles: Association of a dynamin-like protein with the Golgi apparatus in mammalian cells. *J. Cell Biol.*, in press (with Henley).

Upregulation of molecular modor-encoding genes during hepatocyte growth factor- and epidermal growth factor-induced cell motility. *J. Cell Physiol.*, in press (with Török, Urrutia and Nakamura).

Morin, Richard L., Ph.D., University of Oklahoma, 1980, FM-Biophysical Sciences. Electronic medical imaging; computed tomography; magnetic resonance imaging; computer networks in imaging.

Representative articles: CT reconstruction algorithm selection in the evaluation of solitary pulmonary modules. *J. Comp. Assist. Tomog.* 19:932-935, 1995 (with Swensen, Aughenbaugh, et al.).

The technical design and performance of ultrafast computed tomography. *Radiol. Clini. No. Amer.* 32:521-536, 1994 (with McCollough).

Moyer, Thomas P., Ph.D., North Dakota State University, 1975, FM-Pharmacology. Toxicology, clinical correlation studies of diagnostic tests.

Representative articles: Testing for arsenic. *Mayo Clin. Proc.* 68:1210-1211, 1993.

Liver biopsy diagnosis of homozygous hemochromatosis: A diagnostic algorithm. *Mayo Clin. Proc.* 68:263-267, 1993 (with Ludwig, et al.).

Naylor, Stephen, Ph.D., University of Cambridge, United Kingdom, 1987, **DSc** University of East Anglia, United Kingdom, 1991, FM-Pharmacology & AM-

Biochemistry and Molecular Biology. Drug and Xerobrotic metabolism using capillary electrophoeresis - MS. Protein-drug interactions and immunochemical detection of haloperndol - neuroproteins.

Owen, Whyte, G., Ph.D., University of North Carolina, 1975, FM-Biochemistry and Molecular Biology. Regulation of blood coagulation and fibrinolysis, especially protein chemistry of plasma zymogens; thrombin enzymology and physiology; protease inhibitors.

Representative articles: Hirudin as a molecular probe for thrombin in vitro and during systemic coagulation in the pig. *Proc. Nat. Acad. Sci.* 90:1819-1823, 1993 (with Zoldhelyi and Chesebro).

Endogenous antithrombin associated with microvascular endothelium. Quantitative analysis in perfused rat hearts. *Biochemistry* 33:818-822, 1994 (with Felsch).

Pagano, Richard E., Ph.D., University of Virginia, 1968, FM-Biochemistry and Molecular Biology & Molecular Neuroscience. Intracellular transport of lipids; lipid metabolism; liposomes; fluorescence methods.

Representative articles: Ceramide as a modulator of endocytosis. *J. Biol. Chem.* 270:13291-13297, 1995 (with Chen and Rosenwald).

A Chinese hamster ovary cell mutant defective in the non-endocytic uptake of fluorescent analogs of phosphatidylserine: Isolation using a cytosol acidification protocol. *J. Cell Biol.* 128:793-804, 1995 (with Hanada).

Paya, Carlos V., M.D., University of Madrid, 1981, **Ph.D.,** University of Madrid, 1992, FM-Immunology. Viral immunology. Study of the interactions between human pathogenic viruses (HIV, CMV and host cell nuclear transcription factors (NF-kB, CREB) in immune cells (T cells, monocytes).

Pease, Larry R., Ph.D., University of Michigan, 1978, FM-Immunology & Biochemistry and Molecular Biology. Molecular Immunogenetics: Molecular analysis of genetic mechanisms leading to genetic diversity in the major histocompatibility complex. Evolution of class I promoter structure. Structural and functional contributions of sequence diversity among antigen presenting molecules (transplantation antigens) in antigen presentation to T cells and in repertoire selection.

Representative articles: *Immunol.* 150:3375-3381, 1993. *Mol. Cell. Biol.* 13:4374-4381, 1993.

Penniston, John T., Ph.D., Harvard, 1962, FM-Biochemistry and Molecular Biology. Biological membranes; erythrocytes; calmodulin; Ca^{2+} transport.

Representative articles: Mutants in the putative nucleotide-binding region of the plasma membrane Ca^{2+} pump: A reduction in activity due to slow dephosphorylation. *J. Biol. Chem.* 270:30111-30114, 1995 (with Adamo, Filoteo and Enyedi).

Plasma membrane calcium pump isoform 4a has a longer calmodulin-binding domain than 4b. *J. Biol. Chem.* 271:3714-3718, 1996 (with Verma, Enyedi, Filoteo and Strehler).

Persing, David H., M.D., Ph.D., University of California, 1988, FM-Tumor Biology & AM-Immunology. Molecular immunobiology of zoonotic infections, pathogen-pathogen interactions leading to immune suppression, host and pathogen specific determinants of human papillomavirus transformation, intracellular mechanisms of papillomavirus assembly.

Representative articles: Infections with a *Babesia*-like organism in northern California. *N. Engl. J. Med.* 332:298-303, 1995 (with Herwaldt, Glaser, Lane, Thomford, Mathiesen, Krause, Phillip and Conrad).

Perpetuation of the agent of human granulocytic ehrlichiosis in a deer tick-rodent cycle. *PNAS*, in press (with Telford, Dawson, Katavolos, Warner and Kolbert).

Poduslo, Joseph F., Ph.D., University of Pennsylvania, 1973, FM-Biochemistry and Molecular Biology & Molecular Neuroscience & T/E-Neurology. Molecular Neurobiology, Neurochemistry, Membrane Biochemistry. Regulation of myelin gene expression; Role of axon in inducing Schwann cell myelin gene expression; Therapeutic approaches for preventing demyelination; Post-translational protein modifications: glycosylation, sulfation, acylation, and phosphorylation: Quantification of protein permeability at the blood nerve/brain barriers; Delivery of therapeutic proteins into the nervous system.

Representative articles: Polyamine modification increases the permeability of proteins at the blood-nerve and blood-brain barriers. *J. Neurochem.* 66:1599-1609, 1996 (with Curran).

Permeabilities at the blood-brain and blood-nerve barriers of the neurotrophic factors: NGF, CNTF, NT-3, BDNF. *Molecular Brain Res.* 36:280-286, 1996 (with Curran).

Prendergast, Franklyn G., M.D., University of West Indies, 1968, **Ph.D.,** University of Minnesota, 1977, FM-Biochemistry and Molecular Biology, Pharmacology & Tumor Biology. Fluorescence spectroscopy; protein structure and dynamics, microspectrofluorometry. Biochemistry of bioluminescence; membrane biochemistry.

Representative articles: Maximum likelihood method for the analysis of time-resolved fluorescence decay curves. *Eur. Biophys. J.* 20:247-262, 1991 (with Bajzer, Therneau and Sharp).

Fluorescence circular dichroism, attenuated total reflectance (ATR) FT-IR and 13C NMR characterization of the structure and dynamics of synthetic melittin and melittin analogues in lipid environments. *Biochemistry* 31:1301-1313, 1992 (with Weaver, Kemple, Brauner and Mendelsohn).

Tryptophan-47 rotational isometrization in variant-3 scorpion neurotoxin: A combination thermodynamic perturbation and umbrella sampling study. *Biophys J.* 571269-1279, 1990 (with Haydock and Sharp).

Rae, James L., Ph.D., FM-Biophysical Sciences & Physiology. Electrophysiology of ocular epithelia including mechanisms of cataract formation and mechanisms of corneal deturgence.

Representative articles: A cation channel in frog lens epithelia responsive to pressure and calcium. *J. Memb. Biol.* 93:259-269, 1986 (with Cooper, Tang and Eisenberg).

Potassium channels from chick lens epithelium. *Federation Proc.* 45:2718-2722, 1986.

Richelson, Elliott, M.D., Johns Hopkins, 1969, FM-Pharmacology & Molecular Neuroscience & AM-Psychiatry. Basic and clinical neuropsychopharmacology.

Representative articles: Chimeric rat/human neurotensin receptors localize a region of the receptor sensitive to binding of a novel, species specific, picomolar affinity peptide. *Journal of Biological Chemistry,* in press, 1996.

Pharmacological and biochemical profiles of unique neurotensin (8-13) analogs exhibiting species selectivity, stereo-selectivity and super-agonism. *Journal of Biological Chemistry* 270:18359-18366, 1995 (with Cusack, McCormick, Pang, Souder and Garcia).

Riederer, Stephen J., Ph.D., FM-Biophysical Sciences. Technical aspects of medical diagnostic imaging: nuclear magnetic resonance imaging (MRI); digital imaging.

Representative articles: Contrast optimization of fluid-attenuated inversion recovery (FLAIR) imaging. *Magn. Reson. in Med.* 34:868-877, 1995 (with Rydberg, Rydberg and Jack).

Multiple breathhold 3D time-of-flight MR angiography of the renal arteries. *Magn. Reson. in Med.* 35:426-434, 1996 (with Wilman, Grimm, Rossman, Wang, Ehman and King).

Riordan, John R., Ph.D., University of Toronto, 1979, FM-Biochemistry and Molecular Biology. Structure and function of membrane proteins involved in human disease including CFTR, drug transporters and myelin protelipid protein.

Ritman, Erik L., MBBS, Melbourne University Medical School, 1964, **Ph.D.,** University of Minnesota, 1973, FM-Biophysical Sciences, Physiology & AM-Medicine. Cardiovascular physiology; quantitation of cardiac dynamics and coronary circulation by computer assisted analysis of x-ray CT images.

Representative articles: Computed tomography evaluation of regional increases in microvascular permeability after reperfusion of locally ischemic myocardium in intact pigs. *Academic Radiology* 2:952-958, 1995.

Microvascular blood volume-to-flow relationships in porcine heart wall: whole body CT evaluation in vivo. *American Journal of Physiology* 269 (Heart Circ Physiol 38):H1820-H1826, 1995 (with Liu, Bahn, and technical assistance of Beighley).

Robb, Richard A., Ph.D., University of Utah, 1971, FM-Biophysi- cal Sciences, Molecular Neuroscience & Physiology. Computerized analysis of multidimensional biomedical images; scientific visualization; display and analysis of 3-D image data; computer aided surgery and treatment planning; virtual reality; workstations and networks for distributed image processing.

Representative articles: *Three-Dimensional Biomedical Imaging:* R. A. Robb, editor; CRC Press, 1985, Volumes I and II.

Three-Dimensional Biomedical Imaging - Principles and Practice: VCH Publishers, New York, NY, 1994.

Rodriguez, Moses, M.D., Northwestern University, 1975, FM-Immunology & AM-Molecular Neuroscience & Neurology. Viral immunopathology. The laboratory is

concerned with the role of the immune response and virus persistence in demyelination of the central nervous system in diseases such as multiple sclerosis.

Representative articles: Theiler's virus persistence and demyelination in Mayo Histocompatibility Complex Class II-Deficient Mice. *J. Virol.* 70:1729-1737, 1996 (with Njenga, Pavelko, Baish, David, and Leibowitz).

Monoclonal antibody SCH94.03, which promotes central nervous system remyelination, recognizes an antigen on the surface of oligodendrocytes. *J. Neurosci. Res.* 43:273-281, 1996 (with Asakura, Miller, Murray, Bansal, and Pfeiffer).

Romero, Juan C., M.D., University of Cuyo, Argentina, 1964, AM-Medicine & FM-Physiology. Renal and cardiovascular physiology; the role of renal humoral factors in the control of blood pressure.

Representative articles: Role of endothelium-dependent relaxing factor nitric oxide on renal function. *J. Am. Soc. Nephrol.* 2:1371-1387, 1992 (with Lahera, Salom and Biondi).

Are renal hemodynamics a key factor in the development and maintenance of arterial hypertension in humans? *Hypertension* 23:3-9, 1994 (with Ruilope, Lahera and Rodicio).

Salisbury, Jeffrey L., Ph.D., Ohio State University, 1978, FM-Biochemistry and Molecular Biology & Tumor Biology. Cell Biology; Cell Cycle Progression; Centrosomes; Mitotic Spindle Poles; Breast Cancer.

Representative articles: Centrin, centrosomes, and mitotic spindle poles. *Current Opinion in Cell Biol.* 7:39-45, 1995.

Identification of a complex between centrin and heat shock proteins in CSF arrested *Xenopus* oocytes and dissociation of the complex following oocyte activation. *Devel. Biol.* 171:51-59, 1995 (with Uzawa, Grams, Madden and Toft).

Schaff, Hartzell V., M.D., University of Oklahoma, 1973, FM-Physiology. Cardiovascular effects of extracorporeal circulation; alterations in endothelial cell function during global ischemia and reperfusion; myocardial function in valvular heart disease.

Representative articles: Detection of intraluminal release of endothelium-derived felaxing factor from human saphenous veins. *Circulation* 88:II-128-132, November 1993 (with Chua, Pearson and Evora).

Oxygen radical-mediated vascular injury selectively inhibits receptor-dependent release of nitric oxide from canine coronary arteries. *The Journal of Thoracic and Cardiovascular Surgery* 107:505-509, February 1994 (with Seccombe and Pearson).

Schmid, Harald H.O., Ph.D., University of Graz, Austria, 1964, FM-Biochemistry and Molecular Biology. The structure, metabolism and function of complex lipids in biological membranes.

Representative articles: Peroxidative damage to cardiac mitochondria. II. Immunological analysis of modified adenine nucleotide translocase. Arch. Biochem. *Biophys.* 315:1-7, 1994 (with Giron-Calle and Zwizinski).

Generation and remodeling of phospholipid molecular species in rat hepatocytes. *Arch. Biochem. Biophys.* 319:168-176, 1995 (with Schmid, P.C. and Deli).

Sieck, Gary C., Ph.D., University of Nebraska Medical Center, 1976, AM-Anesthesiology & FM-Molecular Neuroscience & Physiology. Plasticity in neuromotor control including: alterations in motor unit mechanical and metabolic properties; alterations in motoneuron morphometry; alterations at neuromuscular junction. Models include postnatal development; neural inactivation; compensatory loading and steroidal treatment.

Representative articles: Mechanical properties of muscle units in the cat diaphragm. *J. Neurophysiol.* 59: 1055-1066, 1988 (with Fournier).

Oxidative capacity and capillary density of diaphragm motor units. *J. Appl. Physiol.* 67: 620-627, 1989 (with Enad, et al).

Sine, Steven M., Ph.D., University of California, San Diego, 1980, FM Biophysical Sciences, Molecular Neuroscience, Physiology.

Representative articles: Activation of Torpedo acetylcholine receptors expressed in mouse fibroblasts: single channel current kinetics reveal distinct agonist binding affinities. *Journal of General Physiology* 96: 395-437, 1990 (with Claudio and Sigworth).

Molecular dissection of subunit interfaces in the acetylcholine receptor: Identification of residues that determine curare selectivity. *Proc. Natl. Acad. Sci. USA* 90:9436-9440, 1993.

Spelsberg, Thomas C., Ph.D., West Virginia, 1967, FM-Biochemistry and Molecular Biology & Tumor Biology. One area pertains to the gene regulation of steroid hormones, including 1) the biological functions of a nuclear matrix receptor binding factor and its DNA binding element, 2) the role this complex plays in the nuclear binding of steroid receptors, and in the steroid regulation of "early" gene's (proto-oncogene) expression. A second area pertains to the biological and molecular actions of steroids (estrogens) and growth factors (TGF-ß) in bone cells (osteoblasts and osteoclasts). This includes the steroid regulation of growth factor production, the growth factor and steroid regulation of a novel human transcription factor, termed TGF-ß inducible early gene (TIEG).

Representative articles: Identification of a novel TGF-ß regulated gene encoding a putative zinc finger protein in human osteoblasts. *Nucleic Acids Res.* 23(23):4907-4912, 1995 (with Subramaniam, Harris, Rasmussen, and Riggs).

Composition and structure of a nuclear matrix acceptor site for the avian progesterone receptor in the c-myc gene promoter. *Recent Progress in Hormone Research* 52:63-96, 1996 (with Lauber, Sandhu and Subramaniam).

Strehler, E. Emanuel, Ph.D., Swiss Fed. Institute of Technology, 1981, FM-Biochemistry and Molecular Biology & Molecular Neuroscience & AM-Tumor Biololgy. Intracellular calcium regulation; Calcium transport; Gene regulation.

Representative articles: Sodium-calcium exchanges and calcium pumps. In: Principles of Medical Biology, Vol. 6 (Bittar, E.E. and Bittar, N., eds.) JAI Press Inc., pp. 125-150, 1996.

Transcript distribution of plasma membrane Ca^{2+} pump isoforms and splice variants in the human brain. *Molec. Brain Res.* 28:263-272, 1995 (with Zacharias and Dalrymple).

Szurszewski, Joseph H., Ph.D., University of Illinois, Urbana, 1966, FM-Biophysical Sciences, Molecular Neuroscience & Physiology. Ionic currents underlying excitability and synaptic transmission in gastrointestinal smooth muscle; mechanisms of neuromodulation in peripheral autonomic ganglia; three dimensional morphology of smooth muscle cells and autonomic neurons; central mechanisms regulating satiety and obesity.

Representative articles: Calcium currents in human and canine jejunal circular smooth muscle cells. *Gastroenterology* 109:707-717, 1995 (with Farrugia, Rich, Rae and Sarr).

Facilitating effect of CCK on nicotinic neurotransmission in cat pancreatic ganglion. *American Jounal of Physiology* 270:G526-G534, 1996 (with Ma).

Taylor, Stuart R., Ph.D., New York University, 1966, FM-Biophysical Sciences, Pharmacology & Physiology. Ca2+ in excitation-contraction coupling; Electronic imaging microscopy; Signal transduction and Ca2+-binding proteins in muscle.

Representative articles: Volume changes during contraction of isolated frog muscle fibers. In: Third International Symposium on Excitation-Contraction Coupling in Skeletal, Cardiac, and Smooth Muscle, Plenum Publ. Corp., *New York Adv. Exp. Med. Biol.* 311:91-101, 1992 (with Neering, Quesenberry and Morris).

High-speed video imaging and digital analysis of microscopic features in contracting striated muscle cells. *Optical Engineering* 32:306-313, 1993 (with Roos).

Tindall, Donald J., Ph.D., University of North Carolina, Chapel Hill, 1973, FM-Biochemistry & Molecular Biology & Tumor Biology. Regulation of gene expression by androgenic steroid hormones.

Representative articles: Characterization of an early growth response gene, which encodes a zinc finger transcription factor, potentially involved in cell cycle regulation. *Molecular Endocrinology* 9:1610-1620, 1995 (with Blok, Grossmann and Perry).

The androgen receptor is transcriptionally suppressed by proteins that bind single-stranded DNA. *J. Biol. Chem.* 270:10968-10975, 1995 (with Grossmann).

Toft, David O., Ph.D., University of Illinois, Urbana, 1967, FM-Biochemistry & Molecular Biology & Tumor Biology. Cellular and molecular basis of steroid receptor and heat shock proteins.

Representative articles: A novel chaperone complex for steroid receptors involving heat shock proteins, immunophilins, and p23. *J. Biol. Chem.* 269:24989-24993, 1994 (with Johnson).

ATP-dependent chaperoning activity of reticulocyte lysate. *J. Biol. Chem.* 269:9493-9499, 1994 (with Schumacher, Hurst, Sullivan, McMahon and Matts).

Turner, Russell T., Ph.D., Pennsylvania State University, 1975, FM-Biochemistry and Molecular Biology, Physiology and AM-Orthopedics. Regulation of bone and mineral homeostasis, gravitational physiology, growth factors, vitamin D metabolism, mechanisms of action of estrogens and antiestrogens.

Representative articles: Mechanism of action of estrogen on intramembranous bone formation: Regulation of osteoblast differentiation and activity. *Endocrinology* 131:883-889, 1992 (with Backup, Sherman, Hill, Evans, and Spelsberg).

Disuse osteopenia is accompanied by down regulation of gene expression for bone proteins in growing rats. *Am. J. Physiol.* 263:E1029-E1034, 1992 (with Wakley and Portwood).

Vetter, Richard J., Ph.D., Purdue, 1969, FM-Biophysical Sciences. Biological effects and dosimetry of ionizing and nonionizing radiation from medical sources; environmental fate of radionuclides.

Representative articles: Effect of Pulsed Progressive Fluoroscopy on Reduction of Radiation Dose in the Cardiac Catheterization Laboratory. *J. Am. Coll. Cardiol.* 15:159-162, 1990 (with Holmes, Wondrow, Gray, Fellows and Julsrud).

Dosimetry and Biodistribution of an Iodine-123-Labeled Somatostatin Analog in Patients with Neuroendocrine Tumors. *J. Nucl. Med.* 33:1613-1619, 1992 (with O'Connor, Kvols, Brown, Hung, Hayostek, and Chuo).

Vuk-Pavlovic, Stanimir, Ph.D., University of Zagreb, Croatia, 1975, FM-Biochemistry and Molecular Biology. Regulation of tumor growth; biological response modifiers; hematopoietic stem cells.

Representative articles: Expression of somatostatin receptor subtypes in breast carcinoma, carcinoid tumor and renal cell carcinoma. *J. Clin. Endocrinol. Metabolism* 80:2974-2979, 1995 (with Vikic-Topic, Raisch and Kvols).

Mathematical modeling of cellular interaction dynamics in multicellular tumor spheroids. In: *Proc. 1st World Congress on Nonlinear Analysts* (V. Lakshmikantham, ed.), Vol. 4, pp. 3645-3654, Walter de Cruyter, Berlin, 1996 (with Bajzer and Marusic).

Weinshilboum, Richard M., M.D., University of Kansas, Lawrence, 1967, FM-Pharmacology, Molecular Neuroscience & Tumor Biology & AM-Medicine. Pharmacogenetics, clinical pharmacology, neuropharmacology, and neurochemistry.

Representative articles: Sulfotransferase enzymes. IN: Conjugation-Deconjugation Reactions in Drug Metabolism and Toxicity, chapter 22, edited by F.C. Kauffman, *"Handbook of Experimental Pharmacology"* series, volume 112, pp. 45-78, Springer-Verlag, Berlin Heidelberg, 1994.

Human liver nicotinamide N-methyltransferase: cDNA cloning, expression and biochemical characterization. *J. Biol. Chem.* 265:14835-14840, 1994.

Wettstein, Peter J., Ph.D., University of North Carolina, 1976, FM-Immunology & Tumor Biology. Investigation of genetic control of allograft rejection and evolution of immunoregulatory gene families.

Representative articles: Differential binding of a minor histocompatibility antigen peptide to H-2 class I molecules correlates with immune responsiveness. *J. of Immunology* 150:2753-2760, 1993 (with van Bleek and Nathenson).

Murine minor histocompatability antigens detected by helper T cells: Recognition of an endogenous peptide. *J. of Immunology.* In press.

Weyand, Cornelia M., M.D., University of Aachen, West Germany, 1979, **Ph.D.,** University of Heidelberg, West Germany, 1988, FM-Immunology. Molecular mechanisms of autoimmune diseases. Research interests center on T lymphocytes in autoimmune diseases and on the genetic elements conferring susceptibility toward autoimmunity.

Representative articles: Distinct vascular lesions in giant cell arteritis share identical T cell clonotypes. *J. Exp. Med.* 179:951-960, 1994 (with Schonberger, Oppitz, Hunder, Hicok, and Goronzy).

Correlation between disease phenotype and genetic heterogeneity in rheumatoid arthritis. *J. Clin. Invest.* 95:2120-2126, 1995 (with McCarthy and Goronzy).

Wieben, Eric D., Ph.D., Yale University, 1979, FM-Biochemistry & Molecular Biology. Post-transcriptional regulation of gene expression, RNA processing, molecular analysis of autoimmune antigens, androgen control of cell growth.

Representative articles: The snRNP E protein gene contains four introns and has upstream homology to genes for ribosomal proteins. *J. Biol. Chem.* 263:17772-17779, 1989 (with Stanford, Holicky, and Perry).

Processing of two protein precursors yields four mature guinea pig seminal vesicle secretory proteins. *Biol. Reprod.* 38:1155-1164, 1988 (with Norvitch, Harvey and Moore).

Windebank, Anthony J., B.M.B.Ch., Oxford, 1974, FM-Molecular Neuroscience & AM-Neurology. Cell biology of the nervous system. Mechanisms of neurotoxicity at the cellular and molecular level with particular emphasis on drugs used to treat cancer. Growth factors and mechanisms of regeneration in the peripheral nervous system.

Representative articles: Role of nerve growth factor in Suramin neurotoxicity studied in vitro. Ann. Neurol. 36:221-228, 1994 (with Russell and Podratz).

The effect of nerve growth factor, ciliary neurotrophic factor, and ACTH analogs on cisplatin neurotoxicity in vitro. *Neurology* 44:488-494, 1994 (with Smith and Russell)

Younkin, Steven G., M.D.,University of Pennsylvania, 1972, **Ph.D.,** University of Pennsylvania 1971, FM-Molecular Neuroscience. Biochemistry and molecular biology of Alzheimer's disease, role of amyloid proteins.

Representativbe articles: Amyloid ß protein (Aß) in Alzheimer's disease brain: Biochemical and immunochemical analysis with antibodies specific for forms ending at Aß40 or Aß42. *J. Biol. Chem.* 270:7013-7016 (with Gravina, Ho, Eckman, Long, Otvos, Younkin and Suzuki).

Age-related CNS disorder and early death in transgenic FVB/N mice overexpressing Alzheimer amyloid precursor proteins. *Neuron.* 15(5):1203-1218, 1995 (with Hsiao, Borchelt, Olson, Johannsdottir, Kitt, Yunis, Xu, Eckman, Price, et al.).

The following faculty members may teach, exam, and advise degree candidates as indicated:

T/E - Teaching/Examining member. Privileges include participation as director of graduate courses and as members of examining or advisory committees.

AM - Associate member; FM - Full member (in non-Ph.D.granting field). Privileges include all of the above, in addition to serving as thesis adviser for Master's degree candidates or co-adviser for Ph.D. degree candidates in the relevant program track.

Aksamit, Allen J., M. D., AM-Molecular Neuroscience & Neurology Molecular pathogenesis of viral infections of the central nervous system.

Amadio, Peter C., M.D., AM-Orthopedics. Tendon healing and biomechanics

An, Kai-Nan, M.D., AM-Orthopedics & T/E-Physiology. Biomechanics of normal and abnormal hand; Artificial ligament replacement; Static force and stability analysis of human elbow; Fluid circulation in bone; Bone fracture fixation; Tendon injury and repair

Andrews, Amy G., D.M.V., 1987, T/E-Physiology & Tumor Biology. Animal models and surgery in biomedical sciences

Bailey, Kent R., Ph.D., T/E-Biostatistics. Design, analysis, interpretation of clinical research protocols, Clinical trials, prospective observational studies; Retrospective studies; Laboratory experiments primarily in cardiovascular diseases

Bajzer, Zeljko, Ph.D., AM-Biochemistry and Molecular Biology. Data reduction and mathematical modeling in biomedical sciences

Baratz, Keith H., M.D., T/E-Ophthalmology

Bartley, George B., M.D., T/E-Ophthalmology. Eyelid disorders and surgery, lacrimal disorders and surgery, orbital disorders and surgery, essential blepharospasm, Graves' ophthalmopathy

Bauch, Christopher D., Ph.D., T/E-Otorhinolaryngology. Comprehensive audiologic assessment, including pure-tone and speech audiometry, hearing aids, and electrophysiologic assessment

Beabout, John W., M.D., AM-Radiology

Beatty, Charles W., M.D., T/E-Otorhinolaryngology

Beckenbaugh, Robert D., M.D., AM-Orthopedics. Studies on the function of hand, upper limb, wrist and finger

Benarroch, Eduardo E., M.D., T/E-Molecular Neuroscience & Neurology. Neurochemistry and neuropharmacology

Bennet, Kevin E., M.S., T/E-Tumor Biology

Berger, Richard A., M.D., AM-Orthopedics. Gross and histomorphology of capsular ligaments with special emphasis on innervation patterns. Kinematics, kinetics, and material property studies related to the upper extremity

Bishop, Allen T., M.D., T/E-Orthopedics

Bite, Uldis, M.D., AM-Biophysical Sciences. Computer simulation of

reconstructive surgery; quantitative analysis of three dimensional CT and MRI data

Bolander, Mark E., M.D., AM-Biochemistry and Molecular Biology & AM-Orthopedics

Bonner, James A., M.D., AM-Biophysical Sciences & T/E-Tumor Biology. Oncology, radiation resistance

Bourne, William M., M.D., AM-Ophthalmology. Corneal disease; Corneal physiology; Corneal preservation; Corneal surgery

Brown, Randall S., T/E-Biophysical Sciences. Digital microelectronics

Brown, Rhoderick E., Ph.D., T/E-Biochemistry and Molecular Biology. Structure and function of glycolipids and sphingolipids in biological and model membranes; Spontaneous and protein-mediated intermembrane lipid transfer with emphasis on glycolipids and gangliosides

Brubaker, Richard F., M.D., FM-Ophthalmology. Physiology of eye pressure control; Pathophysiology of glaucoma; Computer applications in ophthalmology; Quantitative fluorophotometry of the eye

Buettner, Helmut, M.D., AM-Ophthalmology

Burghardt, Thomas P., Ph.D., AM-Biochemistry and Molecular Biology & Molecular Neuroscience. Biophysical investigation of the molecular mechanism of muscle contraction; Physical research into the mechanism of emission from fluorescent probes

Cabanela, Miguel E., M.D., T/E-Orthopedics

Cahill, Donald R., Ph.D., FM-Anatomy. Cross-sectional anatomy; tooth eruption and exfoliation

Campbell, Donald C., II, M.D., T/E-Orthopedics

Campbell, R. Jean, M.D., AM-Ophthalmology & T/E Pathology. Electron microscopy in relation to corneal transplantation; Tumors of the orbit, lid and extraocular muscle

Carlson, Harley C., M.D., Ph.D., AM-Radiology. Motility of gastrointestinal tract; Clinical research in gastroenterologic roentgenology

Carmichael, Stephen W., Ph.D., FM-Anatomy & T/E-Molecular Neuroscience. Basic mechanisms of neurosecretion; Adrenal medullary cytology

Caselli, Richard J., M.D., T/E-Molecular Neuroscience

Christopherson, Mark W., M.D., T/E-Anatomy

Chute, Christopher G., Ph.D., T/E-Health Sciences Research. Classification and information retrieval research related to clinical events. Experimental evaluation on the practical attributes of medical concepts, devoid of trivial modifiers, with respect to clinical epidemiology and outcomes assessment

Cofield, Robert H., M.D., T/E-Orthopedics. Prosthetic shoulder arthroplasty; Rotator cuff disease; Shoulder instability; fractures and dislocations of shoulder girdle

Colligan, Robert C., Ph.D., AM-Psychology. Adolescent characteristics associated with personality inventories; Personality functioning in young children undergoing intensive care

Cooney, William P., M.D., AM-Orthopedics. Orthopedic biomechanic static hand function; Microvascular surgery; Tendon healing

Cunnien, Alan J., M.D., T/E-Psychiatry. Civil and criminal forensic psychiatric evaluations

Currier, Bradford L., M.D., T/E-Orthopedics. Surgery of the spine

Daube, Jasper R., M.D., T/E-Molecular Neuroscience & Neurology. Amyotrophic lateral sclerosis

DeSanto, Lawrence W., M.D., AM-Otorhinolaryngology. Conservation surgery of the larynx; Ophthalmopathy of Graves' disease; Cancer of the base of the tongue; Vocal rehabilitation; Surgery of base of skull; Cancer of external ear

Desjardins, Ronald P., D.M.D., AM-Dentistry. Prosthodontics

Earle, John D., M.D., AM-Radiology. Research in diagnostic and therapeutic radiology

Eberhardt, Norman L., Ph.D., AM-Biochemistry and Molecular Biology. Molecular endocrinology

Eckert, Steven E., D.D.S., T/E-Prosthodontics. Dentistry/oral and maxillofacial prosthodontics; Fixed and removable prosthodontics

Erickson, Bradley J., M.D., Ph.D., T/E-Biophysical Sciences. Application of image processing techniques to solve clinical problems

Erickson, Lisa D., M.D., T/E-Obstetrics and Gynecology. Reproductive endocrinology and infertility, assisted reproductive technologies

Erie, Jay C., M.D., T/E-Ophthalmology

Erlichman, Charles M.D., T/E-Tumor Biology. Oncology, pharmacology of drugs used in cancer therapy

Fabry, David A., Ph.D., AM-Otorhinolaryngology. Hearing aid technology and programming strategies

Facer, George W., M.D., AM-Otorhinolaryngology. Nasal physiology and reconstructive surgery of the nose; Chronic ear disease and reconstruction of the hearing mechanism; Cochlear and middle ear implants

Federspiel, Mark J., Ph.D., AM-Biochemistry and Molecular Biology & Tumor Biology. Molecular medicine, retroviral vectors, antiviral strategies, gene therapy, molecular virology

Felmlee, Joel P., Ph.D., AM-Biophysical Sciences. Correction of motion in magnetic resonance imaging

Felmlee, Teresa, Ph.D., T/E-Biochemistry and Molecular Biology. Bacterial systems

Finlayson, Richard E., M.D., AM-Psychiatry. Addictions; Geriatrics

Frisk, Craig, D.V.M., T/E-Physiology

Garrity, James A., M.D., T/E-Ophthalmology

Gisvold, John J., M.D., T/E-Radiology. Early breast cancer detection

Gloviczki, Peter, M.D., AM-Physiology. Ischemia and reperfusion injury to the spinal cord. Injury to the blood vessels, small vessel vascular grafts

Graff-Radford, Neill R., M.D., T/E-Molecular Neuroscience

Grambsch, Patricia M., Ph.D., T/E-Biostatistics

Grande, Joseph P., M.D., Ph.D., AM-Biochemistry and Molecular Biology & T/E-Tumor Biology. Pathology, transcriptional regulation

Gray, Darryl T., M.D., Sc.D., T/E-Health Sciences Research. Application of methods of clinical epidemiology, cost-effectiveness analysis and decision

analysis to evaluations of clinical procedures

Guenthner, Terry A., D.D.S., T/E-Orthodontics

Gustafson, Ray O., M.D., T/E-Otorhinolaryngology. Tumor immunology

Hansen, Mark R., M.D., T/E-Psychiatry. Brain imaging in psychiatric disorders

Hanson, Norman P., M.D., T/E-Psychiatry. Psychiatric epidemiology; Family psychiatry; Diabetes complications and control trial

Hanssen, Arlen D., M.D., AM-Orthopedics

Harner, Stephen G., M.D., AM-Otorhinolaryngology. Brain stem audiometry; Acoustic neuroma; Temporal bone histopathology

Hartmann , Lynn C., M.D., T/E-Tumor Biology. Oncology, breast and ovarian cancer

Hattery, Robert R., M.D., AM-Radiology. Ultrasound; Computer tomography; Uroradiology; Magnetic resonance imaging

Heise, Robert H., M.D., T/E-Obstetrics and Gynecology

Herman, David C., M.D., T/E-Ophthalmology

Hill, Arnold J., Jr., D.D.S., T/E-Orthodontics

Hohberger, George G., M.D., T/E-Ophthalmology

Holbrook, Margaret A., M.D., T/E-Radiology

Ilstrup, Duane, M.S., T/E-Biostatistics

Ingle, James N., M.D., T/E-Tumor Biology. Breast Cancer

Ivnik, Robert J., Ph.D., AM-Psychology. Neuropsychology and neuro-psychodiagnostics; Neuropsychological correlates of medical diseases; Alzheimer's disease; Epilepsy; ALS; Effects of Aspartame (Nutrasweet) on cognition

Jack, Clifford R., II, M.D., AM-Biophysical Sciences & T/E-Molecular Neuroscience

Jalal, Syed M., Ph.D., T/E-Biochemistry and Molecular Biology. Genetics, especially human cytogenetics

Jenkins, Robert B., M.D., AM-Biochemistry and Molecular Biology & Tumor Biology. Molecular genetic studies of congenital and neoplastic disorders with cytogenetic abnormalities

Johnson, Douglas H., M.D., AM-Ophthalmology

Johnson, Kenneth A., M.D., T/E-Orthopedics

Jones, James D., Ph.D., AM-Biochemistry, Laboratory Medicine & FM-Nutrition. Amino acid toxicities and interrelationships; Metabolism of creatinine and guanidine compounds; Adaptive mechanisms for conservation of nitrogen in mammals

Jorgensen, Edward O., M.D., T/E-Obstetrics and Gynecology

Joyner, Michael J., M.D., AM-Physiology. Neural control of circulation in humans. Oxygen-carrying blood substitutes. Gas exchange

Jung, Sin-Ho, Ph.D., T/E-Health Sciences Research. Survival analysis, generalized linear models, nonparametric statistics, Time series

Kappen, Claudia, Dr.rer.nat., AM-Biochemistry and Molecular Biology & Molecular Neuroscience. The regulation of gene expression during embryonic development

Kasperbauer, Jan L., M.D., T/E-Anatomy & AM-Otorhinolaryngology. Mechanisms of cellular differentiation in human squamous cell carcinoma; head and neck gross anatomy

Katusic, Zvonimir S., M.D., Ph,D., AM-Pharmacology. Nitric oxide and the role of the endothelium in regulating vascular tone

Kavanagh, Brian F., M.D., AM-Orthopedics. Hip reconstruction; Principles of uncemented hip arthroplasty and revision hip arthroplasty

Keller, Eugene E., D.D.S., AM-Dentistry. Radiographic analysis of dental, skeletal and facial development in patients with various endocrine and metabolic diseases

Kern, Eugene B., M.D., FM-Otorhinolaryngology. Nasal physiology; Rhinomanometry

Khraibi, Ali A., Ph.D., T/E-Physiology. The role of interstitial hydrostatic pressure in hypertension

Khosla, Sundeep, M.D., T/E-Physiology. Calcium and bone metabolism; Familial endocrine disorders

Kimmel, David W., M.D., T/E-Molecular Neuroscience

Kitaoka, Harold B., M.D., T/E-Orthopedics. Anatomy of the foot and ankle

Kline, Robert W., Ph.D., AM-Biomedical Imaging. Radiation oncology physics. Treatment beam characterization and planning. Brachytherapy and stereotactic treatment techniques

Kumar, Vijay M., Ph.D., T/E-Biochemistry and Molecular Biology. Regulation of gene expression in prostate, isolation and characterization of 5′-flanking region, in vitro expression

Lagerlund, Terrence D., M.D., T/E-Molecular Neuroscience

Larson, Brent E., D.D.S., AM-Orthodontics. Biomechanics, computer image processing

LaRusso, Nicholas F., M.D., AM-Medicine & Biochemistry and Molecular Biology. Cell biology, intracellular transport and digestion

Leavitt, Jacqueline, M.D., T/E-Ophthalmology

Lee, Nancy A., Ph.D., AM-Biochemistry and Molecular Biology. The expression and function of cell surface proteins during thymopoeisis. The generation of transgenic mice as modes for human disease

Lee, Raymond, A., M.D., AM-Obstetrics and Gynecology

Lewallen, David G., M.D., AM-Orthopedics. Biomechanics; Fracture healing

Liesegang, Thomas J., M.D., AM-Ophthalmology

Limper, Andrew H., M.D., AM-Biochemistry and Molecular Biology. Molecular mechanisms of macrophage recognition of microorganisms

Lingle, Wilma L., Ph.D., T/E-Tumor Biology. Tumor biology, hypertrophic centrosomes in breast and prostate tumors

Litchy, William J., M.D., T/E-Molecular Neuroscience & Neurology. Electrophysiology of nerve and muscle

Logan, Kathleen M., M.D., T/E-Psychiatry. Child and adolescent

Lu, Jian-yu, Ph.D., T/E-Biophysical Sciences. Ultrasound, imaging techniques, and biomedical physics

Lucas, Alexander R., M.D., AM-Psychiatry. Psychopathology of childhood; psychopharmacologic treatment of children; Anorexia Nervosa; Biologic aspects of child psychiatry

Lund, Bruce A., D.D.S., AM-Dentistry. Hypotension anesthesia in orthognathic surgery; Use of durapatite in augmentation for edentulous ridges; Use of heterologous bone in apicoectomies

Lust, John A., M.D., Ph.D., AM-Tumor Biology. Oncology and hematology, cytokines and multiple myeloma

Maguire, Leo J., M.D., T/E-Ophthalmology. Corneal topography; Refractive surgery; Occular allergy

Manduca, Armando, Ph.D., T/E-Biophysical Sciences. Image processing and the application of artificial intelligence and artificial neural network techniques to imaging problems

Maragos, Nicholas E., M.D., T/E-Otorhinolaryngology

Marion, Mitchell S., M.D., AM-Otorhinolaryngology. Temporal bone histopathology

Martin, Maurice J., M.D., FM-Psychiatry. Longitudinal studies of psychiatrically normal groups; Muscle contraction headaches

Martin, William J., M.D., T/E-Pharmacology. Electrophoretic mobility of leukocyte elastase; Alpha antitrypsin and leukocyte elastase interaction; Models of acute lung injury including oxygen toxicity, paraquat toxicity, drug-induced lung injury and neutrophil mediated lung injury

Maruta, Toshihiko, M.D., AM-Psychiatry

McAlpine, Donald E., T/E-Psychiatry

McCaffrey, Thomas V., M.D., Ph.D., AM-Otorhinolaryngology. Cholinergic control of airway resistance

McCollough, Cynthia H., Ph.D., AM-Biophysical Sciences. The physics of diagnostic medical imaging, especially X-ray xomputed tomography, digital radiology, quantitative and cardiac imaging

McCormick, Daniel J., Ph.D., AM-Biochemistry and Molecular Biology. Factors that confer biologic specificity in protein-protein interactions

McDonald, Thomas J., M.D., AM-Otorhinolaryngology. Wegener's Granulomatosis; Sarcoidosis

McEvoy, Kathleen M., M.D., Ph.D., T/E-Molecular Neuroscience

McGee, Richard, Ph.D., AM-Molecular Neuroscience, Pharmacology & Tumor Biology

McLaren, Jay W., Ph.D., AM-Molecular Neuroscience

McLeod, Richard A., M.D., T/E-Radiology

McPhee, Thomas J., M.D., T/E-Ophthalmology

Mellenberg, David E., Ph.D., T/E-Biophysical Sciences. Measurement and calculation of radiation dose as it is applied to radiation oncology as well as the application of X-ray imaging, CT, and MRI to the treatment of tumors with radiation

Melton, L. Joseph, III, M.D., AM-Epidemiology & T/E-Tumor Biology

Meyer, Frederic B., M.D., AM-Molecular Neuroscience

Miller, Laurence J., M.D., AM-Biochemistry and Molecular Biology

Miller, Virginia, Ph.D., T/E-Physiology

Miller, W. Eugene, M.D., AM-Radiology. Chest radiology; Angiography; Detection of early lung cancer; Lymphangiography

Moore, Gordon L., II, M.D., AM-Psychiatry

Morrey, Bernard F., M.D., AM-Orthopedics. Biomechanics of the elbow joint and shoulder; Effect of defects in bone; Pre and postop biomechanical assessment of elbow surgery

Morris, James J., M.D., AM-Physiology. Biomechanical assessment of cardiac performance, pulmonary and arterial flow mechanics, and ventriculo-arterial hydraulic coupling in the intact circulation, as related to cardiovascular disease and cardiac surgery

Morse, Robert M., M.D., AM-Psychiatry. Alcoholism; Drug dependence; Delirium and organic brain syndrome

Muhm, John R., M.D., T/E-Radiology

Murtaugh, Paul A., Ph.D., T/E-Health Sciences Research. Statistical description of dose-response relationships; Repeated-measures screening tests for cancer recurrence; Ecological statistics

Neel, H. Bryan, III, M.D., Ph.D., AM-Microbiology & FM- Otorhinolaryngology. General tumor immunology; Cryosurgery for cancer; Nasopharyngeal carcinoma; Hormone receptors in head and neck cancer; Grafts and implants in head and neck surgery

Nelson, Heidi M.D., T/E-Tumor Biology. Tumor biology, oncology, cancers of the GI track

Newman, Deborah C., M.D., AM-Psychiatry. Affective disorders, psychoneuroendocrinology, psychopharmacology, chemical dependency

O'Brien, Peter C., Ph.D., AM-Biostatistics & T/E-Molecular Neuroscience. Neurology; Ob-Gyn; Endocrinology; Statistical methods

O'Driscoll, Shawn W., M.D., AM-Orthopedics. Cartilage regeneration, physiology, biochemistry, biomechanics and anatomy of the shoulder and elbow

O'Fallon, Judith R., Ph.D., T/E-Biostatistics & Tumor Biology. Cancer clinical trials and data management

O'Fallon, William M., Ph.D., AM-Biostatistics. Statistical methodology in epidemiology

Offord, Kenneth P., M.S., T/E-Biostatistics. Pulmonary physiology; Statistical computing; Linear models; Categorical data analysis; Psychometrics; Smoking cessation

Ogburn, Paul L., Jr., M.D., AM-Obstetrics and Gynecology

O'Kane, Dennis J., Ph.D., AM-Tumor Biology. Telomerase activity as a diagnostic marker for cancer

Olsen, Kerry D., M.D., AM-Otorhinolaryngology

Olsen, Wayne O., Ph.D., FM-Audiology & Otorhinolaryngology. Development of tests for central auditory nervous system dysfunction

Osborne, David, Ph.D., AM-Psychology. Objective personality assessment; Biofeedback; Sexual dysfunction; Psychophysiology problems

Ottesen, Hal H., Ph.D., T/E-Biophysical Sciences. Random processes and noise; Digital signal processing; Systems identification; Magnetic recording and data communication; Artificial intelligence

Oursler-Velasquez, Merry Jo, Ph.D., AM-Biochemistry and Molecular Biology. Actions of steroids and growth factors and cytokines on bone cells-osteoblast and osteoclasts, cancer metastasis to bone, integrins

Pach, John M., M.D., T/E-Ophthalmology

Palmen, Michael A., M.D., T/E-Psychiatry. Low dose Benzodiazapine dependence; Sleep disturbance related to psychoactive chemical use

Pavlicek, William, Ph.D., AM-Biophysical Sciences. Radiologic imaging technologies including ultrasound, magnetic resonance, biomagnetism, computerized tomography, and diagnostic image management

Pearson, Bruce W., M.D., AM-Otorhinolaryngology. Transseptal hypophysectomy; Surgical restoration of voice; Immunodiagnosis in head and neck cancer; Maxilloethmoidal cancer surgery

Pemberton, John H., M.D., T/E-Physiology. Physiology of the colon and anorectum

Petersen, Ronald C., M.D., Ph.D., AM-Neurology & T/E-Molecular Neuroscience. Cognitive function: memory, learning, language; Neuropsychology; Psychopharmacology

Peterson, Gerald C., M.D., T/E-Psychiatry

Peterson, Hamlet A., M.D., T/E-Orthopedics

Pfeiffer, Douglas R., Ph.D., T/E-Biochemistry and Molecular Biology. Cation transport, mechanism, control and role in the control of metabolism and cell function

Pittelkow, Mark, R., M.D., AM-Dermatology & Tumor Biology

Podratz, Karl C., M.D., Ph.D., AM-Obstetrics and Gynecology & Tumor Biology & T/E-Anatomy

Pritchard, Douglas J., M.D., FM-Orthopedics. Immunosurveillance of melanoma; Orthopedic oncology: Circulating tumor cells; Osteosarcoma treatment protocol; Rehabilitation of cancer amputees; Biomechanics of tumor prostheses

Raffel, Corey, M.D., Ph.D., AM-Molecular Neuroscience & Tumor Biology. Tumor biology, pediatric oncology, gene therapy, molecular medicine

Rand, James A., T/E-Orthopedics. Disorders of the knee as well as fracture healing

Reese, David F., M.D., AM-Radiology

Reeve, Charles M., D.D.S., AM-Dentistry. Oral pathology

Richardson, Jarrett W., M.D., T/E-Psychiatry. Sleep disorders; chemical dependency; affective disorders; neuropsychiatric issues in brain-injured patients

Robertson, Dennis M., M.D., AM-Ophthalmology. Long-Term effects of Iodine-125 on the ocular tissues; HLA antigens in alcoholism; Central serous chorioretinopathy

Robinette, Martin S., Ph.D., T/E-Otorhinolaryngology. Audiological assessment of the auditory system: psychoacoustics, hearing aid technology

Rocca, Walter A., M.D., Ph.D., T/E-Health Sciences Research. Epidemiology of Parkinson's disease; epidemiology of dementia; epidemiology of epilepsy

Roche, Patrick C., Ph.D., AM-Biochemistry and Molecular Biology. Development and evaluation of prognostic, immunohistochemical markers for breast, ovarian, and endometrial cancer. Functional, structural, and molecular analysis of gonadotropin receptors in normal and abnormal reproductive states

Rock, Michael G., M.D., AM-Orthopedics & Physiology

Rome, Jeffrey D., M.D., T/E-Psychiatry

Rorie, Duane K., M.D., Ph.D., T/E-Anatomy & Anesthesiology. Effect of anesthetics on autonomic function; Effect of hypoxia on neuroeffector junctions; Neurotransmitter dynamics in hepatic vasculature

Rusnak, Frank M., Ph.D., AM-Biochemistry and Molecular Biology. Enzyme biochemistry, expression vectors

Salassa, Robert R., M.D., AM-Otorhinolaryngology. Evaluation and treatment of dysphagia

Sarr, Michael G., M.D., AM-Physiology. Smooth muscle physiology of gastrointestinal tract, in vivo and in vitro measurements—dogs, man, rats

Sather, A. Howard, D.D.S., AM-Dentistry. Orthodontics

Schaid, Daniel J., Ph.D., T/E-Biostatistics. Statistical methods for clinical trials; Statistical methods in genetics

Schroeder, Alton R., T/E-Orthopedics

Schutt, Ann H., M.D., AM-Physical Medicine and Rehabilitation. Postoperative management of total knee arthroplasties; Cerebral Palsy; Rehabilitation in paraplegia and quadriplegia; Scleroderma; Rheumatoid arthritis of the hand

Schwartz, Mark S., Ph.D., AM-Psychology. Biofeedback and self-regulation; Neuropsychology of memory; Stress and psychopharmacology; Bruxism, nocturnal

Sheedy, Patrick F., M.D., AM-Radiology. Angiography of gastrointestinal bleeding; Pancreatic carcinoma and primary liver tumors; Computerized axial tomograpy pertaining to acute head injury, musculoskeletal disorders, lymphoma tumors and retroperitoneal tumors; Computerized tomography of orbits, liver, pancreas and adrenal glands

Sheridan, Phillip J., D.D.S., AM-Dentistry. Periodontics

Sherris, David A., M.D., AM-Otorhinolaryngology. Facial cosmetic and reconstructive surgery, wound healing and cell culture techniques

Shin, Cheolsu, M.D., AM-Molecular Neuroscience. Kindling model of epilepsy; Hippocampal neuron cell culture; Role of early genes in epileptogenesis; Ischemic and excitotoxic neuronal injury

Shives, Thomas C., M.D., T/E-Orthopedics

Silverstein, Marc D., M.D., T/E-Health Sciences Research. Clinical epidemiology and health services research in respiratory diseases; Diagnostic test assessment; Technology assessment

Silverstein, Murray N., M.D., Ph.D., AM-Medicine & T/E-Health Sciences Research. Hypoglycemia associated with neoplasia; The role of glycolytic inhibitors in leukemia; Myeloproliferative disease

Sim, Franklin H., M.D., T/E-Orthopedics

Sinaki, Mehrsheed, M.D., AM-Physical Medicine and Rehabilitation. Rehabilitation of osteoporosis patients; Back pain syndromes; Rehabilitation of post-stroke patients; Post-stroke depression

Stanhope, C. Robert, M.D., AM-Obstetrics and Gynecology

Stanson, Anthony W., M.D., T/E-Radiology

Steckelberg, James M., M.D., AM-Orthopedics. Bacterial and fungal infections; musculoskeletal infection; infective endocarditis and pneumonia experimental models; epidemiology of infections

Stehno-Bittel, Lisa A., Ph.D., T/E-Pharmacology. The regulation of intracellular calcium with particular focus on calcium release from intracellular stores and its effect on calcium influx from the extracellular space

Stephens, David H., M.D., AM-Radiology. Computerized tomography of abdominal organs; Radiologic investigation of pancreas

Stuart, Michael J., M.D., T/E-Orthopedics. Adult reconstruction, sports medicine, knee anatomy, biomechanics, instrumented testing, arthroplasty and ligament reconstruction

Su, John, Ph.D., T/E-Health Sciences Research. Design and analysis of clinical trials, early stopping rules and group sequential methods

Suman, Vera Jean, Ph.D., T/E-Biostatistics. Estimation of HIV transmission probabilities

Swanson, David W., M.D., FM-Psychiatry. Medical dependency; Psychological aspects of pain

Therneau, Terry M., Ph.D., T/E-Biostatistics

Thibodeau, Stephen N., Ph.D., AM-Biochemistry and Molecular Biology & Tumor Biology. Application of recombinant DNA techniques to medical genetics; Characterization of disease loci by both genetic (Family linkage studies) and physical techniques

Thorsteinsson, Gudni, M.D., AM-Physical Medicine and Rehabilitation. Management of chronic pain; Rehabilitation of spinal cord injury; Multiple sclerosis; Hand dysfunction

Trautmann, James C., M.D., AM-Ophthalmology

Urrutia, Raul A., M.D., AM-Molecular Neuroscience, Biochemistry and Molecular Biology & Tumor Biology. Role of molecular motor enzymes in vesicular transport and morphogenesis

Van Roekel, Ned B., D.D.S., T/E Dentistry. Prosthodontics

Velimirovic, Bratislav M., M.D., Ph.D., T/E-Physiology. Characterization of G protein modulation of inward rectifying potassium channels in the heart and central nervous systems

Vockley, Gerard, M.D., Ph.D., AM-Biochemistry and Molecular Biology. Molecular nature of the defects responsible for Acyl CoA Dehydrogenase deficiencies in humans and structure-function relationships in the Acyl CoA Dehydrogenase family

Vuk-Pavlovic, Zverzdana, Ph.D., T/E-Biochemistry and Molecular Biology. Cellular defense mechanisms in pathogenesis of pulmonary disease

Waller, Robert R., M.D., AM-Ophthalmology. Blindness in blepharoplasty; Meibomian gland carcinoma of the eyelids

Webb, Maurice J., M.D., AM-Obstetrics and Gynecology. Ploidy in ovarian cancer

Wells, Lloyd A., M.D., Ph.D., AM-Psychiatry. Borderline syndromes; Anorexia Nervosa

Westmoreland, Barbara F., M.D., T/E-Molecular Neuroscience & Neurology. Electroencephalography

Wiebers, David O., M.D., AM-Neurology & T/E-Molecular Neuroscience. Cerebrovascular disease

Williamson, Byrn, Jr., M.D., T/E-Radiology. Uroradiology; Computed tomography of the body; Ultrasound

Wilson, Timothy O., M.D., AM-Obstetrics and Gynecology. Endometrial carcinoma; Radioactive colloid chromic phosphate in ovarian carcinoma

Wollan, Peter C., Ph.D., T/E-Health Sciences Research. Constrained estimation and testing; Nonparametric regression; Data visualization; Parallel computing; Design of experiments and quality control

Wood, Michael B., M.D., AM-Orthopedics. Microvascular surgery

Youdas, James W., T/E-Anatomy

Young, Charles Y.F., Ph.D., AM-Biochemistry and Molecular Biology & Tumor Biology. Molecular mechanisms of androgen action; Molecular mechanism of programmed cell death in human prostate

Younge, Brian R., M.D., AM-Ophthalmology. Aerospace medicine

Zinsmeister, Alan, T/E-Biostatistics. Applied stochastic processes; Time series analysis; Survival analysis; Statistical computing; Statistical methodology for analysis of multivariate data

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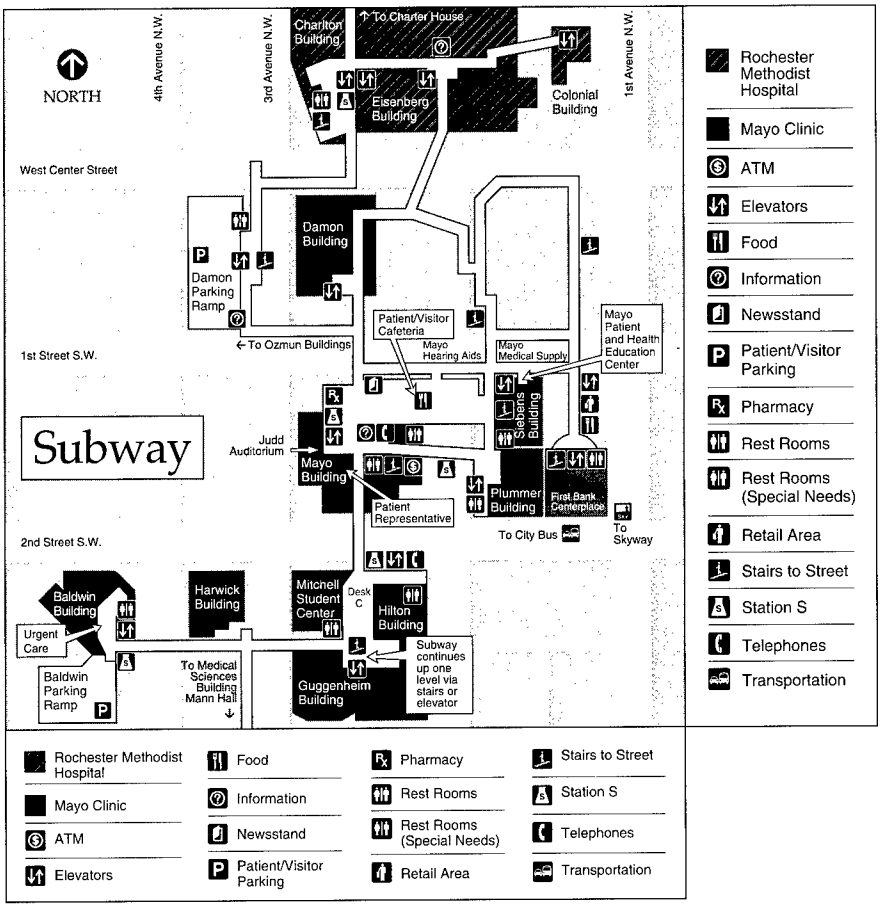
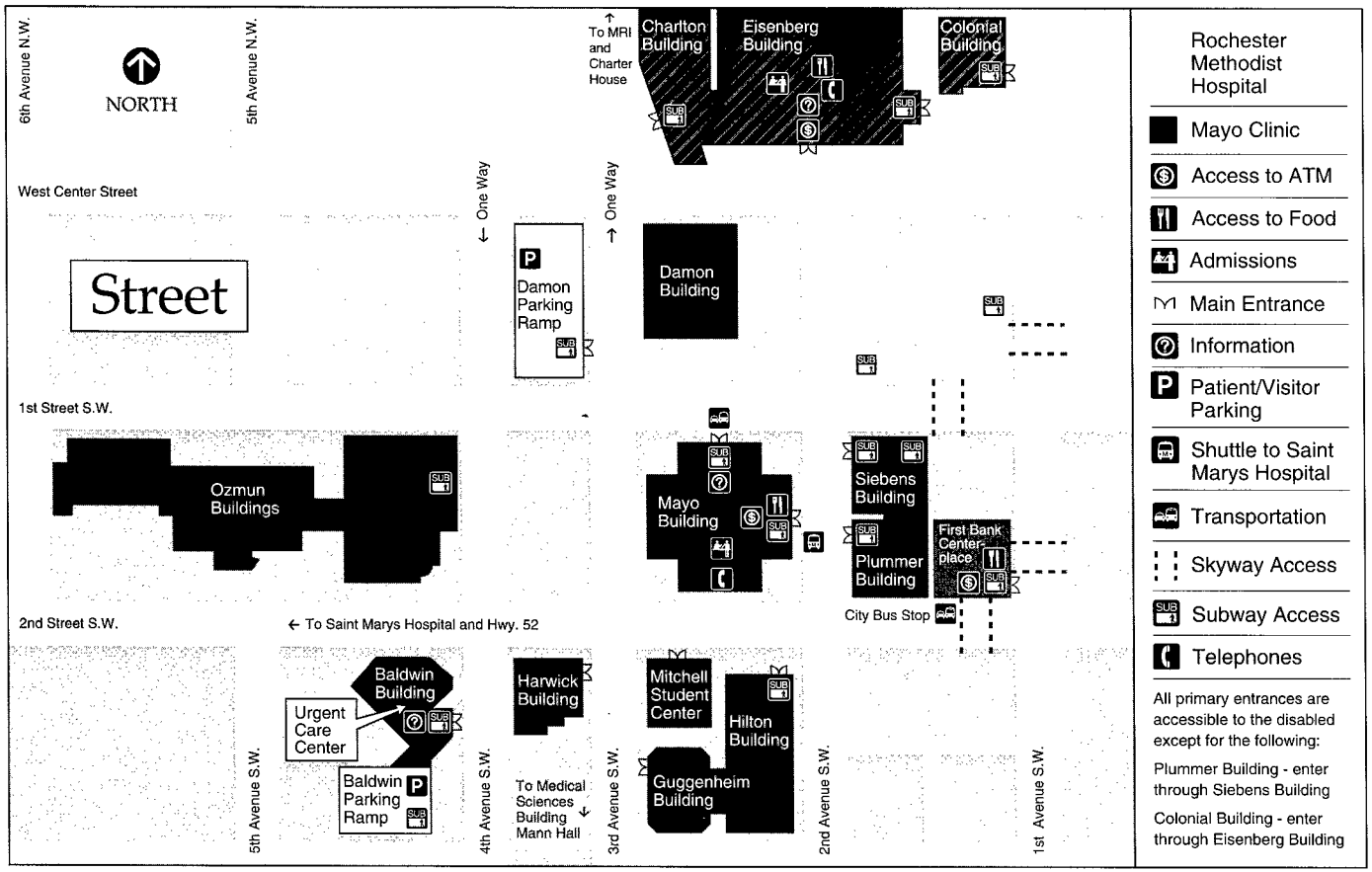

NORTH
4th Avenue N.W.
3rd Avenue N.W.
1st Avenue N.W.
Charlton Building
To Charter House
Eisenberg Building
Colonial Building
West Center Street
Damon Building
Damon Parking Ramp
Patient/Visitor Cafeteria
Mayo Hearing Aids
Mayo Medical Supply
Mayo Patient and Health Education Center
1st Street S.W.
To Ozmun Buildings
Subway
Judd Auditorium
Mayo Building
Gonda Building
Plummer Building
First Bank Centerplace
Patient Representative
To City Bus
To Skyway
2nd Street S.W.
Baldwin Building
Urgent Care
Baldwin Parking Ramp
Harwick Building
Mitchell Student Center
Desk C
Hilton Building
To Medical Sciences Building Mann Hall
Guggenheim Building
Subway continues up one level via stairs or elevator
Rochester Methodist Hospital
Mayo Clinic
ATM
Elevators
Food
Information
Newsstand
Patient/Visitor Parking
Pharmacy
Rest Rooms
Rest Rooms (Special Needs)
Retail Area
Stairs to Street
Station S
Telephones
Transportation


6th Avenue N.W.
NORTH
5th Avenue N.W.
To MRI and Charter House
Charlton Building
Eisenberg Building
Colonial Building
West Center Street
One Way
One Way
Street
Damon Parking Ramp
Damon Building
1st Street S.W.
Ozmun Buildings
Mayo Building
Siebens Building
Plummer Building
First Bank Center-place
City Bus Stop
2nd Street S.W.
To Saint Marys Hospital and Hwy. 52
Baldwin Building
Urgent Care Center
Baldwin Parking Ramp
Harwick Building
Mitchell Student Center
Hilton Building
Guggenheim Building
5th Avenue S.W.
4th Avenue S.W.
To Medical Sciences Building Mann Hall
3rd Avenue S.W.
2nd Avenue S.W.
1st Avenue S.W.
Rochester Methodist Hospital
Mayo Clinic
Access to ATM
Access to Food
Admissions
Main Entrance
Information
Patient/Visitor Parking
Shuttle to Saint Marys Hospital
Transportation
Skyway Access
Subway Access
Telephones
All primary entrances are accessible to the disabled except for the following:
Plummer Building - enter through Siebens Building
Colonial Building - enter through Eisenberg Building

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