AD_____

COOPERATIVE AGREEMENT NUMBER DAMD17-95-2-5012

TITLE: Continuation of a Postdoctoral Research Associateship Program with USAMRMC

PRINCIPAL INVESTIGATOR: Judith K. Nyquist, Ph.D.

CONTRACTING ORGANIZATION: National Academy of Sciences
Washington, DC 20418

REPORT DATE: October 1996

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	October 1996	Annual (4 Sep 95 - 3 Sep 96)

4. TITLE AND SUBTITLE
Continuation of a Postdoctoral Research Associateship Program with USAMRMC

5. FUNDING NUMBERS
DAMD17-95-2-5012

6. AUTHOR(S)
Judith K. Nyquist, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
National Academy of Sciences
Washington, DC 20418

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200*

14. SUBJECT TERMS Postdoctoral Research, Associateship Program, USAMRMC

15. NUMBER OF PAGES 78

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

TABLE OF CONTENTS

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

____ Where copyrighted material is quoted, permission has been obtained to use such material.

____ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

____ Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

____ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

____ For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

____ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

____ In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

Judith K. Nyquist, Ph.D. 15 Nov 96

PI - Signature Date

NATIONAL RESEARCH COUNCIL
OFFICE OF SCIENTIFIC AND ENGINEERING PERSONNEL
2101 Constitution Avenue Washington, D.C. 20418

ASSOCIATESHIP PROGRAMS

(202) 334-2760
GENERAL INFORMATION
FAX (202) 334-2759

NATIONAL RESEARCH COUNCIL

Cooperative Research Associateship Program

with the

US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND

Status Report

October 1, 1995, through September 30, 1996

PUBLICITY

The NRC Research Associateship Programs for 1996 were announced to the scientific community in the Fall of 1995. Publicity materials describing the 1995 Programs were distributed in November to presidents, graduate deans, and heads of appropriate science and engineering departments of all academic degree-granting institutions in the United States. These materials were also sent to Program Representatives and Associateship Advisers at the participating laboratories and to other interested persons.

REQUESTS

Application materials were distributed in response to specific requests for information about the 1996 NRC-AMRMC Associateship Program or as a result of general requests by persons whose fields of specialization appeared to be appropriate for the research opportunities available in the AMRMC laboratories.

COMPETITION

Panel reviews of applicants for the Associateship Programs, including that with the US Army Medical Research and Materiel Command, are conducted in February, June and October of each year.

Enclosed as *Attachment 1* and *Attachment 2* is information on the awardees. *Attachment 3* and *Attachment 4* contain information on the status of the recommended candidates for reviews held during the period of this report.

OCTOBER 1995 REVIEW

Thirteen applications were received for this review. Prior to the review two applications were incomplete due to missing supporting documents, one application was ineligible, and four applications were not approved by the laboratory. *Six applications were presented to the board for review and six were recommended for awards. Two applicants were not given awards due to lack of funding. Four applicants were offered awards of which three accepted and one declined.*

FEBRUARY 1996 REVIEW

Eighteen applications were received for this review. Prior to the review three were not approved by the laboratory. *Fifteen applications were presented to the board for review. Two were not recommended for awards. Ten were recommended for awards of which three were not offered awards due to lack of funding. Ten applicants were offered awards of which nine accepted and one declined.*

JUNE 1996 REVIEW

Nine applications were received for this review. Prior to the review two were not approved by the laboratory. *Seven applications were presented to the board for review and all seven were recommended for awards. Four were not offered awards due to lack of funding. Three were offered awards and accepted.*

ASSOCIATES' ACTIVITIES

Termination Reports

Attachment 1 is a list of Associates, who terminated their appointments during the period of October 1, 1995, and September 30, 1996. It includes their laboratories, their starting and termination dates, and the names of their Advisers. Associates are required to submit reports upon termination (attached to this report), and Advisers are asked to submit final evaluations of each Associate. Associates who have not submitted a termination report have received a follow-up letter.

Associates Who Ended Tenure 10/1/95 - 9/30/96 Attachment 1

U.S. Army Medical Research & Materiel Command 11/8/96 Page 1 of

Associate Name + / Adviser	Center / Term Report Status	Starting Date / Adviser Report Status	Ending Date
Amitai, Gabriel(S)	Walter Reed Army Institute of Research	1/09/95	10/16/95
Dr. Bhupendra P. Doctor	Termination Report: Received	Adviser Report:	Not Receive
Ashcom, James Denny(S)	Medical Research Institute for Infectious Diseases	8/01/94	7/31/96
Dr. Bradley Gene Stiles	Termination Report: Not Received	Adviser Report:	Received
Clifford, Julianne C M	Walter Reed Army Institute of Research	4/08/94	4/07/96
Dr. Thomas Harvey Hudson	Termination Report: Received	Adviser Report:	Received
Diaz Romero, Jose	Walter Reed Army Institute of Research	9/01/95	8/31/96
Dr. Wendell D. Zollinger	Termination Report: Received	Adviser Report:	Received
Gabaree, Catherine Louise	U.S. Army Research Institute of Environmental Medicine	6/01/93	7/15/96
Dr. John F Patton, III	Termination Report: Received	Adviser Report:	Received
Hart, Bruce Weston	Medical Res Inst of Chemical Defense	4/19/93	3/31/96
Dr. John Joseph Schlager	Termination Report: Received	Adviser Report:	Received
Hebert, Mark Andrew	Walter Reed Army Institute of Research	2/05/93	2/04/96
Dr. James L. Meyerhoff	Termination Report: Received	Adviser Report:	Received
Levenson, Vadim Joseph(S)	Walter Reed Army Institute of Research	1/04/93	1/03/96
Dr. Thomas Larry Hale	Termination Report: Not Received	Adviser Report:	Received
Matylevich, Natalya P	U.S. Army Institute of Surgical Research	5/18/92	11/17/95
Dr. Albert Thomas McManus	Termination Report: Received	Adviser Report:	Not Receive
Oberste, Mark Steven(S)	Medical Research Institute for Infectious Diseases	4/25/94	3/28/96
Dr. Jonathan Fowler Smith	Termination Report: Received	Adviser Report:	Not Receive
Okunji, Onyemaechi(S)	Walter Reed Army Institute of Research	3/15/93	3/14/96
Dr. Joan Elise Jackson	Termination Report: Received	Adviser Report:	Not Receive
Qiao, Yiran(S)	Walter Reed Army Institute of Research	2/11/93	2/10/96
Dr. Ludmila V.S. Asher	Termination Report: Not Received	Adviser Report:	Received
Ray, James Paul	Walter Reed Army Institute of Research	12/19/94	12/18/95
Dr. Frank Casper Tortella	Termination Report: Received	Adviser Report:	Received
Reid, Paul Francis	Medical Research Institute for Infectious Diseases	6/21/93	6/20/96
Dr. Leonard Alan Smith	Termination Report: Received	Adviser Report:	Received
Sample, Allen K(S)	Medical Research Institute for Infectious Diseases	10/03/94	6/14/96
Dr. Arthur Michael Friedlander	Termination Report: Received	Adviser Report:	Received
Schmidt, Katherine Ann	Walter Reed Army Institute of Research	5/12/93	5/25/96
Dr. Herman Schneider	Termination Report: Received	Adviser Report:	Not Received
Schoepp, Randal J	Medical Research Institute for Infectious Diseases	9/01/93	9/30/96
Dr. Jonathan Fowler Smith	Termination Report: Not Received	Adviser Report:	Not Received
Srivastava, Ashok Kumar(S)	Walter Reed Army Institute of Research	11/17/92	11/16/95
Dr. Charles Hearn Hoke, Jr	Termination Report: Received	Adviser Report:	Received
Szebeni, Janos(S)	Walter Reed Army Institute of Research	7/09/93	8/08/96
Dr. C. R. Alving	Termination Report: Received	Adviser Report:	Not Received
Triteeraprapab, Surang	Medical Research Institute for Infectious Diseases	3/06/95	6/14/96
Dr. Erik A Henchal	Termination Report: Received	Adviser Report:	Received
Vaughan, Jefferson A(S)	Medical Research Institute for Infectious Diseases	1/03/94	4/02/96
Dr. Michael J Turell	Termination Report: Received	Adviser Report:	Not Received
Wang, Yongqiang	Walter Reed Army Institute of Research	6/14/93	9/13/96
Dr. Wendell D. Zollinger	Termination Report: Received	Adviser Report:	Not Received

Total for Lab: 22

+ (S) indicates the associate was a Senior.

Name + Adviser	Center Citizenship	Starting Date	Ending Date
Abugo, Omoefe Oghenera. (S) Dr. Victor Winslow Macdon	Walter Reed Army Institute of Research Nigeria	4/06/95	4/05/97
Agin, Tonia Sue Dr. Marcia Kay Wolf	Walter Reed Army Institute of Research United States	2/14/94	2/13/97
Asermely, Karen E. Dr. Michael Adler	Medical Res Inst of Chemical Defense United States	5/22/95	5/21/97
Bhattacharjee, Apurba K (S) Dr. Jean Marianne Karle	Walter Reed Army Institute of Research India	7/10/95	7/09/97
Bogusz, Stephen Jude Dr. Charles Edward McQuee	Walter Reed Army Institute of Research United States	3/08/95	3/07/97
Bray, Michael Peter (S) Dr. John W Huggins	Medical Research Institute for Infectious Diseases United States	5/15/95	5/14/97
Britton, Paul Dr. Frank Casper Tortella	Walter Reed Army Institute of Research England, U.K.	7/15/94	1/14/97
Canziani, Gabriela A (S) Dr. Robert Glenn Ulrich	Medical Research Institute for Infectious Diseases Argentina	2/04/94	1/20/97
* Chakrabarti, Arun Kumar (S) Dr. Prabhati Ray	Walter Reed Army Institute of Research India	5/30/96	1/29/97
Connolly, Brett Michael Dr. Peter Becker Jahrling	Medical Research Institute for Infectious Diseases United States	10/18/93	10/17/96
* Das, Rina (S) Dr. Marti Jett	Walter Reed Army Institute of Research India	10/01/96	9/30/97
Ding, Xuan Zhou (S) Dr. Juliann Gong Kiang	Walter Reed Army Institute of Research People's Republic of China	10/03/94	10/02/97
Eze, Michael Okechukwu (S) Dr. David L. Hoover	Walter Reed Army Institute of Research Nigeria	10/03/94	10/02/97
* Fegeding, Konstantin V. Dr. Jeenan Tseng	Walter Reed Army Institute of Research Russia	10/16/95	10/15/97
Fried, Michal Dr. Patrick Emmet Duffy	Walter Reed Army Institute of Research Israel	1/11/95	1/10/97
Gandre, Helene Van Cu.. (S) Dr. Charles Hearn Hoke, Jr	Walter Reed Army Institute of Research France	8/08/94	1/07/97
Gilligan, Kevin James Dr. Kevin Anderson	Medical Research Institute for Infectious Diseases United States	7/18/94	7/17/97
Gorbounov, Nikolai V Dr. Nabil M. Elsayed	Walter Reed Army Institute of Research Russia	6/06/94	6/05/97

* Indicates that the associate started tenure between 10/2/95 and 9/30/96.
+ (S) Associate is a Senior.

Name + Adviser	Center Citizenship	Starting Date	Ending Date
Gouvea, Vera S. (S) Dr. Bruce Lamont Innis	Walter Reed Army Institute of Research United States	10/03/94	10/18/97
* Guebre Xabier, Mimi (S) Dr. Urszula Krzych	Walter Reed Army Institute of Research Ethiopia	5/20/96	5/19/97
* Guttieri, Mary Charity Dr. Connie Sue Schmaljohn	Medical Research Institute for Infectious Diseases United States	10/06/95	10/05/97
Hevey, Michael Carl Dr. Alan L Schmaljohn	Medical Research Institute for Infectious Diseases United States	7/25/94	7/24/97
Hooper, Jay William Dr. Connie Sue Schmaljohn	Medical Research Institute for Infectious Diseases United States	7/05/95	7/04/97
* Kamrud, Kurt Iver Dr. Connie Sue Schmaljohn	Medical Research Institute for Infectious Diseases United States	8/05/96	8/04/97
* Keller, James Erich Dr. Margaret G Filbert	Medical Res Inst of Chemical Defense United States	7/01/96	6/30/97
* Korte, William D (S) Dr. Ming L. Shih	Medical Res Inst of Chemical Defense United States	10/01/96	7/31/97
* Kurtis, Jonathan David Dr. Patrick Emmet Duffy	Walter Reed Army Institute of Research United States	7/01/96	6/30/97
Lee, Dae Taek Dr. Kent B Pandolf	U.S. Army Research Institute of Environmental Med Republic Of Korea	9/15/94	11/15/96
* Li, Guo Dr. Harry Zwick	Walter Reed Army Institute of Research People's Republic of China	9/16/96	9/15/97
Lin, Yu Dr. Joseph Benfer Long	Walter Reed Army Institute of Research People's Republic of China	7/18/94	7/17/97
Lu, Xi-chun May Dr. Frank Casper Tortella	Walter Reed Army Institute of Research People's Republic of China	6/01/94	7/01/97
Luckhart, Shirley Dr. Ronald Rosenberg	Walter Reed Army Institute of Research United States	8/01/95	7/31/97
* Lumley, Lucille Ann Dr. James L. Meyerhoff	Walter Reed Army Institute of Research United States	1/03/96	1/02/97
* Luo, Chunyuan Dr. Bhupendra P. Doctor	Walter Reed Army Institute of Research People's Republic of China	3/12/96	3/11/97
* Marek, Anne Maria Elis Dr. Ai Jeng Lin	Walter Reed Army Institute of Research West Germany	2/12/96	2/11/97
Meyer, Barbara J Dr. Connie Sue Schmaljohn	Medical Research Institute for Infectious Diseases United States	2/01/95	1/31/97

* Indicates that the associate started tenure between 10/2/95 and 9/30/96.
+ (S) Associate is a Senior.

Name + Adviser	Center Citizenship	Starting Date	Ending Date
Morris, Jim Dr. Tsung-Ming Anthony Sh	Medical Res Inst of Chemical Defense United States	9/11/95	9/10/97
Muldoon, Daniel F Dr. Robert Brian Wellner	Medical Research Institute for Infectious Diseases United States	6/05/95	6/04/97
Pakhomov, Andrew G Dr. Harry Zwick	Walter Reed Army Institute of Research Russia	1/26/94	1/25/97
* Palmer, Dupeh Rachel O Dr. Urszula Krzych	Walter Reed Army Institute of Research England, U.K.	11/27/95	11/26/96
Pardhasaradhi, Komandur (S) Dr. Peter K. Chiang	Walter Reed Army Institute of Research India	5/12/94	10/23/96
* Peel, Sheila Anne Dr. Edwin O. Nuzum	Walter Reed Army Institute of Research United States	8/01/96	7/31/97
Pierson, Vicki Lynn D Dr. Patricia Lynne Worsham	Medical Research Institute for Infectious Diseases United States	9/05/95	9/04/97
Pushko, Peter Dr. Jonathan Fowler Smith	Medical Research Institute for Infectious Diseases Latvia	5/20/94	5/19/97
Ryu, Hyoik (S) Dr. Frederick J. Cassels	Walter Reed Army Institute of Research Republic Of Korea	10/03/94	10/02/97
Saikh, Kamal Uddin (S) Dr. Robert Glenn Ulrich	Medical Research Institute for Infectious Diseases India	4/03/95	4/02/97
Santhanam, Kausalya Dr. Jayasree Nath	Walter Reed Army Institute of Research India	7/05/95	7/04/97
* Shitzer, Avraham (S) Dr. Richard R Gonzalez	U.S. Army Research Institute of Environmental Med Israel	8/12/96	8/11/97
Stewart, V Ann Dr. D Gray Heppner, Jr	Research Institute of Medical Sciences United States	1/03/95	1/02/97
Wasieloski, Leonard P Dr. Kevin Anderson	Medical Research Institute for Infectious Diseases United States	4/24/95	4/23/97
Woody, Mary Alice Dr. Bradley Gene Stiles	Medical Research Institute for Infectious Diseases United States	9/21/94	10/20/96
* Wyatt, James Kelley Dr. Harris Ritchie Lieberman	U.S. Army Research Institute of Environmental Med United States	7/01/96	6/30/97
* Yadava, Anjali	Walter Reed Army Institute of Research India	1/02/96	1/01/97
Zhang, Xiaoyan Dr. Marti Jett	Walter Reed Army Institute of Research People's Republic of China	4/10/95	4/09/97

* Indicates that the associate started tenure between 10/2/95 and 9/30/96.
+ (S) Associate is a Senior.

Name + Adviser	Center Citizenship	Starting Date	Ending Date
Zhao, Bangti (S) Dr. Joseph Robert Putnak	Walter Reed Army Institute of Research People's Republic of China	1/10/94	1/09/97

Total for Lab: 55

* Indicates that the associate started tenure between 10/2/95 and 9/30/96.
+ (S) Associate is a Senior.

Name/
Research Title

October 1995 Awardees

Kurtis, Jonathan David
Correlation between Phenotypic T & B Cell Immune Responses against Liver Stage Antigen 1 and the Expression of Naturally Acquired Resistance to Falciparum Malaria in Western Kenya

Luo, Chunyuan
Investigation of Ligand Modulation Mechanism on Reactivation of Phosphonyl Conjugate of Bispyridinium Oximes

Yadava, Anjali
Cloning, Characterization and Immonogenicity of Sequestrin, a Cytoadherence Protein of Malaria

Name/
Research Title

February 1996 Awardees

Chakrabarti, Arun Kumar
Biochemical and Molecular Biological Aspects of Vesicating Agents Induced Protease Stimulation

Crise, Bruce Jeffrey
Phylogenetic Analysis of VEEV IE Strains. Construction of Live-attenuated VEEV IE Vaccine Candidates by Site Directed Mutagenesis of Full-length Clone. Assessment of Polyvalent Vaccines and Extent of Vaccine Interference.

Feaster, Shawn Ray
Determining the Mechanistic Pathway for Product Release in Acetylcholinesterase Catalysis

Guebre Xabier, Mimi
The Role of Liver Stage Antigen 1-specific T Cells in Protective Immunity Induced by Attenuated Plasmodium Falciparum Sporozoites

Kamrud, Kurt Iver
Development and Comparison of Three Recombinant Vaccines to Puumala Virus

Kovach, Ildiko M
Molecular Dynamics Simulation of the Inhibition of Cholinesterases

Lewis, Steven Fred
Effect of Caffeine on Rate of Muscle Fatigue and Recovery during Dynamic Leg Exercise

Li, Guo
Imaging Photoreceptors in the Primate Eye in vivo

Peel, Sheila Anne
Utilize in vitro Biological and Molecular Models to (1) Identify Molecular Determinants which Function in Drug Resistance, thereby Facilitating Drug Development against Multidrug Resistant Strains of P.falciparum, and to (2) Determine whether the Parasite Remodels the structure/function of pfmdr1 to Mediate Resistance to Zenobiotic

Name/
Research Title

June 1996 Awardees

Dailey, Frank
Construction and Testing of Live Vaccine Candidates for Yersinia Pestis, the Causative Agent of Bubonic Plague

Das, Rina
Signal Transduction Pathways for Bioactive Lipids in Breast Cancer

Korte, William D
The Development and Evaluation of Liquid Chromatography-Mass Spectroscopy, Capillary Electrophoresis, or Fluoroimmunoassay Methods For the Detection of Sulfur Mustard Derivatives at Low Concentrations in Biological Samples

Shitzer, Avraham
Development of Mathematical Algorithms for Simultaneous Finger-tip Temperatures and Blood Perfusion Rates during Cold Stress

October 1995

Accepted Award

KURTIS, JONATHAN DAVID
Ph.D. Date:1996
Citizenship: United States
Brown University/RI
Adviser: Dr. Patrick Emmet Duffy
Actual Starting Date: 7/01/96
Research Field: Tropical Medicine
Termination Date: 6/30/97
Research Title: Correlation between Phenotypic T & B Cell Immune Responses against Liver Stage Antigen 1 and the Expression of Naturally Acquired Resistance to Falciparum Malaria in Western Kenya

LUO, CHUNYUAN
Ph.D. Date:1993
Citizenship: People's Republic Of China
China Unknown
Adviser: Dr. Bhupendra P. Doctor
Actual Starting Date: 3/12/96
Research Field: Biochemical Pharmacology
Termination Date: 3/11/97
Research Title: Investigation of Ligand Modulation Mechanism on Reactivation of Phosphonyl Conjugate of Bispyridinium Oximes

YADAVA, ANJALI
Ph.D. Date:1991
Citizenship: India
J Nehru University
Adviser:
Actual Starting Date: 1/02/96
Research Field: Immunology
Termination Date: 1/01/97
Research Title: Cloning, Characterization and Immonogenicity of Sequestrin, a Cytoadherence Protein of Malaria

Declined

BHUSHAN, REVA
Ph.D. Date:1995
Citizenship: United States
State Univ of New York-Buffalo
Adviser: Dr. Susan Lee Welkos
Research Field: Microbiology
Research Title: Mechanism of Action of Plasminogen Activator in Systemic Infection by Virulent Y. Pestis

Recommended/No Funding

LI, JIA
Ph.D. Date:1994
Citizenship: People's Republic Of China
Pennsylvania State U Central Off
Adviser: Dr. Antoinette B. Hartman
Research Field: Infectious Diseases
Research Title: Development of Reagents to Aid in the Study of Cytokine Responses to Shigella Infection in the Guinea Pig Keratoconjunctivitis Model

MALAVASIC, MICHAEL JOHN
Ph.D. Date:1988
Citizenship: United States
University of Chicago/IL
Adviser: Dr. Charles Hearn Hoke, Jr
Research Field: Virology
Research Title: Cloning of Dengue Virus-specific, Display-phage Encoded Mimitopes as Tools to Investigate Dengue Virus Neutralization

February 1996

Recommended

SHALEV, ARIEH YOEL — Ph.D. Date:1972
Citizenship: Israel — Montpellier I, U
Adviser: Dr. Gregory L. Belenky
Research Field: Behavioral Biology
Research Title: Prospective Study of Treatment Intervention Following Exposure to Extreme Stress

Accepted Award

CHAKRABARTI, ARUN KUMAR — Ph.D. Date:1984
Citizenship: India — Calicut, U Of
Adviser: Dr. Prabhati Ray — Actual Starting Date: 5/30/96
Research Field: Toxicology — Termination Date: 1/29/97
Research Title: Biochemical and Molecular Biological Aspects of Vesicating Agents Induced Protease Stimulation

CRISE, BRUCE JEFFREY — Ph.D. Date:1993
Citizenship: United States — Yale University/CT
Adviser: Dr. Michael D Parker — Expected Starting Date: 11/15/96
Research Field: Virology — Termination Date: 11/14/97
Research Title: Phylogenetic Analysis of VEEV IE Strains. Construction of Live-attenuated VEEV IE Vaccine Candidates by Site Directed Mutagenesis of Full-length Clone. Assessment of Polyvalent Vaccines and Extent of Vaccine Interference.

FEASTER, SHAWN RAY — Ph.D. Date:1995
Citizenship: United States — University of Iowa
Adviser: Dr. Bhupendra P. Doctor — Expected Starting Date: 2/01/97
Research Field: Biophysical Chemistry — Termination Date: 1/31/98
Research Title: Determining the Mechanistic Pathway for Product Release in Acetylcholinesterase Catalysis

GUEBRE XABIER, MIMI — Ph.D. Date:1988
Citizenship: Ethiopia — France Unknown
Adviser: Dr. Urszula Krzych — Actual Starting Date: 5/20/96
Research Field: Immunology — Termination Date: 5/19/97
Research Title: The Role of Liver Stage Antigen 1-specific T Cells in Protective Immunity Induced by Attenuated Plasmodium Falciparum Sporozoites

KAMRUD, KURT IVER — Ph.D. Date:1996
Citizenship: United States — Colorado State University
Adviser: Dr. Connie Sue Schmaljohn — Actual Starting Date: 8/05/96
Research Field: Virology — Termination Date: 8/04/97
Research Title: Development and Comparison of Three Recombinant Vaccines to Puumala Virus

KOVACH, ILDIKO M — Ph.D. Date:1974
Citizenship: United States — University of Kansas
Adviser: Dr. Bhupendra P. Doctor — Actual Starting Date: 5/28/96
Research Field: Biochemistry Biophysics — Termination Date: 9/27/96
Research Title: Molecular Dynamics Simulation of the Inhibition of Cholinesterases

February 1996

Accepted Award

LEWIS, STEVEN FRED
Citizenship: United States
Adviser: Dr. Harris Ritchie Lieberman
Research Field: Nutrition
Research Title: Effect of Caffeine on Rate of Muscle Fatigue and Recovery during Dynamic Leg Exercise
Ph.D. Date:1977
Stanford University/CA
Actual Starting Date: 5/16/96
Termination Date: 9/15/97

LI, GUO
Citizenship: People's Republic Of China
Adviser: Dr. Harry Zwick
Research Field: Medical Research
Research Title: Imaging Photoreceptors in the Primate Eye in vivo
Ph.D. Date:1993
University of Mass-Lowell
Actual Starting Date: 9/16/96
Termination Date: 9/15/97

PEEL, SHEILA ANNE
Citizenship: United States
Adviser: Dr. Edwin O. Nuzum
Research Field: Parasitology
Research Title: Utilize in vitro Biological and Molecular Models to (1) Identify Molecular Determinants which Function in Drug Resistance, thereby Facilitating Drug Development against Multidrug Resistant Strains of P.falciparum, and to (2) Determine whether the Parasite Remodels the structure/function
Ph.D. Date:1991
U of North Carolina-Chapel Hill
Actual Starting Date: 8/01/96
Termination Date: 7/31/97

Declined

GIRALDO, LUIS ERNESTO
Citizenship: United States
Adviser: Dr. Alan J. Magill
Research Field: Pathology
Research Title: Isolation and Characterization of a Define Leishmania DTH Antigen and Serological Diagnosis of Leishmania
Ph.D. Date:1996
Tulane University of Louisiana

Withdrew after Review/Recommend

OSORIO, JORGE EMILIO
Citizenship: Colombia
Adviser: Dr. George V Ludwig
Research Field: Virology
Research Title: Effectiveness of the New Generation of Alphavirus Vaccines against Current or newly Emerging Strains
Ph.D. Date:1996
University of Wisconsin-Madison

Recommended/No Funding

MUKHTAR, MAOWIA MOHAMED
Citizenship: United States
Adviser: Dr. Alan J. Magill
Research Field: Immunology
Research Title: Cloning of Recombinant Leishmania Antigens for the Diagnosis and the Development of Vaccines for Visceral Leishmaniasis
Ph.D. Date:1989
Cornell University/NY

June 1996

Recommended

TSAREV, SERGEI ANATOLYEVICH — Ph.D. Date:1989
Citizenship: Russia — Shemyakin Inst Bioorg Chem/Russia
Adviser: Dr. Bruce Lamont Innis
Research Field: Virology
Research Title: Refining the Strategy of Hepatitis E Virus Vaccination through Molecular Virology Studies

Accepted Award

DAILEY, FRANK — Ph.D. Date:1986
Citizenship: United States — University of Michigan-Ann Arbor
Adviser: Dr. Arthur Michael Friedlander — Expected Starting Date: 11/01/96
Research Field: Infectious Diseases — Termination Date: 10/31/97
Research Title: Construction and Testing of Live Vaccine Candidates for Yersinia Pestis, the Causative Agent of Bubonic Plague

DAS, RINA — Ph.D. Date:1987
Citizenship: India — J Nehru University
Adviser: Dr. Marti Jett — Actual Starting Date: 10/01/96
Research Field: Biochemistry — Termination Date: 9/30/97
Research Title: Signal Transduction Pathways for Bioactive Lipids in Breast Cancer

KORTE, WILLIAM D — Ph.D. Date:1966
Citizenship: United States — University of California-Davis
Adviser: Dr. Ming L. Shih — Actual Starting Date: 10/01/96
Research Field: Analytical Chemistry — Termination Date: 7/31/97
Research Title: The Development and Evaluation of Liquid Chromatography-Mass Spectroscopy, Capillary Electrophoresis, or Fluoroimmunoassay Methods For the Detection of Sulfur Mustard Derivatives at Low Concentrations in Biological Samples

SHITZER, AVRAHAM — Ph.D. Date:1971
Citizenship: Israel — U of Illinois-Urbana-Champaign
Adviser: Dr. Richard R Gonzalez — Actual Starting Date: 8/12/96
Research Field: Bioengineering — Termination Date: 8/11/97
Research Title: Development of Mathematical Algorithms for Simultaneous Finger-tip Temperatures and Blood Perfusion Rates during Cold Stress

Withdrew after Review/Recommend

ZANARDI, ALBERT THOMAS — Ph.D. Date:1996
Citizenship: United States — Texas A&M University
Adviser: Dr. Kevin Anderson
Research Field: Virology
Research Title: The Role of Secreted and Membrane-anchored Forms of the Ebola Virus Glycoprotein in Providing Protective Immunity to Virus Challenge

June 1996

Recommended/No Funding

ZUBER, MOHAMMED — Ph.D. Date: 1981
Citizenship: United States — University of Madras/India
Adviser: Dr. Arthur Michael Friedlander
Research Field: Bacteriology
Research Title: Development of Attenuated Live Vaccine Strains for Plague

Final report for NRC Senior Associateship Program

1. Date:

April 28, 1996

2. Name:

Gabriel Amitai, Ph.D.

3. Name and Location of Laboratory and Center:

Division of Biochemistry
Walter Reed Army Institute of Research
Washington DC 20307-5100

4. Dates of Tenure:

January 7 - July 7 1995
October 1 - October 16, 1995

5. Title of Research Project:

Studies on Inhibitors and Reactivators of Acetylcholinesterase

6. Research Advisor's Name:

Dr. B.P. Doctor
Director, Division of Biochemistry
Walter Reed Army Institute of Research

7. Are you on leave from a professional post?

I was on leave from the Israel Institute for Biological Research, Ness Ziona Israel, where I am currently serving as Head, Division of Medicinal Chemistry..

8. Internatonal posts held during tenure

N/A

9. Programmatic travel during tenure

1) Travel to IIBR, Ness Ziona, Israel, March 1995

2) Travel to University of Pittsburgh, Chemical Engineering, Center for Biotechnology and Bioengineering, University of Pittsburgh, PA. May 1995. Working in the laboratory of Dr. Alan J. Russell on covalent binding of AChE to polyurethane foam.

3) Travel to UCSD, La Jolla, Ca. Department of Pharmacology, May 1995. Working with Dr. Zoran Radic and Prof. Palmer Taylor on mouse AChE mutants.

10. Scientific seminars, meetings, and/or consultations

1) APBI Meeting in Columbia, Md., organized by the DOD, March 95.

2) Fourth Meeting on Chemical Protection, ERDEC, APG, Md., April 95.

3) Meetings with Dr. Ken Dretchen, Assistant Dean for Research, Georgetown University, Discussions on oximes and human BChE and visit at the Department of Pharmacology, Georgetown University (March, May, 95).

4) Meetings with Napoleon Monroe, Vice President STI, Inc., Rockville, Md. Discussions, preparation and submission of preproposal (by IIBR) on the improvement of HI-6 stability in automatic combined syringe of STI. (March, April, May, June and October 95).

5) Consultation with Dr. Palmer Taylor on Fasciculin II inhibition kinetics and mouse AChE mutants, (March-July 95, see also programmatic travel).

6) 5th International Symposium on Protection against Chemical and Biological Warfare Agents, Stockholm, Sweden, June 1995 (invited lecturer)..

11. Seminars or lectures delivered at universities and/or institutes:

N/A

12. Meetings attended by specific invitation

5th International Symposium on Protection against Chemical and Biological Warfare Agents, Stockholm, Sweden, June 1995 (invited lecturer)..

13. Teaching, if any as an associate:

N/A

14. Work in progress:

1) Kinetics of inhibition of human plasma cholinesterase and erythrocyte AChE by pyridostigmine

2) Kinetics of inhibition of AChE from various species and AChE mutants by fasciculin II.

3) Delineation of the selectivity and kinetics of inhibition of BChE and AChE by Chlorpyrofos-oxon (CPO).

4) Binding of FBS-AChE to Polyurethane foams and use of insoluble AChE matrix together with oximes for degradation of Nerve Agents.

15. Summary of research during tenure

During my tenure as a senior NRC fellow at the WRAIR I have been involved in four different projects: 1. Construction of kinetic model for the analysis of the time-course of inhibition of human plasma BChE and erythrocyte AChE by pyridostigmine (PYR). 2. Kinetics of inhibition of AChE from various species and AChE mutants by fasiculin II (FAS II).

3. Delineation of the inhibition of BChE and AChE by Chlorpyrofos-oxon (CPO). 4. Covalent binding of FBS-AChE to polyurethane foams and its application for the degradation of nerve-agents. The inhibition of human blood ChE's by pyridostigmine was studied in normal volunteers and out-patients of the Walter Reed hospital in order to find abnormal ChE sensitivity towards PYR. Mouse AChE mutants H287R, D280V, D283N and the double mutant D280V/D283N were prepared to delineate which amino acids affect the affinity of FAS II for FBS and human AChE and are located close to the PAS. Kinetics of inhibition of H287R mutant with FAS II yields K_F value 6 fold higher than that obtained for the wild type. The K_F obtained for the double mutant D280V/D283N is 3 fold larger than that of the wild type. CPO, a metabolite of the widely used insecticide chlorpyrifos, inhibits human plasma BChE and rHBChE with exceptionally high bimolecular rate constant (k_i) $1.3x10^9$ and $1.6x10^9$ M^{-1} min^{-1}, respectively. These values are 140 and 180 fold larger than the k_i value obtained for the inhibition of rHAChE and 340 and 420 fold larger than for human erythrocyte AChE, respectively. The double mutant of the acyl pocket residues of rHAChE F295L/F297V, that display characteristics of BChE active center, shows a 7.5 fold enhanced inhibition rate with CPO as compared to the wild type. These results provide a rationale for higher efficacy of CPO scavanging by BChE as compared to AChE. Furthermore, CPO may serve for differential quantitative determination of BChE active-site concentration especially at low enzyme levels.

16. Publications and papers resulting from research as an associate

1. G. Amitai, Z. Radic, D. Moorad, P. Taylor and B.P Doctor, Interaction of Fasciculin II with mammalian wild-type AChE's and their related mouse AChE mutants, Isr. J. Med. Sci., 31, 732 (1995).

2. G.Amitai, D. Moorad, R. Adani, B. Velan, A. Shafferman and B.P. Doctor, Inhibition of acetylcholinesterase and butyrylcholinesterase by Chlorpyrifos-oxon, 1996 Medical Defense Bioscience Review (1996)

3. K.E. LeJeune, D.S. Frazier, G. Carranto, D.M. Maxwell, G. Amitai, A.J. Russell, and B.P. Doctor, Covalent linkage of mammalian cholinesterases

AMRPC RMILH/SGP

National Research Council Associateship Program Final Report

1. Date: March 18, 1996

2. Name (ID): Julianne Claire Maloney Clifford

3. Dates of Tenure: April 9, 1994 to April 9, 1995
April 9, 1995 to April 9, 1996

4. Title of Research Project: Ricin intoxication in a cell-free system.

5. Research Advisor: Dr. Thomas H. Hudson

6. On leave from a professional post? No

7. International posts held during tenure: NA

8. Programmatic Travel during tenure: NA

9. Scientific seminars, meetings and/or consultations:
   1. December 1994, Annual Meeting of the American Society for Cell Biology, San Francisco, CA
   2. December 1995, Annual Meeting of the American Society for Cell Biology, Washington, DC. (poster presentation)
   3. February 1996, Annual Meeting of American Association for the Advancement of Science
   {4. May 1996, U.S. Army Medical Bioscience Review, Science Applications International Corporation SAIC), Baltimore, MD (poster presentation}

10. Seminars or Lectures delivered at Universities and/or Institutes: NA

11. Meetings attended by specific invitation: NA

12. Teaching, if any, as an associate:
    I was responsible for the training and laboratory supervision of a student hire from May 1995 through February 1996.

13. Work in Progress:

I am currently examining the effects of nonhydrolyzable analogs GTP and GDP on ricin translocation in a permeabilized cell system utilizing the system I have developed for detecting the enzymatic effects of translocated ricin on ribosomal RNA.

14. Summary of Research During Tenure:

In accordance to the proposed goals of this research project I have 1) developed a system for detecting the enzymatic effects of translocated ricin toxin on ribosomal RNA, 2) optimized conditions for generating a permeabilized cell system utilizing the pore forming toxin Staphylococcal alpha oxin and 3) used this unique detection system to investigate the organelle and energy requirements for ricin translocation in the intact and permeabilized cell systems.

15. Publications:

Clifford, J.C.M. & T.H. Hudson. 1995. Detection of ricin-aniline specific RNA fragment: An indicator of ricin translocation. Molecular Biology of the Cell. Vol. 6 Supplement. ASCB Abstracts, # 2361.

16. Patents: NA

17. Future position and address:

Staff Fellow
Laboratory of Bacterial Toxins
Building 29 Rm. 103
Center for Biologics Evaluation & Research
Food and Drug Administration
Bethesda, MD 20892

18. Appraisal of associateship programs:

I consider myself fortunate to have had the opportunity to participate as a postdoctoral fellow in the associateship program. On the whole I have found the system to be responsive to my needs but has allowed pursue my research interests unheeded by administrative distractions. I cannot comment specifically on the performance of any one staff member since I have not experienced any circumstances, complications or problems within the system which required any considerable interaction with the staff. I feel that the associateship program has given me a chance to work in a

unique research environment (Walter Reed Army Institute of Research) and for that I am grateful. The WRAIR liaison office has always been helpful and responsive to my inquiries and needs. The only critical comment I can think of is that I found the system for making travel arrangements and reimbursements to be both confusing and complicated (but I have not had to make arrangements through the travel office since December 1994, so the complaint is a bit outdated).

NATIONAL RESEARCH COUNCIL
ASSOCIATESHIP PROGRAM
2101 CONSTITUTION AVE, NW, TJ2114
WASHINGTON, DC 20418

FINAL REPORT

(1) DATE

7-26-1996

(2) NAME (AND ID NUMBER IF KNOWN)

Jose Diaz Romero

(3) NAME AND LOCATION OF LABORATORY CENTER

Department of Bacterial Diseases
Walter Reed Army Institute of Research
Washington, DC 20307-5100

(4) DATES OF TENURE

9-1-1995/8-31-1996

(5) TITLE OF RESERCH PROJECT

"DEVELOPMENT OF NEW METHODS TO STUDY THE IMMUNE RESPONSE TO NEISSERIA MENINGITIDIS GROUP B"

(6) RESEARCH ADVISER'S NAME

Dr. Wendell D. Zollinger

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?

No

(8) INTERNATIONAL POSTS HELDS DURING TENURE

N/A

(9) PROGRAMMATIC TRAVEL DURING TENURE

N/A

(10) SCIENTIFIC SEMINARS, MEETINGS, AND/O CONSULTATIONS

NATO ASI "Vaccine Design: The Role of Cytokine Networks" 24 June - 5 July 1996, Cape Sounion Beach, Greece.

(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/ OR INSTITUTES

N/A

(12) MEETINGS ATTENDED BY SPECIFIC INVITATION

N/A

(13) TEACHING, IF ANY, AS AN ASOCIATE

N/A

(14) WORK IN PROGRESS.

N/A

(15) SUMMARY OF RESEARCH DURING TENURE

A problem in obtaining a Neisseria meningitidis B vaccine is the lack of capsular polysaccharide immunogenicity. This homopolymer of N-acetyl neuraminic acid residues in alpha 2-8 linkage, polysialic acid, is also present on the surface of animal cells as a unique glycosylation of the neural cellular adhesion molecule (NCAM). NCAM is expressed on hematopoietic cells and recognized by anti-CD56 mAb, a marker of NK cells and lymphocytes that mediate MHC-unrestricted cytotoxicity. A previous report exits about the presence of polysialic acid in NK cells. In this work we reexamine this point by the use of different monoclonal antibodies polysialic acid-specific.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE

Cross-reaction Between Human NK Cells and Group B Meningococci. Yong Q.Wang, Jose Diaz Romero, Craig A. Hammack and Wendell D. Zollinger. (manuscript in preparation)

(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE

N/A

(18) FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS

C/ Oviedo 13, 1 D
28020 Madrid
SPAIN
Tl. and Fax: (34) 1-5343811

(19) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS

Under Article 22(1) of the tax treaty between the United States and Spain, my research grant qualifies for exemption from withholding of federal income tax, but I was not aware of this point until I filled my federal income-tax return; the handbook of Policies, Practices, and Procedures of the N.R.C. in the chapter about tax does not any mention to the possibility of exemptions:

6.3 Federal Tax Liability of Nonresident Aliens
(Exchange Visitors)

6.3.1 – If you are a nonresident alien who holds an Exchange Visitor (J1) Visa, the Research Council is required by the US Tax Code to withhold an amount from your stipend of 30% per month and to report this deduction to the Internal Revenue Service annually.

6.3.2 – Although taxes will be withheld at the 30% level, actual tax liability is determined when you file a federal income-tax return. In the event the tax liability is less than the amount withheld, you will receive a tax refund directly from the IRS.

6.3.3 – As a nonresident alien, you should file Form 1042 NR as early as possible, but not later than the 15th day of June following the close of the tax (calendar) year. For other filing options, you should consult a tax professional and/or the IRS.

FINAL REPORT

(1) **DATE:** 29 July 1996

(2) **NAME:** Catherine L.V. Gabarée, Ph. D.

(3) **NAME AND LOCATION OF LABORATORY:**
U.S. Army Research Institute of Environmental Medicine
Kansas Street
Natick, Massachusetts 01760-5007

(4) **DATES OF TENURE:** 1 June 1993 to 15 July 1996

(5) **TITLE OF RESEARCH PROJECTS:**
A) Assessment of Intra- and Inter-individual Metabolic and Hormonal Variation in Special Operations Forces (SOF) Soldiers.

B) Effects of Topical Skin Protectant on Heat Exchange in Humans.

(6) **RESEARCH ADVISER'S NAME:**
A) John F. Patton III, Ph.D. 1 June 1993-31 May 1994

B) Michael N. Sawka, Ph. D. 1 June 1994-15 July 1996

(7) **ARE YOU ON LEAVE FROM A PROFESSIONAL POST?** N/A

(8) **INTERNATIONAL POSTS HELD DURING TENURE:** N/A

(9) **PROGRAMMATIC TRAVEL DURING TENURE:**
Pennington Biomedical Research Institute, Baton Rouge, LA:
March 1993 (2 days for study preparation)
May 1993 (2 days for study preparation)
June 1993 (3 weeks for data collection)
July 1993 (3 weeks for data collection)

(10) **SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULTATIONS:**
Interagency Committee on Human Nutrition Research, Bethesda, MD, February 23-24, 1994
Experimental Biology '94, Anaheim, CA, April 24-28, 1994
New England American College of Sports Medicine, May 6, 1994
American College of Sports Medicine, Indianapolis, IN, June 1-4, 1994
Experimental Biology '95, Atlanta, GA, April 1995
Experimental Biology '96, Washington D.C., April 1996
American College of Sports Medicine, Cincinnati, Ohio, May 31-June 1, 1996

Final Report
Catherine L.V. Gabarée, Ph.D.

(11) **SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES:** N/A

(12) **MEETINGS ATTENDED BY SPECIFIC INVITATION:** N/A

(13) **TEACHING, IF ANY, AS AN ASSOCIATE:** N/A

(14) **WORK IN PROGRESS:** I am currently working on a research study to determine daily variation in skin blood flow in healthy individuals and individuals who smoke and individuals with high cholesterol. Additionally I am continuing to collect data for a methodological study comparing two methods of determining skin blood flow.

(15) **SUMMARY OF RESEARCH DURING TENURE:**
Study 1: Metabolic and hormonal intra- and inter-individual variation during repeated bouts of prolonged, treadmill exercise was determined in order to evaluate substrate utilization during exercise and recovery. Diet, hydration status, energy expenditure, and ambient conditions were controlled. Extremely low variation in respiratory and biochemical variables indicated insignificant variation between individuals in substrate utilization during exercise.

Study 2: The effects of application of a Topical Skin Protectant (TSP) on heat exchange during exercise in the heat were determined. Esophageal temperature, skin temperature, heart rate, and pre- and post-experimental weights were measured. Mean skin temperature, mean body temperature, changes in esophageal temperature per min of exercise, evaporative heat loss, and sweating rate were calculated. TSP application minimally affected heat exchange under the conditions of this study.

(16) **PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE:**

Gabarée, C.L.V., B.S. Mair, M.A. Kolka, and L.A. Stephenson. Effects of Topical Skin Protectant on Heat Exchange in Humans. In review.

Gabarée, C.L.V., B.S. Mair, M.A. Kolka, and L.A. Stephenson. Effects of Topical Skin Protectant on Heat Exchange in Humans. Technical Report, U.S. Army Research Institute of Environmental Medicine, Natick, MA, 1996. In review.

Gabarée, C.L.V., T.E. Jones, T.C. Murphy, E. Brooks, R.T. Tulley, E.W. Askew. Assessment of Inter-individual Metabolic Variation in Special Operations Forces (SOF) Soldiers during Exercise and Recovery. Technical Report T95-24, U.S. Army Research Institute of Environmental Medicine, Natick, MA, 1995.

Gabarée, C.L.V., T.E. Jones, T.C. Murphy, E. Brooks, R.T. Tulley, E.W. Askew. Intra- and Inter-individual Metabolic and Hormonal Variation During Exercise and Recovery. In preparation.

(17) **PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE:** N/A

(18) **FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS:**
Research Physiologist
U.S. Army Research Institute of Environmental Medicine
Kansas Street
Natick, MA 01760-5007

(19) **APPRAISAL OF THE ASSOCIATESHIP PROGRAM:** My tenure as an NRC associate was most beneficial to me. I have had the opportunity to pursue my interests in basic metabolism as well as thermal effects on metabolism. I particularly appreciated the travel funds available for scientific conferences and presentations.

BM | LH | SGP

AWRDC

Final Report

1. DATE: 3/17/96

2. NAME: Bruce W. Hart #916533

3. NAME AND LOCATION OF LABORATORY:

USAMRICD, APG-EA, MD 21010

4. DATES OF TENURE: 4/93-4/96

5. TITLE OF RESEARCH PROJECT:

The role of p34cdc2 in sulfur mustard-induced G2 block of human epidermal keratinocytes.

6. RESEARCH ADVISER'S NAME: Dr. John Schlager

7. ON LEAVE FROM PROFESSIONAL POST?: no

8. INTERNATIONAL POSTS HELD DURING TENURE: N/A

9. PROGRAMMATIC TRAVEL DURING TENURE:

Beckman Capillary Electrophoresis Training Course, Brea, CA, March 1993.

10. SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULTATIONS:

American Association for Cancer Research Annual Meeting, San Francisco, CA, April 1994
Society of Toxicology Annual Meeting, Baltimore, MD, March 1995
American Association for Cancer Research Annual Meeting, Toronto, ON, April 1995
Society of Toxicology Annual Meeting, Anaheim, CA, March 1996

11. SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES:

Georgetown University, March 1996

12. MEETING ATTENDED BY SPECIFIC INVITATION: NONE

13. TEACHING: none

14. WORK IN PROGRESS:

This work is being continued on a new contract. Studies will focus on the production of reactive oxygen species by the protein phosphatase 2A inhibitors and reversal of the G_2/M cell cycle block.

15. SUMMARY OF RESEARCH DURING TENURE:

Nitrogen and sulfur mustards, both DNA alkylating agents, were shown to produce a G_2/M cell cycle block in normal and transformed human cells. This cell cycle block was completely reversed by substantial inhibition of protein phosphatase 2A. This resulted in an abnormal mitotic state, accompanied by marked changes in protein phosphorylation and DNA integrity. Inhibiton of protein phosphatase 1 had no effect on the mustard-induced G_2/M block. These results suggest that protein phosphatase 2A is involved in the G_2/M block produced by exposure of human cells to low concentrations of nitrogen or sulfur mustard.

16. PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE:

Hart, B.W. and Schlager, J.J. Inhibition of protein phosphatase 2A reverses sulfur mustard-induced G_2/M block of normal human epidermal keratinocytes (in preparation).

Hart, B.W. and Schlager, J.J. Abrogation of nitrogen mustard-induced G_2/M block by inhibitors of protein phosphatase 2A. (Submitted to *J. Biol. Chem.*).

Schlager, J.J., Smith, W.J. and Hart B.W. Sulfur mustard (HD) stress gene induction in transformed Hep G2 cells. *Toxicologist* **30:**328, 1996.

Hart, B.W. and Schlager, J.J. Role of protein phosphatases in nitrogen mustard-induced G_2/M block of HeLa cells. *Proc. Amer. Assoc. Cancer Res.* **36:**174, 1995.

Hart, B.W. and Schlager, J.J. Role of protein phosphatases 1 and 2A in sulfur mustard-induced G_2/M block of normal human epidermal keratinocytes. *Toxicologist* **15:**232, 1995.

17. PATENTS APPLIED FOR: none

18. CURRENT FORWARDING ADDRESS:

30-L Greystone Ct.
Annapolis, MD, 21403

19. APPRAISAL OF THE ASSOCIATESHIP PROGRAMS:

I have been very pleased with the NRC program overall. I have had no problems with any aspect of the program directly controled by the NRC. I believe that the program is a great alternative to the traditional academic postdoc. I do, however, have reservations about the USAMRICD program. There is overwealming pressure at the Institute to generate large numbers of manuscripts. The quality of the manuscripts (or the journals they are submitted to) is not considered, only the number. This is not a healthy attitude for a scientific institution. The credibility of an organization is dictated by the quality of it's work, and I believe that this "bean counter" attitude sends a bad message to young and growing scientists.

92 89030

FINAL REPORT (using attached format)

1. January 12, 1996

2. Mark Andrew Hebert

3. Division of Neurosciences
Walter Reed Army Institute of Research
Walter Reed Army Medical Center
Washington, DC
20307-5100

4. February 4, 1993 - February 4, 1996

5. Defeat-induced pathology in golden hamsters

6. Research Advisor: James L. Meyerhoff

7. No

8. N/A

9. Programmatic Travel: The University of Georgia: May 7-15, 1994

10. Scientific Meetings:

23rd annual meeting of the Society for Neuroscience
Washington, DC
Nov. 7-12, 1993

24th annual meeting of the Society for Neuroscience
Miami Beach, FLA
Nov. 13-18, 1994

25th annual meeting of the Society for Neuroscience
San Diego, CA
Nov. 11-16, 1995

Annual meeting of the International Behavioral Neuroscience Society
Satellite symposium: The Neurobiology of Defensive Behavior
Santiago de Compostela, Spain
May 16-21, 1995

11. N/A

12. N/A

13. N/A

14. Current Work:

Studying effects of acute defeat on immobility in mice. Psychopharmacological drugs are being evaluated to delineate the underlying neuropharmacology of the effect.

15. Summary of Research During Tenure:

Conditioned defeat (CD), an animal model of combat-related psychopathologies such as CSR or PTSD, was examined extensively. Experimental procedures were developed for the acute induction of CD in both Syrian hamsters and DBA/2 mice. Tests were devised for assessing changes in social and non-social behavior following CD acquisition. Benzodiazepines, stress-related neuropeptides, antidepressants, and other compounds were screened for possible effects on CD. None of the drugs tested were found to reverse CD, but diazepam potentiated the syndrome. Neuroendocrine, immunological, and cardiovascular responses were also characterized and neuroanatomical studies were initiated using the CD models.

16. **Peer-reviewed Published Papers**

Hebert, M.A., Potegal, M., Moore, T., Evenson, A.R., & Meyerhoff, J.L. Diazepam enhances conditioned defeat in hamsters (*Mesocricetus auratus*). *Pharmacology, Biochemistry & Behavior*, in press (accepted).

Potegal, M., Hebert, M.A., deCoster, M. & Meyerhoff, J.L. Brief, high frequency stimulation of the corticomedial amygdala induces a delayed and prolonged increase of aggressiveness in male Syrian golden hamsters. *Behavioral Neuroscience*, in press (accepted).

Hebert, M.A., Potegal, M., & Meyerhoff, J.L. (1994). Flight-elicited attack and priming of aggression in non-aggressive hamsters. *Physiology & Behavior, 56*, 671-675.

Potegal, M., Ferris, C., Hebert, M., Meyerhoff, J.L. & Skaredoff, L. Attack priming in female Syrian golden hamsters is mediated by a c-fos coupled process within the corticomedial amygdala (in prep).

Published abstracts

Hebert, M.A., Evenson, A.R., Saxena, H., Saviolakis, G. & Meyerhoff, J.L. Behavioral tests for social and non-social consequences of conditioned defeat in mice. *Society for Neuroscience Abstracts, Vol. 21*, 448, 1995.

Hebert, M.A., Potegal, M., Moore, T. & Meyerhoff, J.L. Diazepam enhances conditioned

fear responses in Syrian golden hamsters. *Society for Neuroscience Abstracts, Vol. 20*, 811, 1994.

17. Patents: Automated activity monitor for activity of rodents in a water medium
Patent application initiated by WRAIR.

18. Future address:

University of Hawaii at Manoa
Pacific Biomedical Research Center
Bekesy Laboratory of Neurobiology
1993 East-West Road
Honolulu
Hawaii
96822

19. Appraisal of Associateships Program:

I was pleased with the program overall. I was disappointed at times with the slowness of the staff in processing travel expense forms. I waited 4 months for reimbursement for one trip. I was also disappointed with the manner in which NRC stipends were increased for new NRCs at WRAIR in the fall of 1993. Second and third year NRCs did not get an increase at that time, which I feel was unfair. The NRC should implement a fair, universal policy with regard to stipend increases with which all laboratories must comply.

BM | LH | SGP

FINAL REPORT

(1) Date: 12/20/95.

(2) Name: Vadim Joseph Levenson.

(3) Name and location of laboratory: Walter Reed Army Institute of Research, Washington, D.C.

(4) Dates of tenure: 1/03/93 - 1/02/96

(5) Title of Research Project: Ribosome as a vaccine vector.

(6) Research adviser's name: T.L.Hale.

(7) Are you on leave from a professional position: No.

(8) International posts held during tenure: No.

(9) Programmatic travel during tenure: No.

(10) Scientific seminars, meetings, consultations:

Microbial Pathogenesis and Immune response. Orlando, Florida. September 6-10, 1993.
Novel Vaccine Strategies. Bethesda, MD. October 6-8, 1993.
Veterinary Vaccines. Bethesda, MD. October 27-28, 1994.
Vaccines: New Technologies and Applications. Alexandria, VA. March 21-23, 1994.
ASM Annual Meeting. Las Vegas, Nevada. May 21-25, 1994.
Vaccines: Novel Strategies. Eilat, Israel,

(11) Seminars or lectures delivered at universities.

Center for Vaccine Development, Baltimore, MD, January 26, 1994.
NIH, August 9, 1995.

(12) Meetings attended by specific invitation: No.

(13) Teaching, if any, as an associate: No.

(14) Work in progress: N/A

(15) Summary of the research during tenure:

Nucleoprotein subcellular (NPS) vaccine from *S.sonnei* was established as a candidate vaccine for humans. Several bench lots were prepared and tested. They elicited in mice an intensive IgG antibody response and the early protection against intranasal challenge with homologous shigellae. In guinea pigs, one parenteral injection of NPS vaccine induced an intensive response of IgA-ASC and about 70% protection against keratoconjunctival challenge. Protocol for the large-scale production of the NPS *S.sonnei* vaccine was elaborated, and the vaccine was produced in 1995 under GMP conditions for clinical trial. Experimental NPS vaccine from *S.flexneri* was obtained to be further tested as a component of the bivalent *Shigella* vaccine.

(16) Publications and papers resulting from research as associate:

Levenson V.J. and T.P. Egorova. 1993. "Effective stimulation of the mucosal immune response by parenteral vaccination with weak antigen associated with nucleoprotein vehicle." In the: "Microbial Pathogenesis and Immune Response", Conference. Orlando, Florida, September 6-10.

Levenson V.J. and T.P. Egorova. 1993. "Effective stimulation of the mucosal immune response by parenteral vaccination with weak antigen associated with nucleoprotein vehicle." Ann. N.Y. Acad. Sci. 730:1-4.

Levenson V.J. 1993. "Nucleoprotein particles as a potent vaccine vector ". In the "Novel Vaccine Strategies". Conference, Bethesda, October 6-8.

Levenson V.J., C.P. Mallett and T. L.Hale. 1994. Protection against lethal *Shigella sonnei* pneumonia in mice by parenteral immunization with a nucleoprotein subcellular vaccine. Abstr. Annual ASM Meeting, p. 150.

Levenson V.J. 1994. Nucleoprotein (ribosomal) vector as a basis for vaccine development: experimental studies with *Shigella* and *Pasteurella*. Veterinary Vaccines. October 27-28, p. 418.

Levenson V.J. 1995. Subcellular dysentery vaccine. 39th OHOLO Conference, Eilat, Israel, p.7P.

Levenson V.J., C.P. Mallett and T.L. Hale. 1995. "Protection against lethal *Shigella* pneumonia in mice by parenteral immunization with nucleoprotein subcellular vaccine." Infection and Immunity, 63: 2762-276.

(17) Patents applied for as a result of research as an associate. No.

(18) Future position and address.

Will participate in the WRAIR CRADA project as an employee of the SBL (Swedish Biological Laboratories). Laboratory of Enteric Infections, WRAIR, Washington, D.C. 20307-5100.

(19) Appraisal of the associateship programs.

The program was very helpful as an opportunity to demonstrate the protective efficacy of parenteral vaccination against shigellosis and to make further steps in the development of parenteral NPS vaccine as a candidate vaccine for humans. It also gave the better understanding of the vaccine research and development practice in the U.S.

FINAL REPORT

(1) DATE

October 16, 1995

(2) NAME (ID#)

Natalya P. Matylevich (9189650)

(3) NAME AND LOCATION OF LABORATORY OR CENTER

Laboratory Department, US Army Institute of Surgical Research, Fort Sam Houston, San Antonio, TX 78234

(4) DATES OF TENURE

May 18, 1992 - November 17, 1995

(5) TITLE

Mechanism of antimicrobial activity of silver nylon dressing.

(6) RESEARCH'S ADVISER'S NAME

Albert T. McManus, PhD

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?

Research Scientist, Institute of Cell Biophysics, Russian Academy Of Sciences, Pushchino, Moscow Reg., 142292

(8) INTERNATIONAL POST HELD DURING TENURE

Research Associate

(9) PROGRAMMATIC TRAVEL DURING TENURE

N/A

(10) SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULTATIONS

(1) National Meetings:

Wound Repair, Gordon Research Conference, June 1993, New London, NH

13th Annual Meeting of the Bioelectrical Repair and Growth Society (BRAGS), October 1993, Dana Point, CA

Galveston Conference on Burn Resuscitation, November 21-23, Galveston, TX

26th annual meeting of the American Burn Association, April 1994, Orlando, FL

27th annual meeting of the American Burn Association, Annual Meeting, April 1995, Albuquerque, NM

5th Annual Wound Healing Society Meeting, Minneapolis, MN, April 1995

Wound Repair, Gordon Research Conference, July 1995, New London, NH

(2) International Meetings:

New Approach in Wound Healing, Scientific Conference, December 18-21, 1993, Pushchino, Russia

9th Congress of the International Society for Burn Injuries, June 1994, Paris, France

6th Congress of European Burn Association, September 1995, Verona, Italy

(3) Seminars

University of Texas at Austin, Bioengineering Department, August 1992

US Army Institute of Surgical Research, Saturday Seminars, 1992-1995

City Trauma Conference, San Antonio, Quarterly, 1994-1995

University of Texas at San Antonio, Health Science Center, Biochemistry and Microbiology Dept., through 1992-1995

(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES

Pushchino State University, December 22, 1993
US Army Institute of Surgical Research, May 6, 1995

(12) MEETINGS ATTENDED BY SPECIFIC INVITATIONS

New Approach in Wound Healing, Scientific Conference, December 1993, Pushchino, Russia Pushchino, Russia

(13) TEACHING, IF ANY, AS AN ASSOCIATE

N/A

(14) WORK IN PROGRESS

MRI study of the effect of silver nylon dressings and direct current on metabolic activity in the burn wound.

(15) SUMMARY OF RESEARCH DURING TENURE

Effect of application of weak direct electric current through silver nylon wound dressing on plasma extravasation in partial and full thickness scald burn wounds in rats have been studied. Fluorescent tracers FITC-albumin and Rhodamine-albumin were used to estimate quantitatively plasma volume and plasma protein concentration in wound tissue. We have used fluorometry and confocal fluorescence microscopy to measure fluorescence intensity signals in plasma and tissue. It was shown that direct current reduces plasma volume loss and decreases protein extravasation in burn wounds after the injury, reduces edema accumulation and induces reabsorption of edema fluid and plasma proteins from interstitium.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE

(1) Matylevich NP, McManus AT, Mason AD Jr, Pruitt BA Jr: Direct current treatment reduces plasma volume loss following

burn injury in rats. Presented at the 6th Congress of the European Burn Association (Abstract 54, p.104), Verona, Italy, September 12-16,1995.

(2) Matylevich NP, McManus AT, Mason AD Jr, Pruitt BA Jr: Direct current reduces albumin extravasation after partial thickness burn injury in rats. Presented at the 4th Annual Wound Healing Society Meeting (Abstract 126), Minneapolis, MI, April 30, 1995.

(3) Chu CS, McManus AT, Matylevich NP,Mason AD Jr, Pruitt BA Jr: Silver-nylon and direct current reduce wound accumulation of Evans Blue following full thickness thermal injury. Presented at the 4th Annual Wound Healing Society Meeting (Abstract 90), Minneapolis, MI, April 29, 1995.

(3) Matylevich NP, McManus AT, Mason AD Jr, Pruitt BA Jr: Direct current reduces plasma extravasation after partial thickness burn injury in rats. Abstract 170 (p.215) of the proceedings. Presented at the 26th annual meeting of the American Burn Association, Albuquerque, NM, 22 Apr 1995.

(4) Chu CS, McManus AT, Matylevich NP, Mason AD Jr, Pruitt BA Jr: Microscopic examination of a mesh auto-epidermal/allodermal composite graft treated with silver-nylon dressing and direct current in rats. Abstract 46 (p.91) of the proceedings. Presented at the 26th annual meeting of the American Burn Association, Albuquerque, NM, 20 Apr 1995.

(5) Matylevich NP, McManus AT, Chu CS, Mason AD Jr, Pruitt BA Jr: Effect of direct current (DC) on microvascular exchange in full thickness burn wounds. Presented at the 9th Congress of the International Society for Burn Injuries, Paris, France, 27 Jun-1 Jul 1994.

(6) Chu CS, McManus AT, Matylevich NP, Mason AD Jr, Pruitt BA Jr: Survival of Dermal allografts in composite (auto/allo) with partial thickness autografts using silver-nylon dressings and direct current. Presented at the 9th Congress of the

International Society for Burn Injuries, Paris, France, 27 Jun-1 Jul 1994.

(7) Chu C, McManus A, Matylevich N, Mason A Jr, Pruitt B Jr: Reduced contraction and hair loss after healing of guinea pig scalds treated with direct current. Presented at the 4th Annual Wound Healing Society Meeting, San Francisco, CA, 20 May 1994.

(8) Chu CS, McManus AT, Matylevich, Mason AD Jr, Pruitt BA Jr: Direct current improves healing of composite auto-epidermal/allodermal grafts. Abstract 125 of the proceedings. Presented at the 26th annual meeting of the American Burn Association, Orlando, FL, 23 Apr 1994.

(9) Matylevich NP, McManus AT, Chu CS, Mason AD Jr, Pruitt BA Jr: Direct current (DC) reduces leakage and accumulation of macromolecules in full thickness burn injuries. Abstract 144 of the proceedings. Presented at the 26th annual meeting of the American Burn Association, Orlando, FL, 23 Apr 1994.

(10) Matylevich NP, McManus AT, Chu CS, Mason AD Jr, Pruitt BA Jr: Direct current (DC) reduces macromolecular leakage after full thickness burn injury in rats. Page 51 of Proceedings. Presented at the American Burn Association, Annual Meeting, April 1995, Orlando, FL.

(11) Chu CS, McManus AT, Matylevich NP, Mason AD Jr, Pruitt AD Jr: Direct current (DC) reduces burn wound edema following full thickness injury in rats. Page 50 of the Proceedings. Presented at the 13th Annual Meeting of the Bioelectrical Repair and Growth Society (BRAGS), Dana Point, CA, 13 Oct 1993.

(12) Chu CS, McManus AT, Matylevich, Mason AD Jr, Pruitt BA Jr: Reduction of dermal ischemia (zone of stasis) by post-scald application of weak direct current (DC). Presented at the International Society of Surgery/35th World Congress of Surgery International Surgical Week 1993, Hong Kong, 22-27 Aug 1993.

(13) Chu CS, McManus AT, Matylevich NP, Mason AD Jr, Pruitt BA Jr: Reduction of dermal ischemia and maintenance of hair

follicle circulation by post scald application of direct current (DC). Page 25 of the Proceedings. Presented at the Third Chino-American Conference on Burns and Trauma, Guangzhou, China, 18-19 Aug 1993.

(14) Matylevich NP, McManus AT, Mason AD Jr, Pruitt BA Jr: Direct current reduces plasma protein extravasation following partial thickness burn injury in rats. Microvascular Research, 1995 (in press).

(15) Chu CS, Matylevich NP, McManus AT, Mason AD Jr, Pruitt BA Jr: Direct current reduces wound edema following full thickness burn injury in rats, Journal of Trauma,(in press).

(16) Chu CS, McManus AT, Matylevich NP, Mason AD Jr, Pruitt BA Jr: Enhanced survival of autoepidermal:allodermal composite grafts in allosensitized animals by use of silver-nylon dressings and direct current. Journal of Trauma, 38(7), July 1995.

(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE

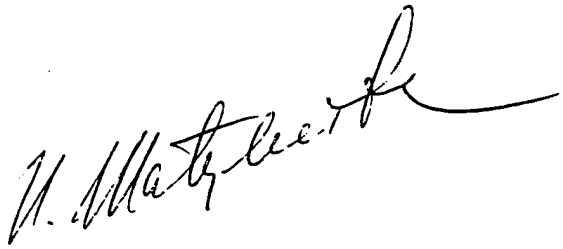
N/A

(18) CURRENT FORWARDING ADDRESS

4031 Thousand Oaks Dr.
Apt. 312
San Antonio, TX 78217

(19) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS

I found this program extremely useful and helpful for my professional growth, including experience as research investigator, communication skills, professional contacts, experience in participation in scientific conferences and discussions. US Army Institute of Surgical Research provides great opportunity for basic research in cell and tissue biology as well as in applied medical studies.



BM | LH | SGP

RECEIVED
MAR 2 6 1996
ASSOCIATESHIP PROGRAMS

Final Report

(1) Date: March 20, 1996

(2) Name: M. Steven Oberste, Ph.D.

(3) Name and location of laboratory or center: Virology Division, US Army Medical Research Institute of Infectious Diseases, USAMRDC, Ft. Detrick, Frederick, MD.

(4) Dates of tenure: 4/24/94-3/28/96

(5) Title of research project: Development of candidate vaccines for enzootic strains of Venezuelan equine encephalitis (VEE) virus

(6) Research advisor: Jonathan F. Smith, Ph.D.

(7) Are you on leave from a professional post? N/A

(8) International posts held during tenure: N/A

(9) Programmatic travel during tenure: N/A

(10) Scientific seminars, meetings, or consultations:
a. 43rd annual meeting, American Society of Tropical Medicine and Hygiene, Cincinnatti, OH, Nov. 13-17, 1994
b. IVth International Symposium on Positive Strand RNA Viruses, Utrecht, the Netherlands, May 25-30, 1995.
c. 44th annual meeting, American Society of Tropical Medicine and Hygiene, San Antonio, TX, Nov. 17-21, 1995.

(11) Seminars or lectures delivered at universities and/or institutes:
Centers for Disease Control and Prevention, Aug. 25, 1995.

(12) Meetings attended by specific invitation: N/A

(13) Teaching, if any, as an Associate: N/A

(14) Work in progress:
Three VEE IAB-IE chimeric viruses have been constructed by recombinant DNA techniques.The first of these is somewhat attenuated in virulence for mice, but it protects mice against subsequent lethal challenge with VEE IE. Additional animal work is in progress with this and the remaining two chimeric viruses. Others in the lab will continue my work by constructing additional chimeric viruses with which to map the viral determinants of differential animal virulence

and mosquito vector competence. Subgenomic cDNA clones have been constructed to be used to construct a full-length VEE IE infectious clone. A mutant gene cassette with which to construct attenuated viruses has also been cloned. Studies on VEE sequence diversity are being completed, using the ns3 and PE2 coding regions to characterize VEE viruses both within a given serotype and among distantly realted VEE strains.

(15) Summary of research during tenure:
The complete sequence of Venezuelan equine encephalitis (VEE) virus subtype IE was determined. Sequence analysis showed that the nsP3 protein contains four conserved domains within a region which is generally hypervariable among alphaviruses. Preliminary animal studies using chimeric viruses, which express one or more VEE IE structural proteins in the context of VEE IAB, suggest that this approach may be useful in developing a live-attenuated VEE IE vaccine. Further sequencing studies have shown that at least three of the four conserved domains are maintained in all VEE strains. Partial sequencing of the structural genes of prototype and sample isolates (approximately 70 isolates) was used to identify VEE strains which were the cause of recent outbreaks in Mexico, Peru, Panama, Colombia, and Venezuela.

(16) Publications and papers resulting from research as an Associate:
(a) **Oberste, M.S.**, M.D. Parker, and J.F. Smith. 1996. Complete sequence of Venezuelan equine encephalitis virus subtype IE reveals conserved and hypervariable domains within the C-terminus of nsP3. Virology (in press).
(b). Weaver, S.C., R.A. Salas, R. Rico-Hesse, G.V. Ludwig, **M.S. Oberste**, J.F. Smith, B. Roberts, A. Barreto, J. Boshell, J. Cardenas, Z. Fernandez, O. Godoy, T. Camacho, E. Rueda, A. Guaqueta, and R.B. Tesh. Re-emergence of epidemic Venezuelan equine encephalomyelitis in South America. Lancet (submitted).
(c) Watts, D.M., J. Callahan, C.B. Cropp, C. Rossi, **M.S. Oberste**, N. Karabatsos, W. Nelson, J.T. Roehrig, M.T. Wooster, J.F. Smith, D.J. Gubler, and C.G. Hayes. Venezuelan equine encephalitis and oropouche viral infections among Peruvian military troops in the Amazon region of Peru. (manuscript in preparation).
(d) Watts, D.M., J. Callahan, C. Rossi, **M.S. Oberste**, J.T. Roehrig, M.T. Wooster, J.F. Smith, C.B. Cropp, N. Karabatsos, D.J. Gubler, and C.G. Hayes Arboviruses associated with human infection in the Peruvian Amazon river basin. (manuscript in preparation).
(e). **Oberste, M.S.**, S.C. Weaver, D.M. Watts, and J.F. Smith. Genetic identification of Panama-genotype Venezuelan equine encephalitis virus subtype ID in Peru: The first occurrance of the Panama genotype outside of the Republic of Panama. (manuscript in preparation).
(f) **Oberste, M.S.**, S. Schmura, S.C. Weaver, and J.F. Smith. Genetic diversity among spatially and temporally separated isolates of Venezuelan equine encephalitis subtype IE. (manuscript in preparation).
(g) **Oberste, M.S.**, S. Schmura, and J.F. Smith. Sequence conservation within the hypervariable C-terminal half of alphavirus nsP3 defines potential functional domains. (manuscript in preparation).

(17) Patents applied for as a result of research as an Associate: N/A

(18) Future position and address or current forwarding address:
Research Microbiologist, GS-13, Respiratory and Enteric Viruses Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Mailstop G17, Atlanta, GA 30333.
Home mailing address, as of 3/30/96: PO Box 95181, Atlanta, GA 30347.

(19) Appraisal of the Associateship programs:
My two years an a Senior Associate have been very rewarding, both personally and professionally. I have had the opportunity to be part of an exciting research program and to develop research, managerial, and interpersonal skills which will be invaluable throughout the rest of my career.

DEPARTMENT OF THE ARMY
WALTER REED ARMY INSTITUTE OF RESEARCH
WALTER REED ARMY MEDICAL CENTER
WASHINGTON, D.C. 20307-5100

REPLY TO
ATTENTION OF

BM/LH/SCP

NATIONAL RESEARCH COUNCIL
ASSOCIATESHIP PROGRAM
2101 CONSTITUTION AVE, NW, TJ2114
WASHINGTON, DC 20418.

FINAL REPORT FORMAT

(1) Date March 6, 1996

(2) NAME **Christopher Onyemaechi OKUNJI** Ph.D

(3) NAME AND LOCATION OF LABORATORY OR CENTER

Walter Reed Army Institute of Research, Washington DC

(4) DATES OF TENURE **March 15, 1993 to March 14, 1996**

(5) TITLE OF RESEARCH PROJECT: **Antileishmanial Agents Based on Isolates from plants used in Traditional Medicine.**

(6) RESEARCH ADVISER'S NAME **Dr. Joan E. Jackson**

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
If so, list position or title and address of facilities

Senior Lecturer, University of Nigeria, Nsukka, Nigeria.

(8) INTERNATIONAL POSTS HELD DURING TENURE:

Secretary/Treasurer Bioresources Development and Conservation Program International (Non-profit Organization)

(9) PROGRAMMATIC TRAVEL DURING TENURE
List location(s) and date(s) N/A

(10) SCIENTIFIC SEMINARS, MEETINGS AND/OR CONSULTATIONS
List location(s) and date(s).List foreign meetings separately

Drug Discovery and Commercial Opportunities in Medicinal plants September 19-20, The Ritz Carlton, Pentagon City, Arlington, VA

American Chemical Society, 208th National Meeting, Washington, DC August 21-25, 1994.

National Institute of Allergy and Infectious Diseases (NIAID) International Centers for Tropical Diseases Research, Second Annual Meeting, April 28-30, 1993

National Institute of Allergy and Infectious Diseases (NIAID) International Centers for Tropical Diseases Research, Third Annual Meeting, April 27-29, 1994

National Institute of Allergy and Infectious Diseases (NIAID) International Centers for Tropical Diseases Research, Fourth Annual Meeting, April 26-28, 1995

HPLC Forum '95 Seminar, Mariot Hotel, Bethesda Maryland, May 15, 1995

Foreign meetings
PRELUDE Symposium on Research and Action: African Medicinal Plants and Human Health within a framework of Sustainable Development, Ouidah, Benin, 27-31, 1995.

IOCD International Symposium on Phytochemical and Pharmacological Properties of African Medicinal Plants, Victoria Falls, Zimbabwe, February 25-28, 1996

Bioresources Development and Conservation Programme Second International Congress on the Utilization of Tropical Plants and Biodiversity Conservation Douala Cameroon, October 23-27, 1995

(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES. List location(s) and date(s)
Division of Experimental Therapeutics Chembio meeting- Screening Nigerian Medicinal Plants for Antileishmanial Activity 1994 Forest Glen, 1994

(12) MEETINGS ATTENDED BY SPECIFIC INVITATION
List location(s) and date(s)

American Chemical Society Meeting Chicago, Illinois August 20-25, 1995

Bioresources Development and Conservation Programme Second International Congress on the Utilization of Tropical Plants and Biodiversity Conservation Douala Cameroon, October 23-27, 1995

(13) TEACHING, IF ANY, AS AN ASSOCIATE N/A

(14) WORK IN PROGRESS.

Two pending patent applications
Structural elucidation of some antileishmanial compounds

(15) SUMMARY OF RESEARCH DURING TENURE

Evaluation of the antileishmanial activity of 110 extracts representing 40 plants species implicated in traditional medicine enabled the identification of new antileishmanial chemotypes that proved highly active and are radically different from the existing drugs. A new bioassay technique was also developed. About 39% of the extracts possess significant *in vitro* antileishmanial activity compared to pentavalent antimonials. Bioassay-directed fractionation of active extracts using a combination of chromatographic techniques yielded lead compounds, from which ten chemically novel antileishmanial compounds were selected based on their chemical class and lack of known toxicity. These findings clearly demonstrate that medicinal plants hold high promise for the development of new antileishmanial drugs.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE

Jackson, J.E., Tally, J. D., **Okunji, C.O.**,Pitchford, S. Oduola,A.M. and Lindquist, A., Microphysiometer methodology (MOM): Nonradioisotopic Techniques for Protozoan Parasite Drug Susceptibility and New Drug Discovery, *American Journal of Tropical Medicine and Hygiene* 51: 171, 1994.

Okunji C.O., Iwu M.M, Jackson J.E. and Tally J.D., Biological Active Saponins from Two Dracaena species, Manuscript accepted for publication in Saponins USED IN TRADITION AND MODERN MEDICINE, edited by George R. Waller and Kazuo Yamasaki, Plenum Publishing Co., New York, NY, 1996 in press. (American Chemical Society presentation and publication).

Jackson J.E., **Okunji C.O.**, Iwu M.M, and Tally J.D., Hanson, W. L., Waits V. B., Nolan L. L., Schuster B. G., Reinventing Antileishmanials: Modern Antileishmanials from Traditional Herb Therapy, *American Journal of Tropical Medicine and Hygiene* 53: 216, 1995.

Okunji C.O., Iwu M.M, Jackson J.E. and Tally J.D., Antileilshmanial activity of Some Nigerian Medicinal Plants Manuscript accepted for publication in PRELUDE Research and Action: African Medicinal Plants and Human Health within a Framework of Sustainable Development edited by Georges Thill, 1995, Benin, 27-31, 1995.

Okunji C.O, Jackson J.E., Tally J.D. and Iwu M.M.,Cytosensor Microphysiometer System (CMS): A New Method of Screening Medicinal Plants for Antileishmanial Activity being an invited paper delivered at the IOCD International Symposium; Chemistry, Biological and Pharmacological Properties of African Medicinal

Plants, Victoria Falls, Zimbabwe, February 25-28, 1996

(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE

- in draft

(18) FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS

Senior Research Associate,
Division of Experimental Therapeutics,
Walter Reed Army Institute of Research,
Washington DC 20305-5100.

(19) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS

The project has been a phenomenal success in identifying new antileishmanial chemotypes as potential leads in the area where there has been no effective therapy. Because such leads have a lengthy history of human use, unacceptable toxicity would not be expected. The data on the in vitro and in vivo studies are significant especially to encourage further investigation.

This program has offered us the opportunity of working as a team in the advancement of knowledge and research in the area of antileishmanial drugs from natural products. Although leishmaniasis is regarded as a major tropical disease affecting humankind, work in this direction has been of low priority due to limited market/investment profit. This important scientific contribution could not have been possible without the NRC program.

The NRC program is an excellent program full of vision and foresight. I personally enjoyed the company of your staff, the interaction was cordial. You have the right calibre of scientific and administrative staff to administer this program. May I use this opportunity to express my appreciation to all of you managing this program. The program has been meaningful, exiting and rewarding. The experience gain during the tenure will obviously constitute an indispensable part of my career. However, arrangement with National Academies Travel concerning travels should be seriously reviewed.

FINAL REPORT

1: DATE October 4, 1995

2: NAME James P. Ray, Ph. D.

3: NAME AND LOCATION OF LABORATORY OR CENTER
Walter Reed Army Institute of Research, Washington, DC

4: DATES OF TENURE
December 19, 1994 - December 18, 1995

5: TITLE OF RESEARCH PROJECT
Studies of cerebral injury and associated penumbral regions

6: RESEARCH ADVISER'S NAME
Dr. Frank C. Tortella

7: ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
No

8: INTERNATIONAL POSTS HELD DURING TENURE
None

9: PROGRAMMATIC TRAVEL DURING TENURE
N/A

10: SCIENTIFIC SEMINARS, MEETINGS AND/OR CONSULTATIONS
25th Annual Meeting of the Society for Neuroscience,
November 11-16, 1995, San Diego, CA

11: SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES
None

12: MEETINGS ATTENDED BY SPECIFIC INVITATION
None

13: TEACHING, IF ANY, AS ASSOCIATE
None

14: WORK IN PROGRESS
None

15: SUMMARY OF RESEARCH DURING TENURE

In an effort to identify the ischemic "penumbra," the viable (and potentially salvagable) but compromised area of neuronal tissue circumscribing the core infarct, I have examined the distribution of markers of cellular viability (beta-actin and c-fos mRNA) in infarcted rat brains using the in situ hybridization technique. Rats received 2 hr of intraluminal middle cerebral artery occlusion and either 4 or 24 hr of reperfusion. In comparison to the contralateral hemisphere, infarcted brain regions exhibited only very low levels of beta-actin or c-fos mRNA. However, the ischemic penumbra exhibited consistently elevated c-fos mRNA at 4 hr, and elevated beta-actin mRNA at 24 hr. The elevated expression of beta-actin gene in the ischemic penumbra may represent a compensatory state of neuronal function following ischemic insults.

16: PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE

Dave, J. R., A. Stankiewicz, A. H. Hogan, L. Clapp, J. Ray, F. C. Tortella, P. Doctor and H. S. Ved (1995) Phospholipase A2 (PLA2) produces differential neurotoxic effects in primary neuronal cultures obtained from different regions of fetal rat brains. Soc. Neurosci. Abstr., Vol. 21, part 1, p. 74

Ray, J. P., P. Britton, X. -C. M. Lu, F. C. Tortella and J. R. Dave (1995) situ hybridization studies of beta-actin gene expression in rat brain tissu following ischemic injury and reperfusion. Soc. Neurosci. Abstr., Vol. 21, part 2, p. 993.

17: PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE

None

18: FUTURE POSITION AND ADDRESS OR CURRENT FOWARDING ADDRESS

Current forwarding address is:

James P. Ray
2445 Lyttonsville Rd., Apt. 402
Silver Spring, MD 20910

20: APPRAISAL OF THE ASSOCIATESHIP PROGRAM

The Associateship Programs serve a vital purpose, to support scholars doing critical research, and they do this very well

BM/LH/EL/LH

RECEIVED
JUN 21 1996
ASSOCIATESHIP PROGRAMS

1. 6-4-1996

2. Paul F. Reid

3. Toxinology Department, USAMRIID, Fort Detrick, Frederick, MD 21702

4. 6-23-1993 to 6-23-1996

5. Cloning and expression of Dendrotoxins

6. Dr. Leonard A. Smith

7. N/A

8. None

9. N/A

10. "Protein Engineering Methodologies", San Diego, June 27-28 1994
"Current topics in gene expression systems", San Diego, October 23-25 1994
"Potassium Channel Modulators", Washington D. C., January 23-25 1995
"5th International Society on Toxinology", Frederick, July 30-4 August 1995.

11. Work in progress seminars given annually at USAMRIID

12. "Cloning and expression of mamba toxins", Genetic Therapy Inc., Rockville, May 24 1996

13. Trained four military technicians to assist in projects.

14. Currently engaged in expression of Dendrotoxin mutants in order to complete additional experiments not possible prior to this time. Creating new mutant toxins by site-directed mutagenesis in an attempt to convert a mamba trypsin inhibitor to a ion channel blocker. Also investigating the possibility of testing the mamba trypsin inhibitor in the prevention of HIV replication. Subcloning other venom genes into the yeast vector, pPic9K, to test expression in yeast. It is

also planned to screen mouse T-cell library to isolate serum immune repressor genes whose protein sequence have some homology to short chain neurotoxins.

15. Forty mutant clones derived from dendrotoxins K and I had been constructed. These mutants were incorporated into a protein expression system as a fusion protein coupled to maltose binding protein. It was my function to solve the expression and purification problems which existed and isolate these mutant toxins. To this end protocols for expression and affinity purification were developed and a final chromatographic procedure was incorporated. Purified mutants were examined by polyacrylamide electrophoresis and N-terminal sequencing before being sent to a laboratory in England for analysis in binding assays. On receipt of binding data, new mutant toxins were designed and created permitting further investigation of toxin structure/function relationships.

16. Smith, L. A., Reid, P. F., Parcej, D., Wang, F., Schmidt, J. and Dolly, J. O. (1996) J. Biol. Chem., submitted

    Wang, F., Reid, P. F., Parcej, D., Schmidt, J., Dolly, J. O. and Smith, L. A. (1996) J. Biol. Chem., in preparation

    Reid, P. F., Wang, F., Schmidt, J., Dolly, J. O. and Smith, L. A. (1996) J. Biol. Chem., in preparation

    Reid, P. F., Assaad, A. and Smith, L. A. (1996) FEBS, in preparation

    Reid, P. F., Wang, F., Schmidt, J., Dolly, J. O. and Smith, L. A. (1996) Biochemistry, in preparation

17. none

18. Current address; 4610 Reels Mill road,
    Frederick,
    MD 21704

19. This program has been of tremendous benefit to post-doctoral people such as myself. It has presented me with the opportunity to work in a modern environment that would not have been possible elsewhere. Through

this position I have greatly expanded my knowledge of snake venoms and their future therapeutic potentials in the field of neurochemistry and in general medicine overall. Through your travel allowance scheme, my attendance of several meetings has given me exposure to experts in related fields which has been useful to us in the laboratory. My only grievance would be that the NRC do not allow their research fellows to attend workshop seminars which would allow them to acquire experience in the latest techniques. Over the course of two or more years new techniques arise and having these skills should aid progress in the laboratory. Aside from that, I consider myself fortunate to have participated in this programme. At this point, I would like to express my gratitude and wish you continuing success.

Final Report for National Research Council Associateship Program

1) September 23, 1996
2) Dr. Allen K. Sample
3) USAMRIID, Ft. Detrick, Maryland
4) October 4, 1994 to July 17, 1996
5) Role of YpkA protein kinase in the pathogenicity of *Yersinia pestis*.
6) Col. Arthur Friedlander
7) No
8) None
9) None
10) 95th ASM General meeting (Washington DC) May 1995
Chemotactic Cytokines (Philadelphia, PA) October 1995
96th ASM General Meeting (New Orleans, LA) May 19-22, 1996
11) None
12) None
13) None
14) None
15) I cloned the gene encoding the protein kinase from *Yersinia pestis* and expressed the protein in *Escherichia coli*. Antibody raised against the purified recombinant protein was used to detect kinase expression in *Y. pestis* and *Y. pseudotuberculosis*. In contrast to the literature, I demonstrated that the kinase was not secreted but was completely cell associated in both species. The entire gene was sequenced and showed little divergence from the published sequence of *Y. pseudotuberculosis*. Immunization of mice with purified recombinant protein kinase did not afford significant protection against challenge with wild-type *Y. pestis*.
16) Plasminogen Activator Protease of *Yersinia pestis* degrades proinflammatory cytokines Allen K. Sample and Arthur M. Friedlander (*Manuscript in preparation*)
17) None
18) Manufacturing Scientist, IDEXX Labs, One IDEXX Drive, Westbrook, ME 04092
19) The Associateship Program gave me the opportunity to move out of the area of academic research and into a more applied industrial-type research. This undoubtably was a major factor in obtaining my current position at IDEXX laboratories.

Allen K Sample
23 Sept 96

National Research Council Associateship Program

Final report

(1) Date 7 May, 1996

(2) Name Katherine Ann Schmidt ID #9354640

(3) Name and Location of Laboratory:
Walter Reed Army Institute of Research
Department of Bacterial Diseases
Bldg 40, Room 2085
Washington DC 20307-5100

(4) Dates of Tenure: 12 May, 1993-25 May, 1996

(5) Title of Research Project: *Neisseria gonorrhoeae* opacity protein expression during infection in human male volunteers.

(6) Research Adviser: Carolyn Deal, Ph.D., Herman Schneider, Ph.D.

(7) Are you on leave from a professiona post? no

(8) International posts held during tenure: none

(9) Programmatic travel during tenure:
USAMRIID, Ft. Detrich, Frederick MD. May 1994, Infectivity study
Kimbrough Hospital, Ft. Meade,MD, May 1995, Infectivity study

(10)Scientific Seminars, Meetings and other Consultations:
March 1994: Vaccine Conference, Alexandria VA.
May 1994: American Society for Microbiology, General Meeting, Las Vegas NV.
May 1995: American Society for Microbiology, General Meeting, Washington DC.
October 1995: IBC International Conference on Mucosal Immunization, Rockville MD.
May 1996: American Society for Microbiology, General Meeting, New Orleans, LA.
International meetings:
September 1994: Neisseria 94, Winchester, England

(11) Seminars or Lectures delivered at Universitites and/or Institutes:
April 1994: Seminar: *Neisseria gonorrhoeae* opacity protein expression during infection in human male volunteers. WRAIR, Washington DC.

(12) Meetings attended by specific invitation: NA

(13) Teaching, if any, as an assistant: Mentor, SEAP program, summer 1993, 1994, 1995

(14) Work in progress: I am continuing study of the opacity protein of *Neisseria gonorrhoeae.*

(15) Summary of research during tenure:

I participated in 4 human volunteer infectivity studies, and analyzed *N. gonorrhoeae* recovered from infected volunteers for opacity protein content: size, and N-terminal sequence. When it became evident that no specific opacity protein was required for human infection, I redirected my studies towards identifying critical common epitopes in the opacity proteins. I showed that an oligopeptide homologous to COOH-terminal outer loop region of opacity protein was recognized by antibodies in the serum of an uninfected volunteer. Specific rabbit polyclonal and mouse monoclonal antibodies, are currently being used to screen a panel of gonococcal isolates for the peptide.

(16) Publications and papers resulting from research as an associate:
Refereed Manuscripts:

1. Schneider, H., **K. A. Schmidt**, D. R. Skillman, L. Van De Verg, R. Warren, H. J. Wylie, J. C. Sadoff, C. D. Deal, and A. S. Cross. 1996 Sialylation lessens the infectivity of *Neisseria gonorrhoeae* MS11mkC. J. Infect. Dis, 173 *In Press.*
2. **Schmidt, K. A.**, C. D. Deal, M. Kwan, E. Thattassery, and H. Schneider. Opacity proteins expressed by strains recovered from volunteers infected with transparent *Neisseria gonorrhoeae* MS11 mkC. J. Infect. Dis. *In preparation*
3. Van De Verg, L.L., R. L. Warren, **K. A. Schmidt**, J. A. Lindstrom, J. Kenner, D. Skillman, C.-H. Zhou, J. W. Boslego, and H. Schneider. Differential antibody and cytokine responses in male volunteers infected with *Neisseria gonorrhoeae* MS11mkC. *In preparation.*
4. **Schmidt, K. A.**, R. Schainker, B. Balignot, and H. Schneider. pH and gonocidal activity in urine of volunteers infected experimentally with *Neisseria gonorrhoeae. In preparation.*

Abstracts and Presentations

1. **Schmidt, K. A.**, C. D. Deal, A. S. Cross, R. Kuschner, D. Skillman, and H. Schneider. 1994. Relationship of the onset of symptoms and dysuria to opacity protein (protein II) in experimental gonorrhea. p. 249. In: J. S. Evans, S. E. Yost, M. C. J. Maiden, I. M. Feavers, ed., Neisseria 94: Proceedings of the Ninth International Pathogenic Neisseria Conference, Winchester, UK.
2. **Schmidt, K. A.**, D. Skillman, J. C. Sadoff, R. Warren, C. D. Deal, L. L. Van De Verg, A. S. Cross, and H. Schneider. 1995. Sialylation of lipooligosaccharide by CMP-NANA does not enhance infectivity of *Neisseria gonorrhoeae* in a human male volunteer trial. B173. American Society for Microbiology General Meeting, Washington DC.
3. Van De Verg, L. L., R. L. Warren, J. Kenner, **K. A. Schmidt**, J. Ruckert, H. Schneider, and J. W. Boslego. 1995. Antibody and cytokine production in human male volunteers infected with *Neisseria gonorrhoea.* Eighth International Congress of Mucosal Immunity. San Diego, CA.
4. **Schmidt, K. A.**, R. Schainker, B. Balignot, J. Lindstrom, J. W. Boslego, L. Van De Verg, R. Warren, and H. Schneider. 1996. Does urine pH effect experimental gonorrhea infections in male volunteers? B312. American Society for Microbiology General Meeting, New Orleans, LA

(17) Patents applied for as a result of research as an associate: none

(18) Future position and address or current forewarding address:
contract employee, WRAIR, Dept. Bacterial Diseases, Washington DC
forewarding address: 9114 Piney Branch Road, Apt 202, Silver Spring MD 20903.

(19) Appraisal of the associateship programs:

The NRC fellowship program provided me with the opportunity to make the transition from student to scientist. The program made it possible for me to meet many of the other scientists involved in the field of STD research. Since my goals are to continue in research, with limited teaching and mentoring, the program was ideal for me.

However, the program might be improved by adding a teacher-track option: where an NRC fellow could do research under an approved mentor at a participating university, with a limited course-load (for example: no more than 1 course per semester, or 10 credit-hours per year). The teacher-track option would allow a young scientist to gain experience teaching, while preventing the usual course overload most part time and even tenure-track instructors face. It would make participants more competitive in the limited job market: many of the universities, and even small colleges place a priority on teaching experience.

BM/LH/SP

National Research Council
Associateship Program
2101 Constitution Avenue, NW, TJ-211,
Washington DC-20418

FINAL REPORT

1. Date:

November 27, 1995

2. Name:

Ashok Kumar Srivastava, DM, DTM, Ph.D.

3. Name and location of laboratory or center:

Department of Virus Diseases
Division of Communicable Diseases and Immunology
Walter Reed Army Institute of Research, Washington DC

4. Dates of tenure:

November 17, 1992 to November 16, 1995.

5. Title of research project:

Development of recombinant vaccine for dengue viruses.

6. Research advisor's name:

Col. Charles H. Hoke, Jr. and Dr. J. Robert Putnak.

7. Are you on leave from a professional post:

None

8. International post held during tenure:

None

9. Programmatic travel during tenure:

None

10. Scientific seminars, meetings, and/or consultation:

1. TROPMED, Atlanta, GA. Oct. 30 - Nov. 4, 1993.
2. First ASM retrovirology meeting, Washington DC., Dec. 11-16, 1993.
3. The vaccine new technology, Alexandria, VA, March 21-23. 1994.
4. TROPMED, Cincinnati, OH., Nov. 16-21, 1994.
5. Second retrovirology meeting, Wasgington DC, Jan. 29-Feb. 2, 1995,
6. Vaccine technology, Bethesda, MD, Feb. 13-15, 1995,
7. Retroviral integrase, NIN, Bethesda, MD, Feb. 19-20, 1995
8. ASM, Meeting, Washington DC., May 22-27, 1995,
9. ASV, University of Wisconsin, Madison, WI. July 9-13, 1995,
10. Serogate markers of HIV, McLean, VA. Oct. 6-18, 1995,
11. WHO meeting on dengue and JE vaccines. San Antonio, Texas, Nov. 16, 1995.

11. Seminar or lectures delivered at Universities and/or institutes:

1. Srivastava, A.K.: Japanese encephalitis vaccine. U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD, May 20, 1993.

2. Srivastava, A.K.: 1. Molecular pathogenesis of HIV-1 in brain. NCI-NIH, Bathesda, MD, August 9, 1993.

3. Srivastava, A.K.: Pathogenesis of HIV- and cytokines in brain and dorsal root ganglia of AIDS patients. Department of Neurology, John Hopkins, Medical Center, Baltimore, MD, January 24, 1994.

4. Srivastava, A.K.: Mice immunized with dengue-2 virus E and NS-1 fusion protein are protected against lethal dengue virus infection. American Society for Virology 13th Annual Meeting, University of Wisconsin, Madison, July 9-13, 1994.

5. Srivastava, A.K.: Expression of HIV-1 and IL-6 in CNS and DRGs of AIDS patients. Department of Microbiology, University of Haward, Washington DC, Oc. 21, 1994.

6. Srivastava, A.K.: Pathogenesis of HIV-1. All India Institute of Medical Sciences, New Delhi, India. February 28, 1995.

7. Srivastava, A.K.: HIV-1 infection in central nervous system of patients with AIDS. UNICEF, Patna Medical, Patna, India., March 13, 1995.

8. Srivastava, A.K.: Mice immunized with dengue-2 virus E and NS-1 fusion protein are protected against lethal dengue virus infection, Annual Conference of TROPMED, Cincinnati, Ohio, November 13 - 17, 1994.

9. Srivastava, A.K.: Dengue vaccine made in Escherichia coli.WHO Working Group on Research, Development and Introduction on Dengue and Japanese encephalitis vaccines and diagnostic tests, San Antonio, Texas, November 16, 1995.

12. Meetings attended by specific invitation:

None

13. Teaching, if any as an associate:

None

14. Work in progress:

1. Evaluation of dengue virus 1, 3 and 4 serotypes recombinant vaccine in monkeys.
2. Immunization of mice with dengue virus type-2 E and NS1 recombinant protein made in baculovirus.

15. Summary of research during tenure:

Srivastava A.K.: Dengue vaccine made in *Escherichia coli.*

A recombinant fusion protein encoding the C-terminus of structural envelope glycoprotein (E) and the N-terminus of non-structural protein (NS-1) of dengue-2 virus (DEN-2) was expressed in *Escherichia coli*, purified and characterized. This fusion protein was reactive with anti-DEN-2 polyclonal sera and monoclonal antibodies which recognize a linear epitope in E. The purified fusion protein was injected into mice subcutaneously. The immunized mice made anti-DEN-2 antibodies measured by the hemaglutination-inhibition (HAI) and neutralization (N) tests, and were protected against lethal challenge with DEN-2 virus administered by intracerebral inoculation. In a separate experiment; a group of Rhesus monkeys were immunized subcutaneously with three different concentration of fusion protein. The monkeys immunized with the higher concentration of protein (100 μg/dose) showed significant N and ELISA antibody titers 2 weeks after the second booster.

16. Publications and papers resulting from research an associate:

1. Srivastava, A.K., Putnak, J.R., Warren, R.L. & Hoke, C.H.: Mice immunized with dengue-2 virus E and NS-1 fusion protein are protected against lethal dengue virus infection. Vaccine, 13, 1251-1258, 1995.

2. Srivastava, A.K., Hoke, Eckels, K.H., Hoke, C.H. Jr., Sadoff, J.C. and Putnak, J.R.: Dengue type-2 virus E and NS1 expressed in Escherichia coli elicits virus-neutralizing antibodies in monkeys and protects from live virus challenge. Under Preparation, 1995.

3. Srivastava, A.K., Hoke, C.H. Jr. and Putnak, J.R.: Immunization of mice with dengue virus 1, 3 and 4 serotypes into mice. Under preparation, 1995.

17. Patent applied for as a result of research as associate:

1. Filed to the Office of Patent Trademarks, Washington DC.

Srivastava, A.K., Putnak, J.R., Warren, R.L. and Hoke, C.H. Jr.: Recombinant vaccine made in Escherichia coli. Office of Patent Trademarks, Washington DC, May 1995.

18. Future position and address or current forwarding address:

Head
Viral Vaccine Production
Department of Biologics Research
Division of Communicable disease and Immunology, Building 40. Room Number 2053
Walter Reed Army Institute of Research, Washington DC
TEL:202-782-7019, TEL:301-427-6609; Fax:202-782-0442

19. Appraisal of the associate programs:

1. The young scientist should be given more chance for such fellowship.

2. NRC Associate program lacks the critical significance such as:

   .Lack of communication between NRC and fellows.

   .NRC does not care much about their fellows related to their progress in science.

   .NRC Associates are not entitled to obtain an Invention Award Money. Although the data have been generated from the original research proposal of an associate and evaluated as a novel finding, and then submitted as an Invention Disclosure followed by filing the patent application.

   .NRC does not provide any kind of document/certificate stating the tenure as associate.

3. NRC is requested to consider these comments carefully.

FINAL REPORT

1/ DATE: 8/9/96

2/ NAME AND ID NUMBER: Janos Szebeni, 929212

3/ NAME AND LOCATION OF LABORATORY CENTER: Lab. Membrane Biochemistry, Walter Reed Army Institute of Research.

4/ DATES OF TENURE: 7/9/94-8/9/96

5/ TITLE OF RESEARCH PROJECT: The influence of hemoglobin-containing liposomes on the immune system

6/ RESEARCH ADVISER'S NAME: COL. Carl. R. Alving

7/ ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
no

8/ INTERNATIONAL POSTS HELD DURING TENURE:
N/A

9/ PROGRAMMATIC TRAVEL DURING TENURE:
N/A

10/ SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULTATIONS:

1) In vitro stability of hemoglobin-containing liposomes: membrane enhancement of phospholipase A_2 activity (Poster)
Janos Szebeni, Nabila Wassef, Helmut H. Spielberg, Alan S. Rudolph and Carl R. Alving
Blood Substitutes and Related Products, IBC Meeting, Philadelphia, Sept. 21-22, 1993

2) Membrane Enhancement of phospholipase A_2 activity in hemoglobin-containing liposomes (Poster) Janos Szebeni, Nabila Wassef, Helmut H. Spielberg, Gary Matyas, Richard O. Cliff, Alan S. Rudolph and Carl R. Alving
Liposomes in Drug Delivery: The Nineties and Beyond. CDDR, School of Pharmacy, London University, London, Dec. 13-17, 1993

3) Complement Consumption, thromboxane B2 secretion and hemolysis following injection of hemoglobin-containing liposomes in rats (lecture)
Janos Szebeni, Nabila Wassef, Helmut H. Spielberg, Gary Matyas, Richard O. Cliff, Alan S. Rudolph and Carl R. Alving
XI Congress of the International Society for Artificial Cells, Blood Substitutes and Immobilization Biotechnology, Boston, July 24-27, 1994

4) Complement activation by liposome-encapsulated hemoglobin (poster)
Janos Szebeni, Nabila Wassef, Helmut H. Spielberg, Alan S. Rudolph and Carl R. Alving
Blood Substitutes and Related Products, IBC Meeting, Washington, DC, Sept. 12-13, 1994

5) The interaction of liposome-encapsulated hemoglobin with blood components: complement activation
(invited lecture)
The Navy's Liposome Encapsulated-Hemoglobin Review Panel, Bethesda, Sept. 14, 1994

6) Complement activation by liposome-encapsulated hemoglobin (invited lecture)
Second annual Conference on "Current Issues in Blood Substitute Research -1995"
San Diego, March 30-April 1, 1995

7) Complement activation by the red cell substitute, liposome-encapsulated hemoglobin, in rats and in human serum in vitro (invited lecture)
Janos Szebeni, Nabila M. Wassef, Helmut Spielberg, Alan S. Rudolph and Carl R. Alving
1st World Meeting on Pahrmaceutics, Biopharmaceutics and Pharmaceutical Technology
Budapest, May 9-11, 1995

8) Complement activation in rats by liposomes and liposome-encapsulated hemoglobin: biological consequences and mechanism (poster)
Janos Szebeni, Nabila M. Wassef, Helmut Spielberg, Alan S. Rudolph and Carl R. Alving
The 9th International Congress of Immunology, San Francisco, 23-29 July, 1995

9) Complement activation in human serum by the red blood cell substitute, liposome-encapsulated hemoglobin. The roles of natural anti-phospholipid antibodies and of vesicle properties. (poster)

Janos Szebeni, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving
Gordon Research Conference on Drug Carriers in Biology and Medicine
Ventura, CA, Feb. 25-March 1, 1996

10) The interaction of liposome-encapsulated hemoglobin with human complement. (invited lecture)
Janos Szebeni, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving
The 6th International Symposium on Blood Substitutes, Montreal, 4-7, August, 1996

11/ SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES:

N/A

12/ MEETINGS ATTENDED BY SPECIFIC INVITATION: Navy Review of the LEH Project, Bethesda, August 94

13/ TEACHING, IF ANY, AS AN ASSOCIATE:

No

14/ WORK IN PROGRESS:

Completion of 2-3 unfinished manuscripts

15/ SUMMARY OF RESEARCH DURING TENURE:

We have demonstrated the presence, and analyzed the mechanism of an adverse immune effect of liposome-encapsulated hemoglobin (LEH), which is currently being developed as an oxygen carrying blood substitute. The effect in question is complement (C) activation, a nonspecific inflammatory reaction of the immune system arising upon the exposure of foreign materials to the blood. The reaction results in increased elimination of activating particles along with numerous cardiovascular and hematological abnormalities. We have studied LEH-induced C activation in rats in vivo, and in rat and human serum, in vitro. It has been established that activation of C in rats proceeds through the alternative pathway, whereas in human serum it can proceed through both the classical and the alternative pathways. In human serum the reaction is mediated, in part, by naturally occurring anti-phospholipid antibodies displaying specific reactivity with LEH. Importantly, we have shown that the reaction can be effectively inhibited with soluble C receptor type 1 (sCR1), a recombinant, truncated form of the natural C inhibitor, CR1. Considering that C activation plays a key role in

the adverse consequences of polytrauma and/or hemorrhagic shock, particularly in the development of adult respiratory distress syndrome, demonstration of potential C activation by LEH and an efficient way to prevent it represents a significant progress in this research area.

16/ PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE:

1) Complement activation in rats by liposomes and liposome-encapsulated hemoglobin: evidence for anti-lipid antibodies and alternative pathway activation.
Janos Szebeni, Nabila M. Wassef, Helmut Spielberg, Alan S. Rudolph and Carl R. Alving
Biochem. Biophys Res. Comm. 205:255-263, 1994

2) Complement activation by liposome-encapsulated hemoglobin in vitro: the role of endotoxin contamination.
Janos Szebeni, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving
Art Cells, Blood Subs. and Immob. Biotechnol. 23: 355-363, 1995

3) Complement activation in vitro by the red blood cell substitute, liposome-encapsulated hemoglobin: Mechanism of activation and inhibition by soluble complement receptor type 1.
Janos Szebeni, K.R. Hartman, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving
Transfusion, In press

4) Complement activation in human serum by liposome-encapsulated hemoglobin: the role of natural anti-phospholipid antibodies.
Janos Szebeni, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving Biochem. Biophym Acta, Submitted for publication.

5) Complement activation and thromboxane secretion by liposome-encapsulated hemoglobin in rats in vivo: Inhibition by soluble complement receptor type 1.
Janos Szebeni, Helmut Spielberg, Richard O. Cliff, Nabila M. Wassef, Alan S. Rudolph and Carl R. Alving Art Cells, Blood Subs. and Immob. Biotechnol., Submitted for publication.

17/ PATENTS APPLIED FOR AS A RESULT FROM RESEARCH AS AN ASSOCIATE:
N/A

18/ FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS:

According to plans I will be working at the National Institute of Hematology and Immunology in Budapest, at the following address:

Dr. Szebeni Janos
Bone Marrow Transplantation Unit
National Institute of Hematology and Immunology
Budapest
1502 Budapest Pf. 44., Hungary
phone: 36-1-209-2311, fax: 36-1-209-2311

19/ APPRAISAL OF THE ASSOCIATESHIP PROGRAMS:

I am sincerely grateful for the opportunity provided by the NRC award I had the fortune to hold, for allowing me to pursue productive research without distraction. The program is excellently organized, the contact persons are nice and helpful, and my award has been generous in benefits in professional, as well as in financial matters.

FINAL REPORT

1. **Date** May 14, 1996
2. **Name** Surang Triteeraprapab
3. **Laboratory** DSD, USAMRIID, Ft. Detrick, Frederick, MD 21702-5011
4. **Date of Tenure** March 6, 1995 - June 14, 1996
5. **Title of Reserach Project**
   Molecular basis of dengue virus-2 S16803 attenuation after serial passage in primary dog kidney cells
6. **Research advisor's name** Lieutenant Colonel Erik A. Henchal
7. **I am on leave from a professional post.**
   Faculty: Instructor and Physician
   Department of Parasitology
   Faculty of Medicine
   Chulalongkorn University
   Bangkok 10330, Thailand
   Telephone: (662)-252-5-944

8. **International posts held during tenure**
   Same as above (7.)
9. **Programmatic travel during tenure**
   N/A
10. **Scientific seminars, meetings, and/or consultations**
    10.1 The IVth International Congress on Positive Strand RNA Viruses held in Utrecht, the Netherlands during May 25-30, 1995.
    10.2 The 7th International Congress for Infectious Diseases to be held in Hong Kong during June 10-13, 1995.
11. **Seminars or lectures delivered at universities and/or institues**
    N/A
12. **Meetings attended by specific invitation**
    N/A
13. **Teaching, if any, as an associate**
    N/A
14. **Work in progress**

Vaccinia virus/T7 RNA polymerase transient-expression system and radio-immunoprecipitation assays were used to compare the levels of expressed C-PrM/M proteins among D2NT57C (wild type clone), D2NT57G, D2NT57A, and D2NT57T (attenuated clone) recombinants, that contained dengue virus-2 5'UTR/C/PrM/M gene fragment with C, G, A and T at nt57, respectively. At 24 hour-post infection, after 2-, 4-, 8- and 12-hour labeling, the expression levels of D2NT57G were 45%, 96%, 74% and 45% of that of D2NT57C, respectively, and the expression levels of D2NT57A were 44%, 43%, 66% and 64% of that of D2NT57C, respectively. Interestingly, the lowest levels of expressed protein were obtained from D2NT57T (attenuated clone), which were 29%, 39%, 29% and 25% of that from D2NT57C, respectively.

To further confirm whether the point mutation at nt57 in the 5'UTR is important for the protein expression. We constructed the four recombinants containing 96-bp 5'UTR (with C, G, A or T at nt57) fused to luciferase gene of the pGEM-luc plasmid. The recombinant plasmid was named C-Luc, G-Luc, A-luc or T-luc, respectively. The levels of luciferase expression were compared among four constructs using vaccinia/SP6 polymerase transient-expression system and luciferase assays. At 3, 5, 8, 12, 24 and 48 hours post-transfection, G-Luc and A-Luc expressed luciferase at the similar level as C-Luc. The expression of C-Luc was significantly higher than that of T-Luc at all time points. All the recombinants expressed luciferase at the highest level at 24 hours post-transfection.

The Northern and dot (RNA) blots were performed to evaluate the transcription messages of D2NT57C, D2NT57G, D2NT57A, and D2NT57T using vaccinia virus/T7 RNA polymerase transient-expression system. There was no significant difference of levels of RNA expression from four recombinants at 3, 5, 8, 12, 24 and 48 hours post-transfection.

These data are consistent with the hypothesis that point mutation at nt57 from C to U reduces the protein expression at the translational level.

15. **Summary of research during tenure (100 words)**

Attenuated dengue virus-2 S16803 (PDK50) contained a point mutation, nt57 (C to U), that may disrupt the 5'UTR stem-loop structure, which is conserved and important for transcription and translation in other positive RNA viruses. We used a vaccinia/T7 RNA polymerase transient-expression system, radio-immunoprecipitation, Northern and dot (RNA) blots to show that this mutation reduced the dengue protein expression. Data from luciferase reporter system confirmed that the mutation effected protein translation. These data provide the basic knowledge of molecular basis of dengue virus attenuation that may help to generate safe and effective vaccines for other flaviviruses.

16. **Pubications and papers resulting from research as an associate**

Molecular basis of dengue virus-2 S16803 attenuation after serial passage in primary dog kidney cells. (in preparation)

17. **Patents applied fro as a result of research as an associate**

N/A

18. **Future position and address or current forwarding address**

Faculty: Instructor and Physician

Before December 15, 1996, please send mail to:

Surang Triteeraprapab
1107A, Donnington Circle,
Towson, MD 21204

After December 15, 1996, please send mail to:

Dr. Surang Triteeraprapab
Department of Parasitology
Faculty of Medicine
Chulalongkorn University
Bangkok 10330, Thailand

19. **Appraisal of the associateship programs**

The associateship programs consist of exemplary programs that provide opportunities for talented researchers to perform their researches on interesting problems in the distinguished institutes. The program help me to gain more experience in doing research under the superb guidance of talented scientists. During the tenure, I also have opportunities to attend scientific meetings, where I can discuss and exchange knowledge with other renowned scientists in various fields. This will definitely enhance the future collaborations between laboratories.

I myself deeply appreciate my advisor, Dr. Erik Henchal, for his guidance, confidence, patience and support during this project. His insight and constructive criticism have made this project a rich and rewarding experience. I am thankful to Dr. Connie Schmaljohn and Dr. Kevin Anderson for the constructive criticism.

I would like to thank Dr. Carol Linden, Dr. Judith Nyquist, Suzanne Polo and Debbie Daugherty for their kindness and helping me with the administrative problems.

National Research Council
Associateship Program
2101 Constitution Ave., NW, TJ2094
Washington, DC 20418

FINAL REPORT

1) **Date:** 28 March 1996

2) **Name and ID Number:** Jefferson Archer Vaughan, (idnumber 938912)

3) **Laboratory:** USAMRIID
Diagnostic Systems Division
Fort Detrick
Frederick, MD 21702

4) **Dates of Tenure:** 3 January 1994 to 3 April 1996

5) **Title of Research Project:** Filaria-mediated enhancement of arboviral transmission

6) **Research Advisor:** Michael J. Turell, Ph.D.

7) **Are you on leave from a professional post?** NO

8) **International posts held during tenure:** N/A

9) **Programmatic travel during tenure:** N/A

10) **Scientific seminars, meetings and/or consultations:**

1. 13-17 November 1994
43rd Annual Meeting of American Society of Tropical Medicine & Hygiene
Cincinnati, OH

2. 15-23 March 1995
61st Annual Meeting of American Mosquito Control Association
Portland, OR

3. 17-21 November 1995
44th Annual Meeting of American Society of Tropical Medicine & Hygiene
San Antonio, TX

4. 24-28 March 1996
62nd Annual Meeting of American Mosquito Control Association
Norfolk, VA

11) Seminars or lectures delivered at universities and/or institutes:

1. 21 March 1996
   Heska, Corp.
   Fort Collins, CO

2. 11 December 1995
   USAMRIID
   Fort Detrick, Frederick, MD

3. 3 February 1995
   Johns Hopkins University
   Baltimore, MD

4. 2 June 1994
   Biting Fly Workshop
   Easton, MD

5. 12 April 1994
   Tropical Medicine Dinner Club
   Baltimore, MD

12) Meetings attended by specific invitation: N/A

13) Teaching as an Associate:

Spring 1994 & 1995.
Guest lectures in Medical Entomology Course
Johns Hopkins University
Baltimore, MD

14) Work in progress: Planned computer simulation studies

15) Summary of research during tenure:

Two groups of mosquito-borne parasites enhanced mosquito transmission of arboviruses. Microfilarial parasites enhanced viral transmission from vertebrate to vector (= mosquito acquisition) by disrupting mosquito midgut barriers to viral dissemination. Malaria sporozoites enhanced viral transmission from vector to vertebrate (= mosquito transmission) by disrupting salivary gland barriers to oral secretion of virus. Because of its greater epidemiological potential, parameters of microfilarial enhancement were further defined. Parameters included; species differences in the capacity of microfilariae to penetrate the mosquito midgut, the amount of virus passing into the mosquito hemocoel during microfilarial penetration, and the innate susceptibility of mosquitoes to hemocoelomically-introduced virus.

16) Publications and papers resulting from research as an Associate:

1. Vaughan JA and MJ Turell. 1996. Dual host infections: enhanced infectivity of eastern equine encephalitis virus to Aedes mosquitoes mediated by Brugia microfilariae. American Journal of Tropical Medicine and Hygiene 54: 105-109.

2. Vaughan JA and MJ Turell. (1996) Plasmodium berghei sporozoites facilitate transmission of Rift Valley fever virus by Anopheles stephensi mosquitoes. American Journal of Tropical Medicine and Hygiene (in press).

3. Vaughan JA and MJ Turell. (1996) Comparative susceptibilities of Aedes and Culex spp. (Diptera: Culicidae) to inoculated virus: eastern equine encephalitis virus, Venezuelan equine encephalitis (Alphaviridae) and Rift Valley fever virus (Bunyaviridae). Journal of Medical Entomology (in preparation).

4. Vaughan JA and MJ Turell. (1996) Penetration efficiencies of microfilariae through the midgut of selected mosquito species. Journal of Parasitology (in preparation).

5. Vaughan JA and MJ Turell. (1996) Brugia malayi microfilarial enhancement of Venezuelan equine encephalitis virus to Aedes taeniorhynchus mosquitoes (Diptera: Culicidae). Journal of Medical Entomology (in preparation).

6. Vaughan JA, DA Focks, and MJ Turell (1996) Microfilarial enhancement of arboviral transmission by mosquitoes: concepts and theoretical considerations. Parasitology Today (in preparation).

17) Patents applied for as a result of research as an Associate: N/A

18) Current fowarding address:

Jefferson A. Vaughan
605 West 39th Street
Baltimore, MD 21211

19) Appraisal of the Associateship Programs:

The NRC Associateship Programs was very useful to me for the following reasons: 1) provided me the opportunity to conduct research in one of the worlds' foremost arbovirology facility; 2) allowed me to expand my scientific network to include workers in military preventive medicine; 3) provided me the opportunity to gather sufficient data to apply for long-term (5 yr) NIH funding. The Program is good and I have been recommending it to both junior and mid-level scientists that are seeking new research experiences.

cc: Dr. Michael J. Turell, Research Advisor
Dr. Carol D. Linden, Laboratory Program Representative

FINAL REPORT ASSOCIATESHIP PROGRAMS

(1) DATE 22 AUGUST 1996

(2) NAME YONGQIANG WANG

(3) NAME AND LOCATION OF LABORATORY OR CENTER
DEPARTMENT OF MOLECULAR PATHOLOGY
WALTER REED ARMY INSTITUTE OF RESEARCH
WASHINGTON, DC 20307-5100

(4) DATES OF TENURE
14 JUNE 1993 TO 13 SEPTEMBER 1996

(5) TITLE OF RESEARCH PROJECT
STUDY OF CROSS REACTION BETWEEN NEURAL CELL ADHESION MOLECULE (N-CAM) ON HUMAN NK CELLS AND CAPSULAR POLYSACCHARIDE OF GROUP B MENINGOCOCCI HETEROPOLYAINS DO NOT INDUCE P-GLYCOPROTEIN ASSOCIATED WITH MULTIDRUG RESISTANCE IN HUMAN BREAST CANCER CELLS

(6) RESEARCH ADVISER'S NAME
DR. WENDELL D. ZOLLINGER
DR. MARTI JETT

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
ASSISTANT RESEARCH PROFESSOR
CANCER INSTITUTE (HOSPITAL)
CHINESE ACADEMY OF MEDICAL SCIENCES
BEIJING 100021
P.R.CHINA

(8) INTERNATIONAL POSTS HELD DURING TENURE
N/A

(9) PROGRAMMATIC TRAVEL DURING TENURE
N/A

(10) SCIENTIFIC SEMINARS, MEETINGS, AND/OR CONSULATIONS
NEISSERIA 94, SEPTEMBER 1994, WINCHESTER, ENGLAND
THIRD ANNUAL VACCINES: NEW TECHNOLOGIES & APPLICATIONS, MARCH 20-22, 1995, ALEXANDRIA, VIRGINIA.

(11) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES
N/A

(12) MEETINGS ATTENDED BY SPECIFIC INVITATION
N/A

(13) TEACHING, IF ANY, AS AN ASSOCIATE
N/A

(14) WORK IN PROGRESS

TWO NEW ENZYME-LINKED IMMUNOSORBENT ASSAYS (ELISA) THAT USE MONOCLONAL ANTIBODIES FOR DETECTION OF LIPOPOLYSACCHARIDE AND OUTER MEMBRANE PROTEIN OF NEISSERIA MENINGITIDIS HAVE BEEN ESTABLISHED.

CELLS EXPRESSING THE EMBRYONIC FORMS OF N-CAM, SUCH AS NK CELLS AND ATT20 CELLS REACTED WITH MONOCLONAL ANTIBODIES TO GROUP B CAPSULAR POLYSACCHARIDE ON MENINGOCOCCI WAS OBSERVED BY INDIRECT IMMUNOFLURORESCENCE, DOT BLOT, WESTERN BLOT AND FLOW CYTOMETRY.

A 170 kDa GLYCOPROTEIN WAS DETECTED FROM THE MCF/ADR (MULTIDRUG RESISTANCE) CELLS BUT NOT THE MCF/WT (DRUG SENSITIVE) CELLS AND HETEROPOLYANIONS (HPA) TREATED CELLS. HPA WHICH DO NOT INDUCE P-GLYCOPROTEIN ASSOCIATED MULTIDRUG RESISTANCE MAY BE A GROUP OF HIGH POTENTIAL COMPOUNDS IN HUMAN BREAST CANCER TREATMENT.

(15) SUMMARY OF RESEARCH DURING TENURE

A CROSS-REACTION BETWEEN NEURAL CELL ADHESION MOLECULE (N-CAM) ON HUMAN NK CELLS AND CAPSULAR POLYSACCHARIDE OF GROUP B MENINGOCOCCI WAS OBSERVED. CELLS EXPRESSING THE EMBRYONIC FORMS OF N-CAM, SUCH AS NK CELLS AND ATT20 CELLS REACTED WITH MONOCLONAL ANTIBODIES TO GROUP B CAPSULAR POLYSACCHARIDE ON MENINGOCOCCI WAS OBSERVED BY INDIRECT IMMUNOFLURORESCENCE, FLOW CYTOMETRY AND WESTERN BLOT ANALYSIS.

MULTIDRUG-RESISTANCE (MDR) IS A MAJOR OBSTACLE TO BREAST CANCER TREATMENT. HETEROPOLYANIONS (HPA) ARE FREE-RADICAL SCAVENGERS AND SHOWED EXCELLENT ANTIPROLIFERATIVE EFFECTS AND DO NOT INDUCE P-GLYCOPROTEIN ASSOCIATED MULTIDRUG RESISTANCE DETECTED BY MDR1 GENE PRODUCTS ON WESTERN BLOT AND PCR ANALYSIS.

(16) PUBLICATIONS AND PAPERS RESULTING FROM RESEARCH AS AN ASSOCIATE

IN PREPARATION

(17) PATENTS APPLIED FOR AS A RESULT OF RESEARCH AS AN ASSOCIATE

N/A

(18) FUTURE POSITION AND ADDRESS OR CURRENT FORWARDING ADDRESS

3007 HUNTINGDON AVE
BALTIMORE, MD 21211

(19) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS

VERY GOOD PROGRAM.