Award Number: W81XWH-10-1-0271

TITLE: Nebraska Prostate Cancer Research Program

PRINCIPAL INVESTIGATOR: Ming-Fong Lin, Ph.D.

CONTRACTING ORGANIZATION: University of Nebraska Medical Center
Omaha, NE 69198

REPORT DATE: May 2012

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14. ABSTRACT

Prostate cancer (PCa) is one of the major cancers threatening US males' life. For improving PCa treatments, better understanding the basic mechanism of this cancer is needed, which would depend on the training of PCa researchers. This proposal is thus to train HBCU undergraduate with science major in PCa research, a joint effort between the University of Nebraska Medical Center (UNMC) and Clark Atlanta University (CAU). Dr. Ming-Fong Lin of UNMC and Dr. Shafiq Khan of CAU have ongoing research collaborations. They will identify interested undergraduates at CAU and institute a summer research program at UNMC where the students will learn basic science for translational application in a lab. Students will spend the majority of their time working at the bench on a research project. They will also participate in a seminar series that will introduce them to different areas of scientific investigation and advanced technological tools used in scientific discovery. After the summer, students will continue their scientific development at CAU and prepare for a graduate career in biomedical sciences or for medical school.

15. SUBJECT TERMS
Prostate Cancer, Training Grant, HBCU students, Biomedical Sciences, Graduate school, Medical school

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Table of Contents

Annual Summary

INTRODUCTION:

The subject of this training grant is to train potential prostate cancer (PCa) researchers via a collaborative effort between University of Nebraska Medical Center (UNMC) at Omaha, NE, and Clark Atlanta University (CAU) at Atlanta, GA. The conception of this Program is based on interactions and collaborations between Dr. Ming-Fong Lin, the PI and a faculty mentor at UNMC, and Dr. Shafiq Khan, a faculty mentor at CAU, since March 2004 (1). The purpose of this proposal is to train undergraduate HBCU students to gain hand-on experience in performing PCa, a high incidence cancer in Africa American males (2), research in UNMC, a research-intensive environment. The scope of training grant is to train CAU undergraduate students to gain hand-on experience in PCa research at UNMC Nebraska Prostate Cancer Research Program (NPCRP). These students will receive training not only in the lab but also in the class room in the format of seminars and visiting biotechnology companies. The goal is to encourage and to prepare HBCU students for academic career, i.e., they will either enter graduate school or medical school with training in, and understand of, PCa research or enter medical school. This will increase the number of PCa researcher at both basic science and clinical science levels.

BODY:

During the past one year (5/2011 – 4/2012) with the second year of funding support from CDMRP, we have trained 4 CAU undergraduate students, and these students have gained hand-on experience in PCa research and made significant accomplishments. There were no technical or unexpected difficulties encountered and/or any deviations from the original Statement of Work. Per Instruction, our training and research accomplishments following each task outlined in the approved Statement of Work are listed as follows:

(**Task 1 - 6 reported in May 2011 Annual Report**)

Task 1: Announcement of the Year 1 Research Program (months 1-3)

Done. Per approved SOW, upon receiving the award notice, Drs. Khan and Odero-Marah at CAU announced the opportunity of conducting PCa research at UNMC, including verbal announcements in their classes during his lectures and also campus-wide posters by Dr. Khan's office. Ms. Priscilla Bakari, the Office Manager, helped prepared all the necessary documents and answered to all questions related to this opportunity. The announcements included the criteria of eligibility, the requirement of documents, and the due date of application.

Task 2: Selection of Trainees (month 4-6)

Done. Drs. Khan and Odero-Marah and Ms. Bakari at CAU went through all application files to ensure all application documents are complete and in place. Due to a short time period between the awarding letter and the student recruitment process, many communications were made possible through phone calls and e-mails. Subsequently, Drs. Lin and Chaney visited CAU, met with Drs. Khan and Odero-Marah, discussed application files and interviewed some eligible student candidates on March 17, 2010. The successful applicants were notified by e-mails and posted the list on board in CAU Prostate Cancer Research Center. The students were given a due date for replying of their acceptance, and all students accepted the offer by April 13, 2010.

In lab assignments, to avoid any potential of conflict of interest, upon request by Dr. Lin, Dr. Chaney coordinated with Dr. Odero-Marah considering students' interests with their priorities in lab selection and made the final matches as follows: Ms. Kiedra Bryant – Dr.

MacDonald, Ms. NeChelle Jack – Dr. Lin, Ms. Lynnette Leffall – Dr. Mehta and Ms. Brittany Jones – Dr. Batra. In the mean time, Dr. Chaney also worked out the Housing for students and coordinated with Ms. Jennifer Pace, the BMB Office Personnel, preparing all necessary documents for students.

Task 3: Summer Research (month 7-9)

Done. All students arrived on May 31, 2010, and Dr. Chaney picked them up at airport, went grocery shopping and settled down in the dorm. Drs. Chaney and Lin had dinner together with all students and provided them with the up-dated information and guidelines for the Program. Dr. Chaney attended students' Monday seminars, which were in conjunction with Idea Networks of Biomedical Research Excellence (**INBRE**) program, and both Drs. Chaney and Lin met with students weekly.

Upon arrival, the students were encouraged to set up a web for the Program. With the support of Jennifer and the UNMC Public Affair Office, the web for NPCRP was finalized and posted in BMB Department web by the end of June 2010. The link is as follows: (http://www.unmc.edu/biochemistry/index.cfm?L1_ID=48&CONREF=84). (**Appendix #1**).

Dr. Odero-Marah was invited to visit UNMC on July 6. She gave a scientific presentation on her research project entitled "Snail Transcription Factor Contributes to Prostate Cancer Tumor Progression via Reactive Oxygen Species", which was excellent and well received by audience. She then met with CAU students and had a lunch together to learn their progresses and to discuss any potential problem during their stays. Subsequently, Dr. Odero-Marah met with Drs. Lin and Chaney for an executive meeting discussing students' issues. While there was one suggestion regarding the payment method for housing; overall, all four students were very happy, enjoyed their stays and had obtained the hand-on experience in their research projects.

The efforts of NPCRP received attention. Dr. Chaney coordinated the efforts and the UNMC Public Affair Office interviewed all four CAU students and reported our Program with Ms. Lynnette Leffall in Dr. Mehta's lab as an example for the story (**Appendix #2**). All students prepared their posters and gave presentations in the UNMC Summer Undergraduate Research Program (**SURP**) poster section on Thursday of Aug. 5, 2010. The abstracts of posters are attached (**Appendix #3**).

Task 4: Evaluation of the Program (month 10-12)

Done. Prior to their departure, all four students met with Drs. Chaney and Lin and other faculty mentors, including Drs. Batra, MacDonald and Mehta, for a final lunch-meeting on Friday of August 6, 2010. We discussed any problem that occurred during their stays and any suggestions that may improve the training by the Program. In the meeting, all students received a certificate for their hard working with the completion of training, cosigned by Drs. Chaney and Lin. The anonymous evaluations that were made by students one week ahead are attached (**Appendix #4**).

Drs. Khan and Odero-Marah and Ms. Bakari met with students at CAU on September 2, 2010, the beginning of Fall semester. The students are very excited by the opportunity of training at UNMC. A Minute taken by Ms. Bakari is attached (**Appendix #5**).

Dr. Chaney met with Dr. Jim Turpen, a member of Executive Committee for NPCRP and the PI of the INBRE program, regarding the results of NPCRP training program during their

INBRE Retreat. With Dr. Turpen's approval, the support from the INBRE program to NPCRP is highly appreciated. We expect continued interactions for the up-coming years.

Drs. Chaney and Lin met and discussed the questions raised by the students and the potential improvement for new students in the summer of 2011.

Task 5: Announcement of the Year 2 Research Program (months 13-15)

Done. Per approved SOW, Drs. Khan and Odero-Marah at CAU announced the opportunity of conducting PCa research at UNMC, including verbal announcements in their classes and also campus-wide posters by Dr. Khan's office in Feb 2011. Ms. Bakari, the office manager, prepared all the necessary paper works and answered to all questions related to this opportunity. The announcements included the criteria of eligibility, the requirement of documents, and the due date of application. For this cycle, the final due date was set as by March 31, 2011.

Task 6: Selection of Trainees (month 16-18)

Done. Drs. Chaney visited CAU on March 29, 2011. He went alone, met with several student candidates and discussed with Dr. Odero-Marah and Ms. Bakari for student recruitment processes. Drs. Odero-Marah sent all information by March 31, 2011, the due date of application to Dr. Chaney. This year, we had 8 students completed their applications. Drs. Odero-Marah and Chaney discussed all the applicants' qualification and made offers to 4 students. All four students accepted the offer. Drs. Odero-Marah and Chaney have worked together and matched these students with mentors in NPCRP at UNMC. Dr. Chaney has also coordinated the Housing issue, and Ms. Pace had mailed the first batch of documents including Housing to students for their attention.

With the support of Dr. Turpen, the NPCRP will again interact with the INBRE program for student training in seminars and site visiting to various research facilities and biotech companies. Currently, we are waiting for the arrival of the new students.

(**Task 7 - 10 for 2012 Annual Report**)

Task 7: Summer Research (month 19-21)

Done. Based on their research interests, four sophomore undergraduate students, including Ms. Shawna Battle (Mentor: Dr. Rakesh Singh), Celeste Scott (Mentor: Dr. Kaustubh Datta), LaTayia Aaron (Mentor: Dr. John Davis) and Hilary Kirwan (Mentor: Dr. Ming-Fong Lin), were matched to the labs in UNMC NPCRP. All four students arrived on May 30, 2011, and Dr. Chaney picked them up at airport, settled down in the dorm and went for grocery shopping. Dr. Chaney also provided them with the up-dated information and guidelines for the Program, including information for the Idea Networks of Biomedical Research Excellence (**INBRE**) and the UNMC Summer Undergraduate Research Program (**SURP**) (**Appendix #6**). Dr. Chaney attended students' Monday seminars, which were in conjunction with the **INBRE** program, and both Drs. Chaney and Lin met with students weekly.

With the support of Ms. Jennifer Pace at BMB and Ms. Lisa Spellman at the UNMC Public Relations Office, the information for 4 new students in NPCRP on BMB Department web was up-dated and posted by the end of June 2011. The link is as follows: (http://www.unmc.edu/biochemistry/index.cfm?L1_ID=48&CONREF=84). (**Appendix #7**).

Dr. Khan visited UNMC on July 6, 2011. He met with CAU students and had a lunch-meeting together to learn their progresses. Drs. Lin and Chaney and also mentors including Drs.

Singh, Davis and Datta all attended the lunch-meeting. Dr. Khan had a private meeting with students discussing any potential problem during their stays. Subsequently, Dr. Khan met with Drs. Lin and Chaney for an executive meeting discussing students' issues. Overall, all four students were very happy, enjoyed their stays and had obtained the hand-on experience in their research projects. They were very pleased with the research environment. Dr. Khan then gave a scientific presentation on his research project and a brief introduction of research environment at the Clark Atlanta University to the UNMC community. His presentation was entitled "Prostate Cancer Research and Education at Clark Atlanta University" (**Appendix #8**), which was excellent and well received by audience including faculty members, post-doctoral fellows and graduate students. Dr. Khan also had a meeting with mentors and other faculty members with research interests in prostate cancer to discuss the potential of collaborations.

The efforts of NPCRP received attention. Dr. Chaney coordinated the efforts and the UNMC Public Relations Office interviewed Drs. Lin and Chaney and reported our NPCRP Program in INBRE IN ROADS, a UNMC INBRE communication (**Appendix #9**). In the last week of training, all students prepared their posters and gave presentations in the UNMC SURP poster section on Aug. 5, 2011. The abstracts of 4 posters are attached (**Appendix #10**).

Prior to their departure, all four students met with Drs. Chaney and Lin for a final lunch-meeting. We discussed any problem that occurred during their stays and any suggestions that may improve the training by the Program. The students in general were very happy for their training and no comment was raised. They were strongly encouraged to continue their research in CAU faculty members' labs. Dr. Chaney provided all necessary transportation and supports back to the airport.

Task 8: Evaluation of the Program (month 22-24)

Done. Drs. Khan and Odero-Marah and Ms. Bakari met with students at CAU after the beginning of Fall semester. The students were happy with the opportunity of training at UNMC. Again, no issue was raised.

Dr. Chaney met with Dr. Jim Turpen, the PI of the INBRE program and a member of Executive Committee for NPCRP, regarding the results of NPCRP training program during their INBRE Retreat. With Dr. Turpen's approval and supports, we appreciate very much for the support from the INBRE program to NPCRP because the students can expose more to different technologies applicable toward research and career development. We expect the continuing interaction in the up-coming years. Drs. Chaney and Lin met and discussed the potential improvement for new students in the summer of 2012.

Task 9: Announcement of the Year 3 Research Program (months 25-27)

Done. Per approved SOW, on Jan 11, 2012, Drs. Khan and Odero-Marah at CAU and Drs. Lin and Chaney at UNMC started to up-date the flier announcing the opportunity of conducting PCa research at UNMC. The wording in the flier was finalized by the end of January, and Drs. Khan and Odero-Marah immediately announced the opportunity by distributing the flier and verbal announcements in their classes and also campus-wide posters by Dr. Khan's office in Feb 2012. The announcements included the criteria of eligibility, the requirement of documents, and the due date of application. Ms. Bakari, the office manager, prepared all the necessary paper works and answered to all questions related to this opportunity. For this cycle, the final due date was set as by March 31, 2012.

Task 10: **Selection of Trainees (month 28-30)**

Done. Drs. Chaney and Lin visited CAU on March 18, 2012, discussed with Drs. Khan and Odero-Marah for student recruitment processes, and also met with four student candidates on March 19, 2012. Drs. Odero-Marah sent all applicants' information to Dr. Chaney in the early April of 2012, after the due date of application. This year, we had 10 students who filed their applications. With the inputs of Dr. Odero-Marah, Drs. Chaney and Lin discussed all the applicants' qualification. Four successful applicants were identified and notified by e-mails from Dr. Chaney and also contacted by a secretary at CAU Cancer Research Center. The students were given a due date for replying of their acceptance. Nevertheless, one student declined the offer. Dr. Chaney has matched these three students to the labs in NPCRP at UNMC: Ms. Alexandra M. White (Mentor: Dr. Mehta), Alexus S. Devine (Mentor: Dr. Lin) and Sierra R. Coleman (Mentor: Dr. Datta). Dr. Chaney has also coordinated the Housing issue, and Ms. Jennifer Pace at Department of Biochemistry and Molecular Biology, UNMC, had mailed the first batch of documents including Housing to students for their attention.

With the support of Dr. Turpen, the NPCRP will again interact with the INBRE program for student training in seminars and site visiting to various research facilities and biotech companies. We also register these students for the UNMC SURP program. Currently, we are waiting for the arrival of the new students.

It should be noted that our 2011 trainees continue their research in CAU cancer center faculty members' labs. Importantly, two of trainees gave poster presentation in the 8th Annual National Symposium on Prostate Cancer organized by CCRTD, CAU, March 18-20, 2012. The three abstracts were attached (**Appendix #11**).

Task 11: ***Summer Research (month 31-33) - Task 12: Evaluation of the Program (month 34-36)***

To be accomplished in the up-coming summer.

KEY RESEARCH ACCOMPLISHMENTS:

(**Reported in May 2011 Annual Report**)

- We successfully recruited 4 excellent HBCU undergraduate students from CAU in the first year of award for summer 2010.
- Based on their research interests, these four students were assigned to different labs with matched expertise in prostate cancer research for their respective prostate cancer research training.
- All four students attended the Monday seminar jointly with the INBRE program through the entire period.
- The students also visited different research institutions and BioPharm companies locally to expand their knowledge and scopes in future career developments.
- These CAU students also attended the seminars set by the UNMC SURP every Tuesday at noon through the entire training period.
- By attending the INBRE and the UNMC SURP activities, the students expand their view and social activities to different student communities.
- The students actively worked together with BMB Personnel and with the support of UNMC Public Affair Office, a web for our NPCRP training program was prepared and

posted on the BMB at UNMC web in July 2010. The link is as follows: (http://www.unmc.edu/biochemistry/index.cfm?L1_ID=48&CONREF=84).

- UNMC Public Affairs reported the NPCRP program with one student as the story in August 2010.
- As a part of training and requirement, all four students prepared their results and gave poster presentations jointly in the UNMC SURP poster section, the last Thursday of their training, August 5, 2010.
- All four students submitted their abstracts to the DOD PCa IMPaCT meeting at Orlando, FL, March 9-12, 2011.
- Dr. Lin attended the Undergraduate Student Luncheon and Networking Session in the IMPaCT meeting on March 11, 2011, interacting with other program leaders and students to learn more about the potential significance of this training program.

(**For 2012 Annual Report**)

- For 2011 summer training program, we successfully recruited 4 excellent HBCU undergraduate students from CAU.
- These four students were matched to different labs based on their research interests.
- All four students attended the Monday seminar offered by the INBRE program through the entire period.
- These students also visited regional universities and local BioPharm companies to expand their knowledge and scopes in future career developments.
- The students actively worked together with Ms. Jennifer Pace, the administrator for NPCRP and with the support of UNMC Public Relations Office, the web for our NPCRP training program was updated and posted on the BMB web within UNMC web by the end of June 2011. The link is as follows: (http://www.unmc.edu/biochemistry/index.cfm?L1_ID=48&CONREF=84).
- The UNMC INBRE IN ROADS, an INBRE communication reported the NPCRP efforts and the interaction between two programs.
- All four students prepared their results and gave poster presentations jointly in the UNMC SURP poster section, the last Thursday of their training, August 5, 2011.
- The success of the training program is strongly supported by the fact that the CAU trainees of 2011 UNMC NPCRP continue their junior year research in the CAU Cancer Center faculty members' labs.
- Ms. Celeste Scott as the first author gave a poster presentation with up-dated data in the 8th Annual National Symposium on Prostate Cancer organized by CCRTD, CAU, March 18-20, 2012.
- Ms. LaTayia Aaron continues her research in prostate cancer research in Dr. Joann Powell's lab at CAU. She is the first author of one poster and 2nd co-author of another poster in the 8th Annual National Symposium on Prostate Cancer by CCRTD, CAU, March 18-20, 2012.
- For 2012 summer training program, we successfully recruited 3 excellent HBCU undergraduate students from CAU.

REPORTABLE OUTCOMES: (Names for NPCRP Trainees are in bold.)

(**Reported in May 2011 Annual Report**)

- **Brittany T. Jones**, Poomy Pandey, Srustidhar Das, and Surinder K. Batra. (2010). Therapeutic Potential of Curcumin: Inhibition of MIC-1/GDF-15 Expression in Prostate Cancer Cells Exposed to Heavy Metal Carcinogen. UNMC Summer Undergraduate Research Program, August 2010.
- **Keidra A. Bryant**, Joseph R. Wheeler, Michelle A. Montgomery, and Richard G. MacDonald. (2010). Effect of Metal Ion Chelators on Mannose 6-Phosphate/Insulin-like Growth Factor II Receptor in DU145 Prostate Cancer Cells. UNMC Summer Undergraduate Research Program, August 2010.
- **Lynnette Leffall**, Kristen E. Johnson, Parul Katoch, Linda Kelsey, and Parmender Mehta. (2010). Aspects of Gap Junction Assembly and Disassembly in Prostate Cancer Progression. UNMC Summer Undergraduate Research Program, August 2010.
- **NeChelle L. Jack**, Yu Wei Chou, Laurenee London, Xiu R. Bu, and Ming-Fong Lin. (2010). The Effect of 4'-Bis-Thiosemicarbazide, a New Ribonucleotide Reductase Inhibitor, on Prostate Cancer Cell Proliferation. UNMC Summer Undergraduate Research Program, August 2010.

(**For 2012 Annual Report**)

- **Hilary Kirwan**, Yu Wei Chou, Sakthivel Muniyan, Ming-Fong Lin. (2011). Growth suppression of new ribonucleotide reductase inhibitors in prostate cancer cells. UNMC Summer Undergraduate Research Program, August 5, 2011.
- **LaTayia Aaron**, Chao Jiang, and John S. Davis. (2011). Effects of TGFβ1 and PGE2 on Cellular Signaling in Bovine Corpora Luteal Fibroblasts. UNMC Summer Undergraduate Research Program, August 5, 2011.
- **Celeste Scott**, Marissa Stanton, Samikshan Dutta, Heyu Zhang, Kaustubh Datta. (2011). VEGF-C Promotes Autophagy and Survival in Prostate Cancer Cells Following Chemotherapeutic Stress. UNMC Summer Undergraduate Research Program, August 5, 2011.
- **Shawna Battle**, Michelle L. Varney, Mitsuru Futakuchi, Rakesh K. Singh. (2011). Upregulation of matrix metalloproteinase (MMP) 13 expression at the tumor-bone in prostate cancer. UNMC Summer Undergraduate Research Program, August 5, 2011.
- **LaTayia Aaron** and Joann Powell. (2012). Dioxin exposure enhances nuclear localization of androgen receptor. The 8th Annual National Symposium on Prostate Cancer by CCRTD, CAU, March 18-20, 2012.
- Cindy Tran, **LaTayia Aaron** and Joann Powell (2012). The aryl hydrocarbon receptor sustains androgen receptor signalling in androgen independent prostate cancer cells. The 8th Annual National Symposium on Prostate Cancer by CCRTD, CAU, March 18-20, 2012.
- **Celeste Scott**, Marissa Stanton, Samikshan Dutta, Heyu Zhang, Kaustubh Datta. (2012). VEGF-C Promotes Autophagy and Survival in Prostate Cancer Cells Following Chemotherapeutic Stress. The 8th Annual National Symposium on Prostate Cancer by CCRTD, CAU, March 18-20, 2012.

CONCLUSION:

The purpose of this award is to train HBCU undergraduate students from CAU to gain hand-on experience in performing PCa research in a research-intensive focus group, the UNMC

Nebraska Prostate Cancer Research Program (NPCRP). We are very pleased with the outcomes for the continuing success of the second year training at UNMC. These students have received training not only in the lab but also in the class room in the format of seminars and visiting biotechnology companies. Our goals of training are to encourage and to prepare HBCU undergraduate students for academic career in graduate school or medical school with training in, and understand of, prostate cancer research. We propose that by this way, we can increase the number of PCa researcher from the minority group at both the basic science and the clinical science levels. With the two years of award support from the DOD PCa Research Program, as evidenced by the scientific outcomes of student posters and student comments, we are very excited by the success of our training program. We are expecting that more exciting results will be done in the up-coming years of the support.

REFERENCES:

1. Dillard, P.R., **Lin, M.F.**, and **Khan, S.A.** (2008). Androgen-independent prostate cancer cells acquire the complete steroidogenic potential of synthesizing testosterone from cholesterol. Mol. Cellu. Endo. 295:115-120.
2. Siegel, R., Naishadham, D., and Jemal, A. (2012). Cancer Statistics, 2012. CA Cancer J Clin 62: 10-29.

APPENDICES:

(**Reported in May 2011 Annual Report**)

1. Appendix #1: The web information for 2010 NPCRP posted on the BMB at UNMC web is attached.
2. Appendix #2: UNMC Public Affairs reported 2010 NPCRP student.
3. Appendix #3: Four abstracts prepared by 2010 four CAU students are attached.
4. Appendix #4: Evaluation by 2010 CAU students upon their completion of training at UNMC prior to their departure.
5. Appendix #5: A Minute taken by Ms. Bakari at CAU for students' evaluation and comments during the meeting after their return to CAU in September 2010.

(**For 2012 Annual Report**)

6. Appendix #6: The schedules for UNMC INBRE and UNMC SURP programs.
7. Appendix #7: The up-dated web information for 2011 NPCRP trainees posted on the BMB at UNMC web.
8. Appendix #8: Announcement by BMB for Dr. Shafiq Khan's presentation at UNMC.
9. Appendix #9: UNMC INBRE IN ROADS reported CAU students in NPCRP training.
10. Appendix #10: Four abstracts for the posters prepared by 2011 four CAU students in the UNMC SURP poster section.
11. Appendix #11: Three abstracts for UNMC-CAU trainees' posters in the 8th Annual National Symposium on Prostate Cancer by CCRTD, CAU, March 18-20, 2012.

2011 INBRE Weekly Seminar Schedule
(all on Mondays)

June	6	UNMC 1005 DRC	9:00	James Eudy Robert Boissy	DNA Sequencing Core and Genomic Analysis
			10:30	Vimla Band	Breast Cancer
June	13	UNL	9:00	Arrival at Morrison Virology Building	
			9:15	Jack Morris – Welcome and outline of today's program	
			9:30	Deb Brown – Biological Sciences	
			10:30	TBA	
			11:30	Tour of Nebraska Center for Virology	
June	20	CU	9:00		
June	27	Lincoln Biotech	9:00	Doc Chavez, Li-Cor	
July	4	No Seminar			
July	11	Omaha Biotech 1005 DRC	9:00	M. Dixon, UNEMED	
			10:30	T. Wasmoen, Schering-Plough Invertis	
July	18	UNMC 1005 DRC	9:00	Charles Kuszynski	Flow Cytometric Analysis Of Cells
			10:30	Kenneth Bayles	*Staphlococcus aureus* Research at UNMC
July	25	UNL	9:00	Arrive at Beadle Center	
			9:15	Jack Morris – Welcome	
			9:30	Rick Bevins – Dept of Psychology	
			10:30	Karrie Weber – Biological Sciences	
			11:00	Joe Zhou, Rik Barrera—Tours of Microscopy facility and Beadle Center	
Aug	1	CU	9:00		

2011 INBRE-BRIN Scholars First Week Schedule

Michael Sorrell Center Room 4053
UNMC

Tuesday-May 31

8:00	Welcome and Introductions	J. Turpen P. Davis
9:00	Use of Animals in Research	J. Turpen
9:45	Laboratory Safety	W. Chaney
10:45	Introduction to Bioinformatics	D. Bastola
12:00	Lunch	
1:00	Library Access	M. Helms
1:45	Responsible Conduct in Research	D. Crouse
2:30	Proteomic Analysis Tools	P. Ciborowski
3:45	Radiation Safety Usage and Video	W. Chaney
4:45	Wrap-up and Questions	
5:30	Barbeque Welcome Banquet	J. Turpen

Wednesday-June 1

9:00	Science as a Career	D. Crouse
9:50	Graduate Studies at UNMC	J. Zheng
10:30	MD/PhD Program at UNMC	S. Smith
10:50	Graduate Studies at Creighton	R. Hallworth
11:20	Graduate Studies at UNL	J. Morris
12:00	Lunch	

Go meet mentors and labs.

Denise M Chapman to: 05/24/2011 12:57 PM

Cc: Diane C Torrey, Sonja A Cox, Myrna Newland, Janine M Wilson, Olivia R McGregor, Leticia A Tran, Selaba Travis, Jennifer Pace, Tuire Cechin, Erin M Plouzek, Mary McNamee, Rebecca McCaw,

SURP Students:

Welcome to the 2011 Summer Undergraduate Research Program. There were almost 500 applicants this year so this is a great accomplishment for you all. This year our Program will run from June 6st - August 5th.

Please join us at the Orientation on June 6th at 10:00 am in the Durham Research Center, Room 1002. Dr. David Crouse, Vice Chancellor of Academic Affairs, will be there to welcome everyone and you will also have the opportunity to meet the other students. Breakfast will be served at 9:30am.

Compliance Training will also be held on June 6th at 1:00 pm in the Sorrell Center room 3002. Registration begins at 12:30 pm. This session is mandatory and every student must attend, even if you were here last year. Attached you will find a copy of the Agenda for the Orientation Session

Luncheon Seminars are held every Tuesday from 12:00-1:00 in Eppley Science Hall, Room 3010. There will be guest speakers from all over campus and lunch will be provided on a first come, first serve basis. Any student who attends 6 out of 7 Luncheon Seminars will receive a certificate of completion from Academic Affairs. This certificate is in addition to any other certificate you may receive from your Department.

If you are interested in additional volunteer opportunities at the Hospital, please visit the Nebraska Medical Center's website and contact Patty Ostronic directly at postronic@nebraskamed.com. Please note: You must contact Patty by June 1st in order to register.

If you have any questions, please let the SURP Office or the coordinators in your department know. We are looking forward to a great summer!

Thank you,

Denise Chapman BA, MFA
Coordinator- Office of Postdoctoral Education
Community Liaison
University of Nebraska Medical Center
987810 Nebraska Medical Center
Omaha, NE 68198-7810
(402) 559-3662 Phone

Summer Undergraduate Research Program Orientation Agenda.docx

Summer Undergraduate Research Program Orientation
Monday June 6, 2011
DRC 1 Room 1002

9:30-10:00

Breakfast/Registration

10:00-10:10 am

Welcome-Dr. Crouse, Interim Vice Chancellor for Academic Affairs

10:10-10:35

Overview of SURP Program

Luncheon Seminars

Poster Session

Free summer events in Omaha

10:40-11:00

Networking Activity/Icebreaker

11:00-12:30

Lunch on your own (Vendor available in DRC 2 Commons or Cafeteria across the street)

12:30-1:00

Sign in for Compliance Training Begins

Sorrell Center Room 3002

1:00-3:00-

Compliance Training

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Nebraska Prostate Cancer Research Program (NPCRP)

This program is supported by the Department of Defense Prostate Cancer Research Program - Grant PC094595

Overview of NPCRP

Nearly 200,000 men in the U.S. will be diagnosed with prostate cancer and over 30,000 will die of this disease annually. While surgery and chemotherapy can cure the disease, in many cases it will spread and kill the patient. Better basic scientific understanding of this disease is needed to enable the development of more effective preventive and therapeutic treatments toward this cancer.

The development of better prostate cancer treatments depends on the training of prostate cancer researchers. This program is designed to train undergraduate science majors in prostate cancer research. It is a collaborative effort between the University of Nebraska Medical Center (UNMC), Omaha, NE and Clark Atlanta University (CAU), Atlanta, GA. Dr. Ming-Fong Lin of UNMC and Dr. Shafiq Khan of CAU have ongoing research collaborations. They will identify interested undergraduates at CAU for summer research at UNMC where the students will do basic science or translational research in a laboratory. Students will spend the great majority of their time working at the bench on a research project. They will also participate in a seminar series that will introduce them to different areas of scientific investigation and advanced technological tools used in scientific discovery.

After the summer, the students will continue research in a prostate cancer lab at CAU. They will thus continue their scientific development throughout the academic year in preparation for a graduate career in the biomedical sciences or for medical school.

Mission Statement of NPCRP

This Program will train undergraduate students to perform prostate cancer research in a research-

intensive environment. They will continue to perform research during their undergraduate academic career. After graduation, the student participants will be prepared to enter graduate school or medical school with training in, and understanding of, prostate cancer research. This will increase the number of prostate cancer researchers in both the basic and the clinical sciences.

Focus Areas of Research in NPCRP

Since our faculty members are engaged in a variety of research projects, students will have the opportunity to be trained in different areas of prostate cancer research. For example, the focus areas or research include Biomarkers, Therapy, Genetics, and Tumor Biology as outlined by the laboratory research descriptions in the table below.

NPCRP: Program Director, Staff Members and Mentors

Dr. Ming-Fong Lin, PD/PI of NPCRP, has served as the Coordinator/Leader of the UNMC Eppley Cancer Center Prostate Cancer Research Focus Group since 1997. Dr. Lin is a veteran in prostate cancer research for over twenty years. He was initially involved in the early investigation on the potential of prostate-specific antigen (PSA) as a surrogate marker for prostate cancer, comparing with the classical marker, circulating prostate acid phosphatase (PAcP). For investigating the molecular mechanism of hormone-refractory prostate cancer progression, Dr. Lin has established clinic-relevant, U.S. patent-awarded prostate cancer cell lines, which are well accepted by scientists in the field. Dr. Lin has also made the seminal discovery on the novel role of cellar PAcP in prostate cancer progression, corroborating clinic phenomena. Since 1995, he has served in various study sections for National Institutes of Health, Department of Defense Congressionally Directed Prostate Cancer Research Program, American Cancer Society and others.

The concept of training of undergraduate HBCU students from CAU is based on long-term interactions between Dr. Lin and Dr. Shafiq Khan, the faculty mentor at CAU. Dr. Lin has been a member of the Executive Advisory Committee for the NIH Research Center in Minority Institute (RCMI) at CAU and Dr. Khan is the Director of the Center since March 2004. Recently, Dr. Khan's Center, with Dr. Lin's inputs, was awarded a grant from NIH National Center on Minority Health and Health Disparities (NCMHD) for establishing a Center of Excellence for Prostate Cancer Research, Education and Services at CAU. To strengthen the research efforts in prostate cancer at CAU, Dr. Lin has provided necessary expertise and reagents to Dr. Khan and his faculty members. Dr. Lin and Dr. Khan have research collaborations as well; Dr. Lin is a consultant in Dr. Khan's DOD PCa Idea Award which has resulted in a co-authored publication in 2008 and additional collaborative articles are under construction or pending reviewing.

Dr. William Chaney serves as the Program Coordinator organizing orientation sessions and a summer seminar series for the students. He has over fifteen years of experience with undergraduate summer programs, having organized the first one provided by the College of Medicine at UNMC. He currently is the Program Coordinator of the NIH-supported Nebraska Center for Functional Genomics INBRE grant (The P.I. of the grant is Dr. James Turpen of UNMC). In this role, he organizes summer orientation and seminar presentations for undergraduate students. The concept is supported by Dr. Turpen, and the CAU students will also attend the INBRE activity during their summer research at UNMC. Thus, Dr. Chaney brings a tremendous amount of experience and activities to the CAU students in the NPCRP.

In NPCRP, fourteen faculty members from Creighton University (CU) in Omaha; University of Nebraska – Lincoln (UNL) and University of Nebraska Medical Center (UNMC) have agreed to serve as potential research mentors for this proposal. Their research areas cover a wide range of expertise and interest in cancer research including prostate cancer (the detail of research activity is described in the table below). Thus, a student entering this program can find a research mentor who is working in an area of interest to that student.

Faculty Advisors at CAU

Dr. Shafiq Khan, Professor of Biological Sciences at CAU, will serve as the faculty advisor for the undergraduate students participating in this program. He currently coordinates undergraduate research efforts at CAU and is extensively involved in their research experiences. Dr. Khan is the Director of Research Center in Minority Institute (RCMI) program and also is the PI of the Prostate Cancer Research Center at CAU supported by NCMHD, NIH. Dr. Khan has an active research lab and is funded externally including the DOD Prostate Cancer Research Program Idea award. To strengthen the effort of this training program, upon discussion with Dr. Lin, Dr. Khan recruited Dr. Valerie Odero-Marah, Assistant Professor of Biology at CAU, who is also funded by the DOD Prostate Cancer Research Program to serve as the Program Coordinator supporting Dr. Khan in student recruitment and mentoring at CAU.

Research Mentors and Projects

Investigator	Institution	Project
S. Batra	UNMC	Genetic Alterations in Prostate Cancer Progression
J. Christman	UNMC	Regulation of DNA Methylation in Prostate Cancer
W. Chaney	UNMC	Glycobiology in Prostate Cancer
P. Cheng	UNMC	Glycomics in Prostate Cancer Metastasis and Gene Therapy
J. Davis	UNMC	Hormone Regulation of Tumor Cell Development
R. Lewis	UNMC	IGF Receptors in Prostate Cancer
M.-F. Lin	UNMC	Androgen Regulation of Prostate Cancer Growth and Development
R. MacDonald	UNMC	IGF Axis in Prostate Cancer Growth
P. Mehta	UNMC	Gap Junction Proteins in Prostate Cancer Metastasis
E. Rogan	UNMC	Metabolism of Dietary and Environmental Chemicals to Mutagenic and Genotoxic Species
M. Simpson	UNL	The Role of Hylauronate in Prostate Cancer Development
R. Singh	UNMC	Prostate Cancer Metastasis and Immunology
Y. Tu	CU	Regulation of G-Protein-Coupled Receptors in Prostate Cancer
D. Wang	UNMC	Targeted Therapies for Prostate Cancer Bone Metastasis

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2011 Clark Atlanta University Students

**We would like to acknowledge Lisa Spellman and the Public Relations Office for taking the photos below of the Clark Atlanta University Students (group photo). We would also like to acknowledge Jim Turpen for taking the individual headshots of the students below We appreciate their support.

Dr. Ming-Fong Lin, Shawna Battle, Celeste Scott, LaTayia Aaron, Hilary Kirwan, Dr. Bill Chaney

LaTayia Aaron

Shawna Battle

Hilary Kirwan

Celeste Scott

University of Nebraska Medical Center

Department of Biochemistry & Molecular Biology

Seminar Series

"Prostate Cancer Research and Education at Clark Atlanta University"

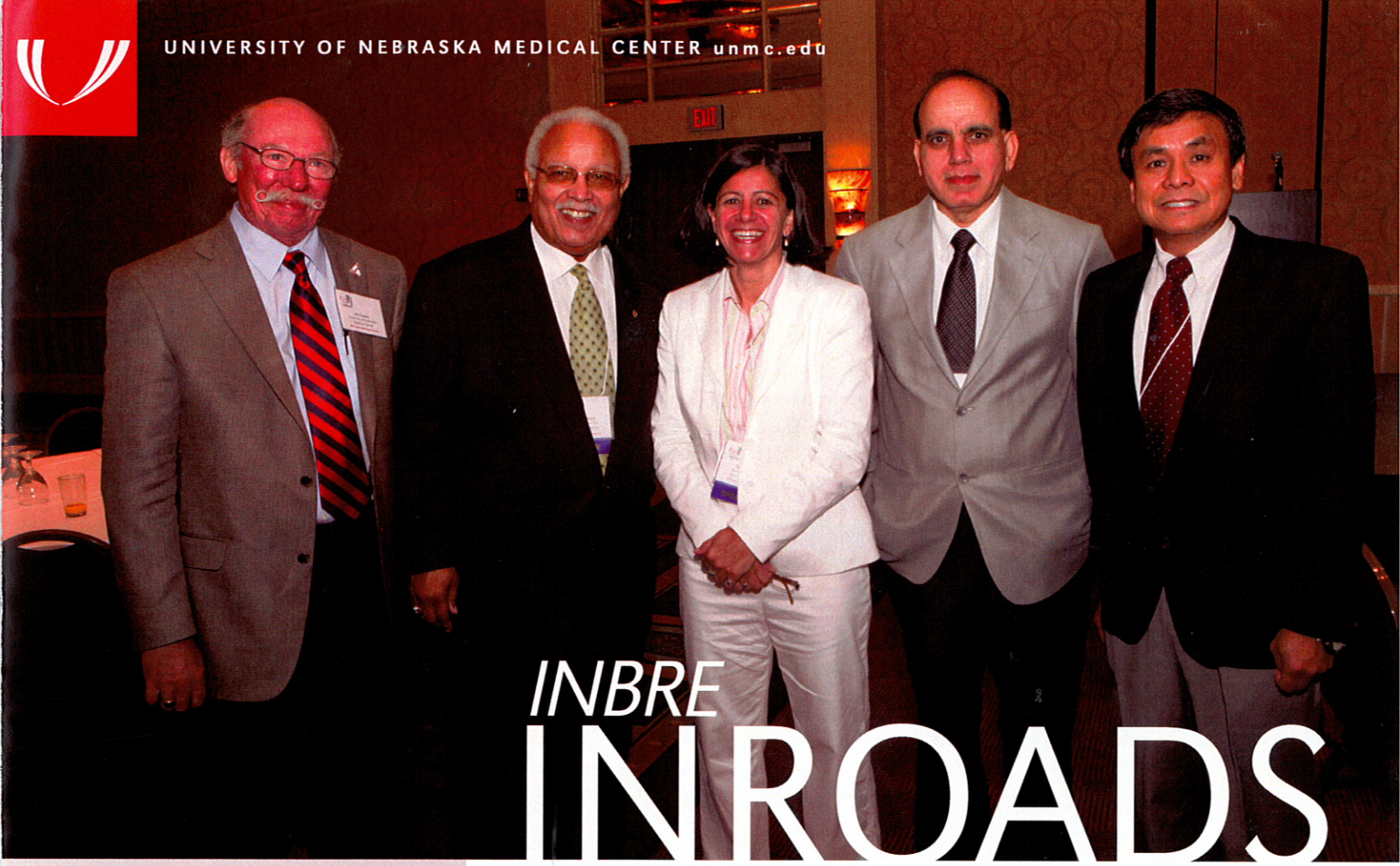
Shafiq Khan, PhD
Professor
Dept of Biological Sciences
Clark Atlanta University

Wednesday, July 6, 2011

3:00 p.m.

DRC1 1004

UNIVERSITY OF NEBRASKA MEDICAL CENTER unmc.edu



INBRE INROADS

Sidney McNairy, Jr., Ph.D., D.Sc., Division Director of the research infrastructure at the National Center for Research Resources, gave an overview of the NCRR at the 2011 Central Region IDeA conference in Omaha in May. Pictured from left to right are: James Turpen, Ph.D., Nebraska INBRE Principal Investigator, Dr. McNairy, Sheila Caldwell, Ph.D., Health Scientist Administrator (NCRR), Krishan Arora, Ph.D., INBRE Program Officer (NCRR), and Charles Woods, Ph.D., director of the Center for Virology at the University of Nebraska-Lincoln.

IDeA conference showcases best of regional science

You believe in your programs.

You know the value of them and you know the impact.

The IDeA program is magnificent and you are the reason it works so well.

Those were the key messages Sidney McNairy Jr., Ph.D., left with attendees at the Central Region IDeA Networks of Biomedical Research Excellence conference held in Omaha in May.

"I am proud to say that in the heartland there is great science," said the director of the division of research infrastructure with the National Center for Research Resources, a division of the National Institutes of Health, which funds the IDeA program.

More than 200 people attended the three-day conference which featured 100 poster presentations, 28 oral presentations, and faculty and students representing colleges and universities in five states.

"It's great to come and see the work being done around the region," said Narayanaganesh Balasubramanian, a graduate student from North Dakota State University.

Although he studies chemistry, Balsubramanian said seeing the work being done in the various fields reveals a lot about how interconnected science really is.

"It's good to see how the different areas of science complement each other," he said.

A highlight of the conference was a regional multi-user core facility marketplace that featured 16 different facilities in North Dakota, Nebraska and Kansas.

"I would like to personally thank-you, commend you and salute you for what you've been able to do," Dr. McNairy Jr. told attendees.

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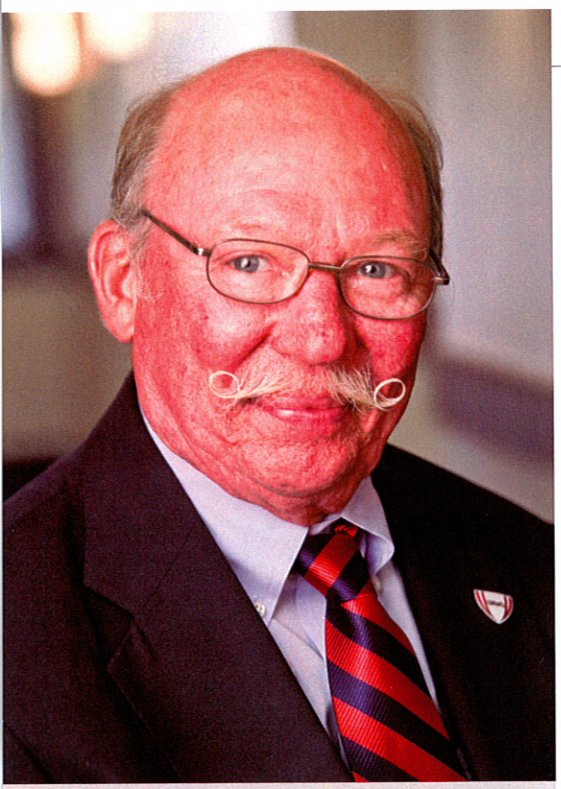

INBRE INROADS

A newsletter of Nebraska's Institutional Development Awards (IDeA) Networks of Biomedical Research Excellence (INBRE)

The Nebraska INBRE is funded through a grant from the National Center for Research Resources, a division of the National Institutes of Health.

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INROADS participating institutions 2011

Creighton University College of Arts and Science; College of Saint Mary's, Doane College; Little Priest Tribal College; Nebraska Wesleyan University; the University of Nebraska at Kearney; the University of Nebraska at Omaha; the University of Nebraska-Lincoln; Wayne State College; Chadron State College; Western Nebraska Community College.

brin.unmc.edu

From the director

This is always an exciting time of the year as we welcome a new class of INBRE Scholars to our program. As usual, we have some outstanding students joining us as Scholars. I am especially pleased to welcome Melina Baeza-Villa to our program since she is the first in her family to go to college.

I am partial to first generation college students, both my wife and I were the first in our families to go to college and we both loved it so much we stayed there for the rest of our lives. It is also rewarding to welcome the new Clark-Atlanta students to our program. The Scholars program is all about opportunity and it is gratifying that we are extending opportunity to such a diverse group of students and will be able to highlight your success in future issues of INROADS.

Our Central Region IDeA Conference was a success beyond our expectations. We had initially projected around 150 attendees and significantly exceeded that projection with 207 attendees. Our projection of 50 poster presentations mushroomed to over 100 and we met our goal of booking 75 rooms at the hotel.

More importantly, around 40 percent of our attendees were students, which bodes very well for our scientific future. Thanks to all of you for attending and providing such a warm welcome to Dr. Sidney McNary.

As most of you know, Dr. McNary has been the architect of and driving force behind the IDeA program since its inception. He had never been to Omaha before and was genuinely impressed with all that he saw in Nebraska and the Central Region.

A special thanks goes to our organizing committee and especially Penni Davis for all the work she did in putting the Conference together. We are looking forward seeing you all at to the Grand Island Conference in August. Have a productive and fun summer.

Q&A with UNK's Kim Carlson, Ph.D.

Q. What is your lab working on right now?

A. We are looking at characterization of differential gene regulation during natural aging using large populations of Drosophila melanogaster with my INBRE mentor, Dr. Larry Harshman, from UNL. Our interest is in the factors that may perturb gene expression during aging and contribute to the aging process as a whole. From one of our earlier studies, we hypothesized that the frass (feces) of D. melanogaster (fruit fly) might contain micro-organisms that can affect aging. Therefore, we set out to characterize these micro-organisms. In doing so, we uncovered a novel RNA virus, Nora Virus that is largely uncharacterized. We are working in collaboration with Dr. Dan Hultmark's lab in Sweden, who first discovered Nora Virus, to work on characterizing it.

Q. How has being a part of the INBRE program helped your research and your students?

A. It has made the research possible. Without INBRE, we would not have the space, equipment, or connections with other faculty and core facilities to carry out our research. Also, the students get to travel with INBRE faculty to national meetings and meet the scientists whose work they've only read in research papers. I doubt without INBRE we would have ever gotten to the point of finding the Nora Virus and establishing a collaboration with Dr. Hultmark.

Q. What is the best part about the INBRE program?

A. The best part of the program is the ability to incorporate undergraduate research in my teaching and have student collaborators. These high motivated students are able to work on large projects in the lab and feel a sense of ownership. The support from UNMC is phenomenal and so are the connections with UNL and Creighton. I have talked to faculty in other departments at UNK and they are surprised by the connection we have with the other campuses and the resources allotted to us.

Exploring careers in biomedical research

Kelvin Chin isn't sure what he wants to do in science, but knows that he needs more experience before he can decide on a career.

"How do you decide on a career without exploring it first?" Chin asks.

This summer the computer science major joins 30 students from throughout the state of Nebraska immersed in research labs at the University of Nebraska Medical Center, Creighton University and the University of Nebraska-Lincoln.

He is a part of the latest class of INBRE Scholars who spend 10 weeks every year exploring the world of biomedical sciences. Chin is curious to see how his talent for computer science can enhance research through the use of bioinformatics.

He will work alongside graduate students in the lab of Elena Batrakova, Ph.D., an associate professor in the UNMC College of Pharmacy, who studies the development of polymer-based drug delivery systems for chemotherapy and disorders of the central nervous system.

"I'm excited to learn how bioinformatics is used and applied to laboratory research," Chin said.

His enthusiasm mirrors that of fellow INBRE Scholar Melina Baeza-Villa, who will spend the summer working with Joseph Vetro, Ph.D., an assistant professor in the UNMC College of Pharmacy, who studies nanomedicine.

Baeza-Villa is an undergraduate student at the College of Saint Mary and the first in her family to go to college. She was 10 years old when her family moved to the United States from Mexico. Baeza-Villa said she struggled with English concepts but excelled in math and science and enjoyed taking extra courses in high school.

"I decided to major in biology and chemistry in college and am planning to go to medical school. I would like to be a pediatrician," she said.

Baeza-Villa hopes her experience in the INBRE program will enhance her education and laboratory skills.

"Just the experience of working in a lab and all the people I will meet in the INBRE program is going to help me later on," she said.

Clark Atlanta University students Celeste Scott, Hilary Kirwan, Shawna Battle and LaTayia Aaron.

Longtime collaboration opens door to new undergraduate opportunities

An ongoing collaboration between two cancer researchers has opened a world of opportunities for four young undergraduate students from Clark Atlanta University (CAU), a well-respected, historically black college in Georgia.

LaTayia Aaron, Hilary Kirwan, Celeste Scott and Shawna Battle, are spending the summer conducting research at the University of Nebraska Medical Center through the Nebraska Prostate Cancer Training Program.

The program, which is supported by a three-year, $200,000 department of defense grant, also collaborates with the successful INBRE scholar program at UNMC to provide training for the Clark Atlanta students. This is the second year for the undergraduate training program. To date eight students, including those listed above, have participated.

Program director, Ming-Fong Lin, Ph.D., a prostate cancer researcher at UNMC, and Shafiq Khan, Ph.D., director of the Prostate Cancer Research Center at CAU, developed the program.

Inspiring undergraduate students to consider a career in biomedical research specifically targeting prostate cancer is the goal of the program, Dr. Lin said.

"The incidence of prostate cancer is 65 percent higher and the mortality rate is more than double in African-American men compared to Caucasians," he said.

It's also important for students to get a good foundation in laboratory research whether they plan to go into medicine or become a scientist, Aaron said.

The junior biology major is interested in pursuing a career in pediatrics, but applied to the training program for exactly that reason.

"Discovering what causes disease and the science behind it gives you valuable insight," Aaron said.

University of Nebraska Medical Center

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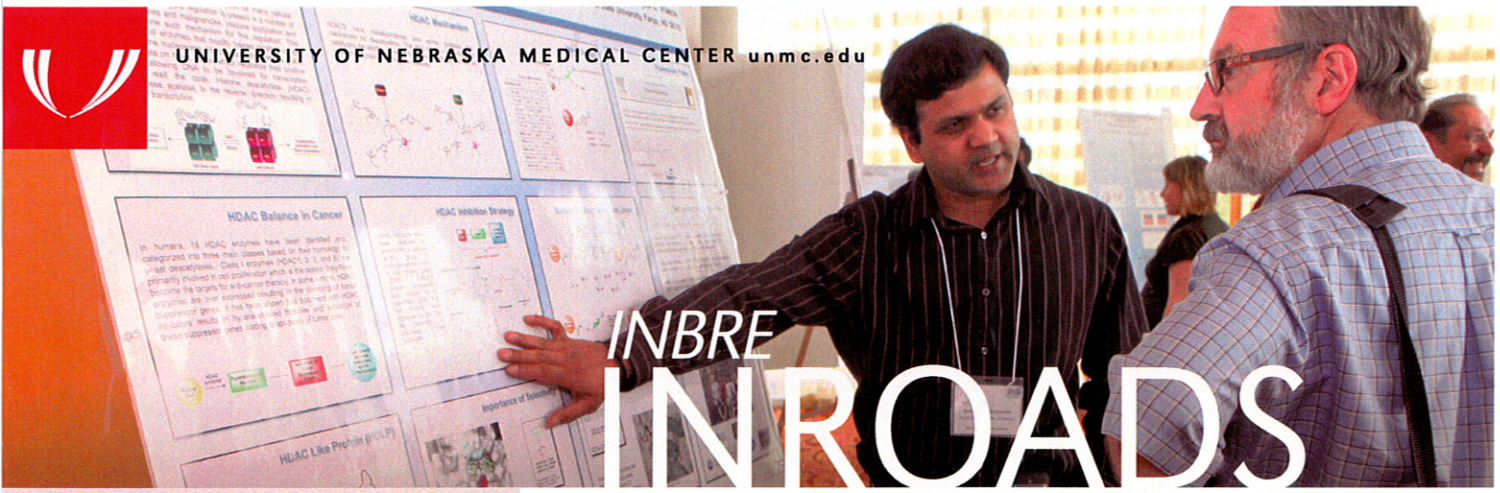
John Karanicolas, Ph.D., a researcher from The University of Kansas, kicked off the genomics, proteomics and bioinformatics symposium during the 2001 Central Region IDeA conference in May, with a talk on building biomolecular switches by chemical rescue.

Ming-Fong Lin
University of Nebraska Medical Center
Dept. of Biochemistry & Molecular Biology
zip 5870



in this issue

The INBRE program is funded by the National Center for Research Resources. NCRR is part of the National Institutes of Health, U.S. Department of Health and Human Services.

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Growth suppression of new ribonucleotide reductase inhibitors in prostate cancer cells

Hilary Kirwan[1,2], Yu Wei Chou[2], Sakthivel Muniyan[2] , Ming-Fong Lin[2]

[1]Department of Biology, Clark Atlanta University, Atlanta, GA
[2]Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE

Background:
Many approaches have been utilized in the treatment of early stage prostate cancer (PCa), including surgery and radiation therapy; the treatment for the advanced castration-resistant PCa is limited. It is very important to develop new effective treatments for castration-resistant PCa. The ribonucleotide reductase (RR) plays a important role in cell growth and tumor progression. The new synthesized RR inhibitors, thiosemicarbonzones, have been tested for growth suppression on cancer cells. We examined new compounds from this family on PCa cells.

Methods:
The four new RR inhibitors (4-Bis, AMN, AMD, PHE) were investigated on the cell growth inhibition in androgen-independent PCa cells (LNCaP C-81) in regular medium. We also examined the dosage effect of 4-Bis compound in LNCaP C-81 cells.

Results:
In four RR inhibitors treated PCa cells, growth suppression was seen for 4-Bis, AMD and PHE. In 4-Bis treated PCa cells, the cell growth inhibition followed a dose-dependent fashion.

Conclusion:
These findings suggest that the newly synthesized RR inhibitors, thiosemicarbonzones, exhibit the efficacy on cell growth suppression and follow the dosage effect in LNCaP C-81 cells.

Effects of TGFβ1 and PGE2 on Cellular Signaling in Bovine Corpora Luteal Fibroblasts

LaTayia Aaron[2], Chao Jiang[3], and John S. Davis[1,3,4]

[1]Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE; [2]Clark Atlanta University, Atlanta, GA;
[3]Department of Obstetrics and Gynecology University of Nebraska Medical Center, Omaha, NE;
[4]Veterans Affairs Medical Center, Omaha, NE

Objective

The purpose of this study was to determine if PGE2 inhibits the actions of TGFβ1 in corpora luteal fibroblast cells. For this experiment, fibroblasts cells were isolated from the bovine corpus luteum. After preliminary experiments to find out if PGE2 was present in the fibroblast cells and to see if PGE2 inhibits TGFβ1 action, we sought out to determine which specific EP receptor caused this inhibition. By doing RT-PCR we found that almost all EP receptors were present in the fibroblast cells isolated. Due to time constraints, we were only able to test for EP2. We conducted a test that inhibited as well as promoted EP2 function using its agonist, butaprost, and its antagonist, AH6809.

Conclusions

- **Corpora luteal fibroblast cells expressed PGE2 receptors.**
- **TGFβ1 stimulated phosphorylation of SMAD2 and P38MAPK.**
- **PGE2 stimulated phosphorylation of PKA substrates.**
- **Immunofluorescence staining shows that the addition of PGE2 or butaprost and TGFβ1 alters cell morphology.**

VEGF-C Promotes Autophagy and Survival in Prostate Cancer Cells Following Chemotherapeutic Stress

Celeste Scott[1], Marissa Stanton[2], Samikshan Dutta[2], Heyu Zhang[3], Kaustubh Datta[2]

[1] Clark Atlanta University, Atlanta, GA;
[2] University of Nebraska Medical Center, Omaha, NE ;[3] The Mayo Clinic, Rochester, MN

Introduction

About 218,000 men in the United States were diagnosed with prostate cancer. From this number, about 32,000 men died from prostate cancer in the United States. The primary cause of prostate cancer death is a failure to treat metastatic disease. The expression of VEGF family members, VEGF-C in particular, has been linked to radiation and chemotherapy resistance.

Summary

Based on the collected data, we conclude that VEGF-C promotes the survival of prostate cancer cells following nutrient and chemotherapeutic stress.

UPREGULATION OF MATRIX METALLOPROTEINASE (MMP)13 EXPRESSION AT THE TUMOR-BONE IN PROSTATE CANCER

SHAWNA BATTLE[1], MICHELLE L. VARNEY[2], MITSURU FUTAKUCHI[2], RAKESH K. SINGH[2]

[1] Clark Atlanta University, Atlanta, GA;
[2]Department of Pathology & Microbiology, University of Nebraska Medical Center, Omaha, NE 68198

ABSTRACT

According to the American Cancer society, prostate cancer is the second leading cause of cancer death in American men, only behind lung cancer. In the year of 2011, it is estimated that about 240,890 new cases of prostate cancer will be diagnosed and about 33,720 of these men will die from prostate cancer. Bone is one of the most common sites of metastasis, in human prostate cancer. The tropism of prostate cancer cells for bone and their tendency to induce osteolytic/osteoblastic phenotype is a result of interactions between malignant cells and stromal cells, and is of paramount importance for bone metastasis of prostate cancer. However, the underlying molecular mechanisms remain poorly understood. The capacity of prostate cancer cells to collaborate with bone stromal cells is likely to be specific and also critical for the formation of bone metastases.

In this report, we examined whether interaction between prostate cancer cells and stromal cells in the bone microenvironment play a critical role in the formation of bone metastases determine the molecular mechanism of this regulation. We have developed a rat model to examine tumor-stromal interactions in osteolytic/osteoblastic bone metastasis. Using this model, we analyzed whether tumor-bone (TB) microenvironment regulates expression of proteases. We used microarray analysis for gene expression profiling at the TB interface versus the tumor alone area from syngenic rat injected with malignant prostate cancer cells.

We observed the up-regulation of matrix metalloproteinase (MMP)-3, 7, 9 and -13 at the TB interface. Our data suggests that MMP-13 expression is specifically upregulated at the tumor bone in prostate cancer suggesting its importance in determining the molecular mechanism of bone metastases regulation.

U1

DIOXIN EXPOSURE ENHANCES NUCLEAR LOCALIZATION OF ANDROGEN RECEPTOR, ***LaTayia Aaron***, *and Joann Powell, Center for Cancer Research and Therapeutic Development, Clark Atlanta University, Atlanta, Georgia, USA.*

Androgen receptor (AR) signaling is involved in a number of developmental and physiological processes. AR is localized in the cytoplasm of stromal and secretory epithelial cells. Upon binding with androgens, AR enters the nucleus and regulates transcription of genes involved in diverse biological process such as proliferation, differentiation and apoptosis. Androgens are especially important in male sexual development and growth of the prostate gland. Early stage prostate cancers are dependent on androgens for growth. Therefore, androgen deprivation therapy is the predominant form of treatment. However, when prostate cancers progress following androgen depletion therapy, the cells gain the ability to thrive despite low levels of circulating androgens. Treatment options for androgen-independent prostate cancer are scarce with docetaxel being the only agent shown to prolong survival. Previously, 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD/Dioxin) has been shown to inhibit growth of androgen dependent prostate cancer cell line, LNCAP. Dioxin, is the most potent agonist for the aryl hydrocarbon receptor (AhR). AhR, has been shown to interact with multiple signaling pathways during prostate development and may provide a new target to regulate androgen signaling. The objective of this study is to establish dioxin's ability to regulate androgen receptor localization in androgen-dependent cell lines. We hypothesize that dioxin increases AR nuclear localization. Dioxin activity may regulate androgen receptor signaling by direct heterodimerization with AhR.
Androgen-dependent prostate cancer cell line (LNCaP), as well as, androgen-independent prostate cancer cell lines (C-42) was grown on coverslips and treated with TCDD alone and in combination with an androgen derivative, R1881. Immunofluorescence staining was used to label AhR and AR within the cells. Fluorescence microscopy was utilized to determine location of both AhR and AR following exposure to TCDD and R1881. In addition to inducing nuclear localization of AhR, TCDD treatment also enhanced nuclear localization of AR.

Acknowledgements: This work was supported by the NIH/NIGMS MBRS RISE Grant #5R25GM060414 and RCMI grant 2G12RR003062-22.

U2

THE SYNTHESIS OF METAL ORGANIC FRAMEWORKS (MOFs), ***Brandon Dennis***, *Conrad W. Ingram, Esmerelda Castaneda and Liang Liao, Clark Atlanta University, Department of Chemistry, Atlanta, GA.*

Metal organic frameworks (MOFs) are crystalline compounds that are formed by the binding of metals to organic compounds known as ligands. The metal ion and ligand chosen, the ratio of metal to ligand, temperature, and solvent used for the reaction all affect the ability of the reaction to form a MOF. These factors also affect the structure and properties of these coordination polymers. The purpose of this study was to synthesize MOFs using transition and lanthanide metal ions in combination with 3, 6-dimethylpyrazine-2, 5-dicarboxylic acid as the organic linker. The first experiment involved the use of lanthanum (III) nitrate hexahydrate in two ratios of ligand to metal: 1:3 and 1:2. The second experiment used which was cobalt (II) nitrate hexahydrate was in the same ratios as experiment one. The reactions are being monitored for the formation of crystalline MOFs. The porous structures of MOFs will be studied for their use in gas storage, absorption, gas separation, and catalysis.

Acknowledgements: This study was supported by the NIH/NIGMS, MBRS RISE Grant #2R25GM060414.

Acknowledgements: Supported by the MBRS RISE Interdisciplinary Early Inquiry-Based Research Training Program, NIH/NIGMS Grant #2R25GM060414. The Pure Cocoa Powder was generously provided by Mr. Emmanuel Frimpong of Cocoa Gold, Atlanta, GA.

U7

INHIBITION OF CONSTITUTIVELY ACTIVE ARYL HYDROCARBON RECEPTOR (AhR) SIGNALING REDUCES PROLIFERATION OF C4-2 PROSTATE CANCER CELLS,

Oliver Richmond, *Cindy Tran and Joann Powell, Center for Cancer Research and Therapeutic Development, Clark Atlanta University, Atlanta, Georgia, USA.*

The aryl hydrocarbon receptor is a member of the basic helix loop helix family of transcription factors. AhR is known to mediate the biochemical and toxic effects of a number of polyaromatic hydrocarbons such as 2,3,7,8, tetrachloro-dibenzo-dioxin (TCDD). AhR is widely known for regulating transcription of drug metabolizing enzymes, such as cytochrome P450 1A1 (CYP1A1), involved in the xenobiotic metabolism of carcinogens and therapeutic agents. AhR has also been shown to play a role in cell cycle regulation and proliferation of a number of cancers. AhR has two binding sites for retinoblastoma tumor suppressor protein (pRb) which controls cell cycle progression through G1. This interaction has been shown to regulate proliferation in human skin, neuronal (neural) and breast cancer cells. Activation of the receptor by TCDD inhibits androgen dependent proliferation in prostate cancer cells. However, the effect of AhR signaling on androgen independent proliferation has not been studied. Here we investigate the effect of AhR signaling on the androgen independent growth of prostate cancer cells. Immunoblot analysis shows that AhR expression is increased in androgen independent (C4-2) prostate cancer cells. RT-PCR studies revealed enhanced AhR activity in C4-2 cells without ligand activation. Reduction of AhR activity by pharmacologic inhibitors or short RNA mediated silencing reduces proliferation of C4-2 cells in an androgen depleted environment. This data indicates that AhR is essential to maintain androgen independent growth and may provide insight into the molecular mechanisms responsible for the hormone refractory phenotype.

Acknowledgements: These studies were supported by the RCMI grant 2G12RR003062-22.

U8

VEGF-C PROMOTES AUTOPHAGY AND SURVIVAL IN PROSTATE CANCER CELLS FOLLOWING CHEMOTHERAPEUTIC STRESS,

Celeste Scott[1], *Marissa Stanton*[2], *Samikshan Dutta*[2], *Heyu Zhang*[3], *Kaustubh Datta*[2,1] *Clark Atlanta University, Department of Biological Sciences, Atlanta, GA;*[2] *University of Nebraska Medical Center, Omaha, NE ;*[3] *The Mayo Clinic, Rochester, MN.*

In 2010, about 218,000 men in the United States were diagnosed with prostate cancer. From this number, about 32,000 men died from prostate cancer in the United States The primary cause of prostate cancer death is a failure to treat metastatic disease. The expression of VEGF family members, VEGF-C in particular, has been linked to radiation and chemotherapy resistance. VEGF family proteins are closely related cytokines that exert critical functions in vasculogenesis, pathological and physiological angiogenesis and lymphangiogenesis. Based on data from tumors that overexpress VEGF-C but do not promote lymphangiogeneis, we hypothesize that VEGF-C has non-lymhangiogenic functions that promote tumor cell survival and metastatic spread. Our goal for this research project is to determine the role VEGF-C plays in the survival of tumor cells following therapy. In order to test our hypothesis, we took sets of PC3 cells, transfected one of the sets of PC3 cells with scrambled siRNA, and transfected the second set with VEGF-C siRNA. We also conducted

other tests in order to obtain the rest of our data results such as a clonogenic assay test following γ-irradiation, microarray studies to determine the differential expression of genes followed by validation via quantitative, real-time PCR, western blots, and cell death assay tests. The results of this analysis can be used to find whether or not VEGF-C promotes the survival of prostate cancer cells following nutrient and chemotherapeutic stress. The findings from this research may be useful in creating a new prostate cancer drug that will eliminate VEGF-C and stop the survival of prostate cancer tumor cells.

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THE UNIQUE EXPRESSION OF NEURAL REGULATION FROM IMMOBILIZATION STRESS, ***Elena Washington***[1], *Mary I. Smith*[2], *J.Shead*[2], *B. Winston*[1], *L. French*[2] *and T. O. Moore*[1], *Department of Psychology*[1], *Department of Biological Sciences*[2], *Clark Atlanta University, Atlanta, Georgia.*

In this study a gaseous neurotransmitter known as nitric oxide was the unique neural substrate that was studied in our immobilization stress experiment. The presence of nitric oxide synthase (NOS) was used in combination with cFOS, a genetic marker for neural activity. It was hypothesized that there would be a positive relationship between the presence of neural nitric oxide synthase (nNOS) in relation to cFOS expression. The nNOS and cFOS were measured in hypothalamic regions of the brain. Immobilized stress occurred by placing the rats into a small tube. There were four groups tested in this study: 1. control; 2. 1 hour; 3. 3 hour; and 4. 6 hour group. The stains that were used were diaminobenzidine (DAB) and NADPH to measure the neural structure of nNOS and cFOS. We have found the control and the one hour group appeared to not release large amounts of nNOS and cFOS. However, the three hour group released the highest levels. In the six hour group, the cFOS and nNOS appeared to be less prominent than the three hour group. This study is currently being continued by using different stains to investigate neural changes. This study could possibly aid in future treatment of stress related disorders and diseases.

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OUTPATIENT FOLLOW-UP AND RE-HOSPITALIZATION RATES OF SICKLE CELL DISEASE PATIENTS FOLLOWING INDEX HOSPITALIZATION FOR PAIN CRISIS, 2006-2007, ***Benjamin Ansa,*** *Adamkiewicz Thomas, Yvonne Fry-Johnson, Barbara Moore, George Rust, Morehouse School of Medicine, Atlanta, Georgia.*

Sickle cell disease (SCD) affects 80,000-100,000 Americans. Acute pain is the most common reason for hospitalization among SCD patients. The cost of hospital care and the burden of the disease on the patients, their families and the community are enormous. Most chronic diseases currently have measures for quality of care assessment, but SCD does not. Re-hospitalization within thirty days after index hospitalization for SCD was developed by the National Association of Children's Hospitals (NACHRI) as a way to drive internal hospital quality improvement. However, there are very few studies to validate this marker and debate remains as to its value. Several factors may influence re-hospitalization rates among SCD patients, and outpatient follow-up after index hospitalization is considered as one of those factors. We aimed to examine the rates of re-hospitalization and out-patient follow-up visits among children and adults with SCD, and to determine any association between out-patient follow-up visit and re-hospitalization in this group of individuals. We analyzed the Medicaid

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THE ARYL HYDROCARBON RECEPTOR SUSTAINS ANDROGEN RECEPTOR SIGNALING IN ANDROGEN INDEPENDENT PROSTATE CANCER CELLS, ***Cindy Tran,*** *LaTayia Aaron and Joann Powell, Center for Cancer Research and Therapeutic Development and Department, Clark Atlanta University, Atlanta, Georgia.*

The aryl hydrocarbon receptor (AhR) is a basic helix-loop-helix (bHLH) transcription factor that is well characterized for mediating the carcinogenic responses to environmental polyaromatic hydrocarbons (PAH), such as 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin (TCDD). Traditionally, AhR has been studied for its transcriptional regulation of metabolizing enzymes such as cytochrome P450-1A1 (CYP1A1). However, AhR has also been shown to interact with multiple signaling pathways during prostate development and may provide a new target to regulate androgen signaling. Early stage prostate cancers are dependent on androgens for growth. Therefore, androgen deprivation therapy is the predominant form of treatment. However, more advanced forms of prostate cancer are hormone refractory and do not rely on the presence of androgens for growth. The molecular mechanisms responsible for the sustained androgen receptor (AR) signaling during androgen deprivation therapy are not clearly understood. The objective of this study is to determine the ability of AhR to enhance AR signaling in prostate cancer cells. For these experiments, androgen independent C4-2 and androgen dependent LNCaP cell lines were treated with TCDD. AhR and AR expression, activity and localization were accessed by RT-PCR, Western immunoblotting and immunofluorescence. AhR was found to be overexpressed in the castration independent cell lines. In addition, AhR and AR are localized in the nucleus without ligand treatment in the androgen independent cell line. In contrast, the LNCaP cells required ligand activation for translocation of AhR and AR to the nucleus. Also, CYP1A1 was found to be expressed independent of ligand treatment in C4-2 cells while activation of AhR with TCDD was needed for expression of both CYP1A1 and PSA in LNCaP cells. These results indicate the presence of a constitutively active AhR as well as cross-talk with AR in castration independent prostate cancer cell lines.

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STRESS AND APOPTOTIC PROTEINS EXPRESSION IN ARSENIC TRIOXIDE-TREATED BREAST AND LUNG CANCER CELLS, ***Alice M.Walker,*** *Laurin Paris, Jacqueline J. Stevens, and Paul B Tchounwou, Jackson State University, Environmental Science Program, Center for Environmental Health and Murrah High School, Jackson, MS.*

Breast cancer is a malignant tumor that starts in the cells of the breast. It is second to lung cancer among estimated cancer deaths and first overall in estimated diagnosed cases in women. Hence, lung cancer has the highest number of cases and death in both women and men. Arsenic trioxide (ATO) has been used in the treatment of relapsed/refractory acute promyelocytic leukemias. However, its effects on breast and lung cancer are not known. We hypothesize that ATO may also have a bioactivity against breast cancer, and its mechanisms of action may involve changes in stress-related proteins and apoptosis in breast and lung cancer cells. Using breast (MCF-7) and lung (A549) cancer cells as test model, the effects of ATO were examined by western blot analysis for stress related proteins (*Hsp70 and cfos*) and apoptotic protein (*Bcl-2*, and *cytochrome c*) expressions. MCF-7 and A549 cells were treated with arsenic trioxide at 0, 2, and 4 μg/ml for 48 hr. There was a decreased in *Hsp70* and *cfos* expressions at 4μg/ml in MCF-7. In A549 cells, *Hsp70* increased and cfos decrease in expression. However, there was a slight increase in the *Bcl-2* expression at 4μg/ml of ATO in both MCF-7 and