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W81XWH-09-1-0270

TITLE: 
Prostate Cancer Research Training Program

PRINCIPAL INVESTIGATOR: 
David M. Lubaroff, PhD

CONTRACTING ORGANIZATION: 
University of Iowa 
Iowa City, IA  52242

REPORT DATE: 
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designated by other documentation.
The HBCU Summer Research Training Program accepted a total of 8 students from Lincoln University for the eight week session during the summer of 2012. Four of the students were supported by this grant and four of the students were supported by the second grant awarded in 2010. Each student was assigned to a laboratory of a participating mentor and also paired with a member of the mentor’s laboratory. This laboratory member assisted with day to day aspects of the research project. During the summer the students worked diligently on their research project, participated in meetings of the mentor’s laboratory, attended workshops and seminars associated with our and other summer programs, and attended a special course in prostate cancer. We integrated the Lincoln students into social programs held throughout the campus for summer interns. At the end of the summer sessions the students presented a poster of the research results from the summer experience. They also presented the results of their research in the fall at Lincoln University. One of the students graduated and has been accepted into the Interdisciplinary Graduate Program in Immunology at the University of Iowa. All of the remaining students are continuing their undergraduate education at Lincoln University.
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Introduction:

In our initial award (W81XWH-06-1-0266), begun in 2006, we were funded for five students from Lincoln University of Pennsylvania. Because of a large number of qualified student applicants we were funded for additional three students in 2007 (W81XWH-07-1-0241), allowing our program to support a total of eight Lincoln students each summer. We applied for, and were awarded, three additional grants (W81XWH-12-1-0117), (W81XWH-10-1-0459) and this award (W81XWH-09-1-0270) after the original grants had been completed. For the year reported here we had the following faculty participants: David M. Lubaroff, PhD, Principal Investigator, Paul Heidger, PhD, University of Iowa Faculty Advisor, Derek Swinton, PhD, Lincoln University Faculty Advisor, and the following mentors: James Brown, MD, Frederick Domann, PhD, Paloma Giangrande, PhD. Prabhat Goswami, PhD, Michael Henry, PhD; Yi Luo, MD, PhD, Lyse Norian, PhD, Aliasger Salem, PhD, Michael Schultz, PhD, Andraean Simons-Burnet, PhD, Elaine Smith, PhD, Douglas Spitz, PhD, Chad Tracy, MD, George Weiner, MD, Michael Wright, PhD, and Nicholas Zavazava, MD.

Body:

Recruitment and Admission:

Brochures, application forms, and posters were designed and printed and sent to Dr. Swinton at Lincoln and the PI traveled to Lincoln University in January 2012, met with Dr. Swinton, Dr. John Chikwem, and the Chairmen of the Departments of Chemistry and Biology. A presentation was made about the summer training program to a group of students at a special seminar. Nineteen applications were received for the 2012. The applications were reviewed by the Admissions Committee whose membership consisted of Dr. Lubaroff, Dr. Heidger, Dr. Henry, Dr. Domann, and Dr. Swinton. Admission was offered to a total of 8 students.

Students Accepted for the 2012 Program
Laurie-Ann Davis
Chalwe Diallo
Shauna Ebanks
Ashley Ellis
Shakeema Jones
Candice Lynch
Jhanelle Markes
Rasheid Smith

For the summer session of 2013, the PI again visited Lincoln University to recruit students. The date was January 17, 2013. Accompanying the PI on this trip was Dr. Sherree Wilson, the recently appointed Associate Dean for Cultural Affairs and Diversity at the University of Iowa’s Carve College of Medicine. Both the PI and Dr. Wilson made presentations to the students at Lincoln. Fifteen applications were received and reviewed by the Admissions Committee, this year included Dr. Lubaroff, Dr. Heidger, Dr. Doman, Dr. Simons-Burnet, Dr. Swinton, and Dr. Karen Baskerville. Dr. Baskerville was added as an additional Faculty Advisor at Lincoln University, working closely with Dr. Derrick Swinton. Admission was offered to 8 students.

Students Accepted for the 2013 Program
Daniel Appeah
Precious de-Winton Cummings
Jodi-Ann Foster
Lehnae Linkins
Advance Preparation and Information Distribution:
Following acceptance of the students into the program we assigned each student a mentor based upon his/her choices listed in their applications. Each mentor then assigned a member of the lab as a “big brother/big sister,” a person that partners with the student during the 8 week summer session. The mentor also prepared a portfolio of articles covering the area of research the student would be working on, including published papers by the mentor. These materials were sent to the students in advance of their arrival at the University of Iowa.

In 2012 a six week course on Prostate Cancer was organized with six faculty assigned to deliver lectures. The following represents the course schedule with lecturers:

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Key Research Accomplishments

Each of the students worked on research projects that were part of an overall program within the laboratory of their mentors. As such, it is difficult to identify key research accomplishments for each student research project. Continuation of the research program by each mentor will certainly produce important research findings, aided in part by the summer research of the Lincoln University students. What is key is the mentoring and counseling of the students to aid in their future as scientists in the area of prostate cancer research. The high percentage of the students that are graduate programs or medical schools is an outstanding accomplishment as these future scientists will most certainly provide key research accomplishments in the years to come.

Reportable Outcomes:

The students have reported their findings to the University of Iowa faculty, to the faculty and students at Lincoln University, and at national competitions and conferences.
Conclusion

This award was highly successful as evidenced by the amount of work accomplished by each student and by their motivation to continue in a science career. The PI applied, and received funding, for additional HBCU training grants that will enable us to continue accepting students for a number of years, thus increasing the number of African American scientists in the area of prostate cancer.

Appendices: Brochures for 2012 and 2012
2012 Prostate Cancer Research Summer Training Program

A Collaboration Between the University of Iowa and Lincoln University of Pennsylvania

Students in the 2011 Program
**Summary of Program:** The partnership of the University of Iowa and Lincoln University is designed to provide an outstanding atmosphere to train undergraduate students from Lincoln in prostate cancer research. We propose to have fifteen mentors available for each of the trainees to choose from for their summer research project. The mentors are from seven departments and three colleges at the University of Iowa and the prostate cancer research in their laboratories covers a wide area of interest. The proposed mentors have extensive training experience at all levels; undergraduate, graduate, medical, and postdoctoral.

In addition to the fifteen faculty mentors both the University of Iowa and Lincoln University have designated Faculty Advisors for the students. Dr. Paul Heidger serves as the advisor at the University of Iowa and Dr. Derrick Swinton serves as the advisor at Lincoln University. Both individuals are available for advice and assistance throughout the summer and the regular academic year. The faculty members are listed below as well as a brief description of research in the laboratories of each University of Iowa mentor.

At this point in time the program is 8 weeks long, beginning on Monday, June 4, 2012 and ending on Friday, July 27, 2012.

**Faculty Advisor at Lincoln University:** Derrick Swinton, PhD.; Associate Professor, Department of Analytical Chemistry (610- 932-8300, ext.3470)  
http://www.lincoln.edu/chemistry/swinton.html

**University of Iowa Faculty and Their Research**

**Director and Research Mentor:** David Lubaroff, PhD; Professor, Department of Urology & Director of the Summer Research Program (319-335-8423)  

The work in this laboratory concentrates on the area of tumor immunology with an emphasis on immunotherapy. We have constructed microbial vaccines to be used for the investigation of gene and immunotherapy of prostate cancer. Investigations on the ability of immunized animals to produce immune responses to the transgene product induced by the vaccine are underway. Additionally, we are carrying our "translational" research in the form of clinical trials of our adenovirus vaccine in men with prostate cancer. Important in these trials is the safety of the vaccine and its ability to induce anti-tumor immunity. We have recently completed a Phase I clinical trial of the vaccine that demonstrated its safety. We have initiated a therapeutic Phase II trial. Finally, we have been collaborating on studies of psychosocial effects on immune status in cancer patients.

**Faculty Advisor:** Paul Heidger, PhD; Professor, Dept. of Anatomy & Cell Biology (319-335-7722)  
http://www.anatomy.uiowa.edu/personnel.shtml?id=heidger

Dr. Heidger will assist in the recruitment and evaluation of summer students and will assist students in career planning.

**Research Mentors**

Elizabeth Chrischilles, PhD; Professor, Department of Epidemiology (319-384-5009)  
http://www.public-health.uiowa.edu/faculty-staff/faculty/directory/faculty-detail.asp?emailAddress=e-chrischilles@uiowa.edu

Dr. Chrischilles directs the Health Effectiveness Research Center (HERCe) (www.public-health.uiowa.edu/herec/), a collaborative research enterprise between the Department of Epidemiology and the College of Pharmacy at the University of Iowa. HERCe focuses on understanding the reasons for and consequences of treatment variation in clinical practice. It is a center for research, learning, and education that is comprised of epidemiologists, economists, biostatisticians, clinicians, database specialists, geographers, and graduate students from colleges and departments across campus. Areas of expertise include conceptualization and measurement of preventive care and treatments from retrospective data; methodologies for addressing treatment selection bias including instrumental variables and direct statistical and design control for confounding; population-based sampling; analysis of complex sample surveys and longitudinal data; geographical analysis of healthcare access; data linkage and application of encryption methodologies to maintain confidentiality; and synthesis of drug information to evaluate medication safety. Examples of HERCe research include recent publications on breast cancer treatments, complications of chemotherapy for lymphoma patients, invasive treatments for acute myocardial infarction, and an evaluation of the Iowa Medicaid Pharmaceutical Case Management program.

Frederick Domann, PhD; Professor, Dept. of Radiation Oncology. (319-335-8018)  
http://www.uiowa.edu/~frrbp/domann_lab.html

The Domann laboratory is predominantly interested in the regulation of gene expression in cancer that does not involve classical changes in the DNA sequence, but rather is mediated through so-called “epigenetic” events. These include DNA methylation, histone modifications that affect DNA accessibility, and chromatin conformational changes that render genes available or unavailable for efficient
transcription. During a typical summer research experience the undergraduate student would learn how to develop and test a scientific hypothesis related to a fundamental question in cancer research using state of the art techniques and approaches. Methods learned would include human cell culture, nucleic acid extraction, conventional PCR, reverse-transcriptase-PCR to measure mRNA, real-time quantitative PCR, DNA sequencing, DNA methylation analysis, western blotting, enzyme assays, and molecular cloning. The student would become proficient at the techniques through daily interactions with laboratory staff. In addition, the student would become familiar with the theory behind each technique and interpretation of their laboratory results through twice weekly meetings with Professor Domann. It is the goal of this research experience to allow the student the opportunity to participate in larger ongoing research projects in the lab in a substantive way so that he or she can contribute to a publication

**Michael Henry, PhD; Associate Professor, Department of Physiology & Biophysics (319-335-7886)  
http://www.physiology.uiowa.edu/henry.shtml?menu=1&tab=facultyTab**

Research in the Henry laboratory is geared toward understanding the molecular and cellular biology underlying the spread of cancer cells from the prostate to other vital organs such as bone, liver and lung. They have developed animal models of prostate cancer metastasis that employ bioluminescence imaging to visualize metastatic cancer cells in living animals. A summer research project would be to engineer and characterize a prostate cancer cell line for expression of the firefly luciferase gene so that it might be used in our animal models.

**Siegfried Janz, MD; Professor, Department of Pathology (319-384-2869)  
http://www.healthcare.uiowa.edu/pathology/site/faculty/janz/janz.html**

Siegfried Janz’ primary research interest concerns mouse models of human B cell and plasma cell neoplasms that are induced by the deregulated expression of the cellular oncogene MYC (c-myc). His laboratory has recently generated gene-insertion mice that mimic three different states of the human genetic alterations. He is now developing genetic methods for the detection of the homologous Myc-activating translocations in mice. As leader of the Cancer Genetics and Computational Biology Program at the Holden Comprehensive Cancer Center, he is also actively engaged in research on human blood cancers.

**Yi Luo, MD, PhD; Associate Professor, Department of Urology (319-335-9835)  

A major research project in our laboratory is to develop a novel therapeutic strategy to cope with the limitations of the current modalities for prostate cancer treatment. We will use prostate-specific antigen (PSA), a protein known to be aberrantly expressed in prostate cancer, as a target for immunotherapy of prostate cancer. In fact, PSA has been demonstrated to be a useful immunotherapeutic target in clinical trials as well as in animal models. In addition, PSA has also been demonstrated to be antigenic and capable of inducing specific immune responses in both humans and mice. However, up to date, all currently available PSA-targeted immunotherapies have only demonstrated limited antitumor effects. To improve this immunotherapeutic approach, we will use both bacillus Calmette-Guérin (BCG, a bacterial vaccine strain) and adenovirus (Ad, a replication-defective strain) to deliver PSA for animal immunization. Both BCG and Ad microbes have been demonstrated to be safe and effective for antigen delivery in humans and mice. Since these two microbes are known to be different in their infectious modes and host anti-infection responses, rationally combined use of BCG and Ad recombinants for vaccination will provide a synergistic/complementary immune induction and thus likely result in enhanced antitumor immunity. Indeed, we have previously observed a robust induction of PSA-specific T cell responses by vaccination with combined BCG-PSA (primer vaccine) and Ad-PSA (booster vaccine) in mice. In this study, we will further evaluate the effects of this vaccination method on preventing or treating experimental prostate tumors. The objective of this study is to provide a proof of principle that enhanced antitumor immunity can be achieved by combined vaccination with BCG and Ad recombinants.

**Lyse Norian, PhD; Assistant Professor, Department of Urology (319-335-3013)**

Dr. Norian’s research is focused on developing novel, highly efficacious combinatorial anti-tumor immunotherapies by utilizing pre-clinical models that accurately reflect the diverse physiologies of cancer patients. To accomplish this, it will be imperative to explore and understand interactions between the immune system and other organ systems, particularly as they relate to anti-tumor immunity. Therefore, her investigations focus not only on the inter-relationships between positive and negative immune cell populations, but also on how the microenvironment of different organ sites impacts anti-tumor immunity. Dr. Norian has developed a robust pre-clinical murine model of metastatic renal cell carcinoma, as well as a...
model of metastatic prostate cancer, and now plans to use these models to investigate mechanisms of site-specific tumor-induced dysfunction in dendritic cells and T cells. She has previously worked with a Lincoln student in collaboration with Drs. Lubaroff and Salem during the summer of 2010.

Aliasger K. Salem, PhD; Associate Professor, Division of Pharmaceutics, College of Pharmacy (319-335-8810) [http://www.pharmacy.uiowa.edu/pharmaceutics/people/Salem.htm](http://www.pharmacy.uiowa.edu/pharmaceutics/people/Salem.htm)

Dr. Salem's research interests are primarily focused on self-assembling systems, the rational design of novel drug and gene delivery systems and on the development of sophisticated scaffolds for tissue-specific regeneration. In tissue engineering, Dr. Salem's laboratory applies microfabrication techniques to novel biomaterials to provide spatial control over tissue formation and to integrate minimally invasive scaffold delivery strategies. In drug/gene delivery, he is currently exploring the synergistic application of degradable particle technology, CpG oligonucleotides and heat shock proteins for generating sustained immunotherapeutic responses against cancer. Dr. Salem’s laboratory also collaborates with Dr. Lubaroff on the use of microparticles in association with cancer vaccines for the induction of strong anti-tumor immune responses and tumor destruction.

Michael Schultz, PhD; Assistant Professor, Department of Radiology (319-356-4159) [http://www.medicine.uiowa.edu/Radiology/faculty-staff/faculty/schultz-michael.html](http://www.medicine.uiowa.edu/Radiology/faculty-staff/faculty/schultz-michael.html)

Dr. Schultz’s laboratory is interested in exploring cell-surface protein expression (e.g., G-coupled protein receptors) that is amplified in specific cancer cell lines and developing peptide- and RNA-aptamer-based molecular targeting mechanisms for delivering radionuclides specifically to the site of cancerous tissue in the body. Examples of Dr. Schultz’s research include the development of novel radiolabeled peptide-analogs of neupeptide Y (NPY) that are designed to bind with high affinity to neupeptide Y subtype 2 receptors (Y2). In a second example of Schultz laboratory research, an ribonucleic acid (RNA) compound (known as an aptamer) has been synthesized that binds tightly to a cell surface protein receptor (referred to as PSMA) whose expression is amplified on the surface of prostate cancer cells relative to normal cells. Through the development of a novel chelator derivative, Dr. Schultz and colleagues are able to radiolabel the aptamer for imaging by PET. These exciting imaging agents serve not only as high resolution probes for evaluating the location and extent of disease, but also pave the way for the development of molecularly-guided therapeutic agents that hold promise in the development of curative approaches to these enigmatic cancers.

Andreas Simons-Burnett, PhD; Assistant Professor, Department of Radiation Oncology (319-384-4450)

Dr. Simons-Burnett has been an active participant in the summer program, previously acting as a “big sister” to students while a member of Dr. Douglas Spitz’s laboratory. Her research interests include metabolic oxidative stress in tumors and the role oxidative stress plays in signal transduction pathways. Her current interests focus on the EGFR/PI3K/Akt signaling pathway and its involvement with NADPH oxidase activation, glucose metabolism and autophagy in cancer. Additionally she is interested in investigating novel combined modality therapies that target the EGFR/PI3K/Akt pathway and how one can predict sensitivity to these therapies in cancer disease sites.

Elaine Smith, PhD; Professor, Department of Epidemiology, College of Public Health (319-384-5014)

Dr. Smith, a recent addition to our mentors, is a Professor of Epidemiology in the College of Public Health. She has a number of research interests that will benefit training of our summer students. These include etiology of oncogenic diseases, focused on molecular epidemiology, HPV effects on the development of genital and other cancers; hormones and risk of HPV detection and replication; HPV and perinatal vertical transmission, head and neck cancers and reproductive diseases: HPV and vestibulitis; prostate cancer risk associated with pesticides and sex steroid hormone alterations.

Douglas Spitz, PhD; Professor, Department of Radiation Oncology (319-335-8001) [http://www.uiowa.edu/~frrbp/spitz_lab.html](http://www.uiowa.edu/~frrbp/spitz_lab.html)

Research in the Spitz laboratory is concentrated on the role of free radicals and oxidative events in cancers. For example, combinations of inhibitors of glucose metabolism, 2-deoxy-D-glucose (2-DG), and of hydroperoxide detoxification, dehydroisoandrosterone (DHEA) and L-buthionine sulfoximine (BSO), have been shown to be effective in killing human tumor cells via oxidative stress. 2-DG has also been shown to increase radiosensitivity in human cancer cells both in vitro and in vivo. These results have led us to test the ability of 20 mM 2-DG + 300 μM DHEA + 1 mM BSO to induce radiosensitization following exposure to 4 Gy ionizing radiation. Clonogenic survival was used as the parameter indicative of cytotoxicity. Prostate cancer cells (PC-3) treated with 2-DG or DHEA alone as well as the combinations of
2-DG + DHEA, 2-DG + BSO, DHEA + BSO, or 2-DG + DHEA + BSO all demonstrated some degree of radiosensitization, and the effect was most pronounced in the group treated with 2-DG + DHEA + BSO, relative to the other combinations (< 2% survival in the 2-DG + DHEA + BSO group versus > 5% with other agents). In another human prostate cancer cell line, DU145, 2-DG + DHEA + BSO also resulted in substantially enhanced radiosensitization when compared to any of the other combinations. These results support the hypothesis that the combining inhibitors of glucose metabolism with inhibitors of hydroperoxide detoxification increases radiation sensitivity in human cancer cells.

George Weiner, MD; Professor, Department of Internal Medicine and Director, Holden Comprehensive Cancer Center (319-353-8620)
http://www.healthcare.uiowa.edu/Labs/Weiner/

The laboratory of Dr. George Weiner focuses on exploring methods to enhance the efficacy of monoclonal antibody therapy of cancer. Preclinical and clinical studies are exploring the relative role of various effector cells in antibody dependent cellular cytotoxicity, how complement impacts on the efficacy of monoclonal antibody therapy and how therapy can be improved. Dr. Weiner’s laboratory is also evaluating the use of other immunotherapy agents such as immunostimulatory CpG oligodeoxynucleotides (CpG ODN). He works closely with Dr. Brian Link who leads the clinical research aspects of their collaborative research program. Dr. Weiner is the Director of the University of Iowa Holden Comprehensive Cancer Center, and of the Iowa/Mayo Clinic Specialized Program of Research Excellence (SPORE) in lymphoma. He is also the principal investigator of additional research grants from the National Cancer Institute and the Leukemia and Lymphoma Society in the field of immunotherapy of cancer.

Nicholas Zavazava, MD, PhD; Professor, Department of Internal Medicine (319-384-6577)
http://www.intmed.uiowa.edu/Divisions/Immunology/Directory/NicholasZavazava.html

Research in the Zavazava laboratory is devoted to the characterization of primate embryonic stem cells. The motivation for this emphasis is that cancer appears to originate from cancer stem cells. These cancer cells have not been well characterized, but appear to share basic characteristics with embryonic stem cells, for example the property of uncontrolled growth. Characterization of these cells will some day lead to better treatment of cancer. Our laboratory is interested in characterizing primate embryonic stem cells and understanding their properties that allow self renewal and immune evasion. Further, the lab is interested in differentiating these cells in vitro into T cells that could be used for the treatment of cancer in the in vivo situation.
Research Facilities - The research laboratories of the faculty mentors at the University of Iowa are located on the west side of Iowa City on the Health Sciences Campus. The facilities include the Medical Laboratories, Bowen Sciences Building, Pharmacy Building, UI General Hospital, Medical Education and Biomedical Research Facility, and the Veterans Affairs Medical Center. Support for the research is provided by a large number of Shared Core Facilities that include the Gene Transfer Vector Core, DNA Core, Flow Cytometry Core, to name but a few. For research that includes laboratory animals, professional, humane veterinary care is provided by the Animal Care Facilities of the University of Iowa and the Veterans Affairs Medical Center.

Opportunities for Learning - Students will have a large number of opportunities to learn about research, prostate cancer, and cancer in general. These include meeting with other members of the HBCU SRT and mentors, joint laboratory meetings with other investigators collaborating with the mentor, journal clubs, and a six-week course designed to educate the students about prostate cancer, its origins, genetics, epidemiology, and treatment.

Living in Iowa City for the Summer

Housing and Meals - All students will be housed in the Mayflower Residence Hall on the Campus of the University of Iowa. It is conveniently located on the northern edge of the campus and is served by the free Cambus transportation system. The Mayflower has kitchen facilities and double air conditioned rooms. The living quarters are also across the Iowa River from the Iowa City Park.

Arrival and Welcome – For the 8 week program, students will be expected to arrive on Sunday, June 3, 2012. Flights by most major airlines are available to the Cedar Rapids Eastern Iowa Airport (CID). These include American, Delta, and United Airlines. A welcoming barbecue will be held on Sunday, June 3rd with members of other summer research programs that include the Iowa Biosciences Advantage, and the Student Summer Research Opportunities Program.

Activities In and Around Iowa City - There are a number of activities in the Iowa City Area that students can find during the summer research program. These include, but are not limited to, the following:

Friday and Saturday Night Concert Series – Free musical concerts held each Friday and Saturday night from 6:30 to 9:30 pm on the downtown Pedestrian Mall.

Iowa City Jazz Festival – A free, three-day jazz concert featuring local, regional, and national jazz groups during the July 4th celebration. The festival will be held on the Pentacrest on the campus of the University of Iowa.

Thursday Night Concerts in Coralville – These musical concerts, held in Morrison Park in the adjacent town of Coralville, IA, are also free and open to the public.

Saturday Night Free Movies Series – This is the newest addition to Iowa City's long tradition of free, outdoor family-friendly entertainment that literally brings our community together. It is held outdoors on the Pentacrest from June through August.

Other Activities – there are a large number of indoor & outdoor activities that can be accessed through the Cities of Iowa City and Coralville and the University of Iowa. These include exercise facilities (running, tennis, basketball, volleyball, handball/racquetball, weights, biking, and swimming), local beaches, and museums (art, natural history, and sports). In addition, there are a large number of restaurants ranging from fast food to fine dining.

Application to the Program - Application forms, distributed with this brochure, must be completed and returned either to Dr. Swinton at Lincoln University or to Dr. Lubaroff at the University of Iowa. The deadline for submission is March 2, 2012. A committee composed of Dr. Swinton, Dr. Lubaroff, Dr. Heidger and two additional faculty from the University of Iowa will meet and make final decisions. Students will be notified of the decisions no later than March 16, 2012 pending prompt receipt of all applications.

Financial Support - The housing, meal, and transportation costs will be paid by the program. In addition, each student will be provided a stipend, the amount of which is currently being negotiated with the University of Iowa and Lincoln University.

For additional information please contact one of the following:

David Lubaroff, PhD, Department of Urology, University of Iowa, 375 Newton Road, 3209 MERF, Iowa City, IA 52242; 319-335-8425; david-lubaroff@uiowa.edu

Paul Heidger, PhD, Department of Anatomy & Cell Biology, University of Iowa, 51 Newton Road, Iowa City, IA 52242; 319-335-7722; paul-heidger@uiowa.edu

Derrick Swinton, PhD, Department of Analytical Chemistry, Lincoln University, 1570 Baltimore Pike, Lincoln University, PA 19352; 610-932-8300, ext. 3470; dswinton@lincoln.edu

Diane Morman, Program Coordinator, Department of Urology, University of Iowa, 375 Newton Road, 3209 MERF, Iowa City, IA 52242; 319-335-8425; diane-morman@uiowa.edu
2013
Prostate Cancer Research
Summer Training Program

A Collaboration Between the University of Iowa and Lincoln University of Pennsylvania

Students in the 2012 Program
Summary of Program: The partnership of the University of Iowa and Lincoln University is designed to provide an outstanding atmosphere to train undergraduate students from Lincoln in prostate cancer research. We propose to have sixteen mentors available for each of the trainees to choose from for their summer research project. The mentors are from seven departments and three colleges at the University of Iowa and the prostate cancer research in their laboratories covers a wide area of interest. The proposed mentors have extensive training experience at all levels; undergraduate, graduate, medical, and postdoctoral.

In addition to the sixteen faculty mentors both the University of Iowa and Lincoln University have designated Faculty Advisors for the students. Dr. Paul Heidger serves as the advisor at the University of Iowa and Dr. Derrick Swinton serves as the advisor at Lincoln University. Both individuals are available for advice and assistance throughout the summer and the regular academic year. The faculty members are listed below as well as a brief description of research in the laboratories of each University of Iowa mentor.

At this point in time the program is 8 weeks long, beginning on Monday, June 10, 2013 and ending on Friday, August 2, 2013.

Faculty Advisor at Lincoln University: Derrick Swinton, PhD.; Professor and Chair, Department of Chemistry (484-365-7470)  
http://www.lincoln.edu/chemistry/index.html

Dr. Swinton is the contact person for the summer program at Lincoln University. He is active in the recruitment, retention, and career planning for our summer students. He also visits the University of Iowa during the program.

University of Iowa Faculty and Their Research

Director and Research Mentor: David Lubaroff, PhD; Professor, Department of Urology & Director of the Summer Research Program (319-335-8423)  
http://www.medicine.uiowa.edu/dept_primary.aspx?appointment=Urology&id=907659

The work in this laboratory concentrates on the area of tumor immunology with an emphasis on immunotherapy. We have constructed microbial vaccines to be used for the investigation of gene and immunotherapy of prostate cancer. Investigations on the ability of immunized animals to produce immune responses to the transgene product induced by the vaccine are underway. Additionally, we are carrying our "translational" research in the form of clinical trials of our adenovirus vaccine in men with prostate cancer. Important in these trials is the safety of the vaccine and its ability to induce anti-tumor immunity.

We have recently completed a Phase I clinical trial of the vaccine that demonstrated its safety. We have initiated a therapeutic Phase II trial. Finally, we have been collaborating on studies of psychosocial effects on immune status in cancer patients.

Faculty Advisor: Paul Heidger, PhD; Emeritus Professor, Dept. of Anatomy & Cell Biology (319-335-7722)  
http://www.anatomy.uiowa.edu/personnel.shtml?id=heidgerp

Dr. Heidger will assist in the recruitment and evaluation of summer students and will assist students in career planning.

Research Mentors

James Brown, MD. Professor, Department of Urology (319-353-8702)  
http://www.medicine.uiowa.edu/dept_primary.aspx?appointment=Urology&id=296546

Dr. Brown’s clinical practice and research interests focus on urologic oncology, with specific interest in minimally invasive procedures, new techniques, and outcomes. Dr. Brown initiated many of the laparoscopic and robotic programs at his former institution, the Medical College of Georgia, and currently serves as Chair of the urology research protocols evaluation committee. He is the Residency Program Director in the Department of Urology and has trained a large number of individuals that include resident physicians, medical students, and undergraduate students. Dr. Brown’s research interest include molecular epidemiology and pathology of urologic cancers.

Frederick Domann, PhD; Professor, Dept. of Radiation Oncology. (319-335-8018)  
http://www.uiowa.edu/~frrbp/domann_lab.html

The Domann laboratory focuses on how chromatin structure participates in the transcriptional regulation of cancer related genes including oncogenes and tumor suppressor genes. They study the molecular mechanisms by which aberrant cytosine methylation of CpG dinucleotides and post-translational modifications on histones affect gene expression during the development and progression of cancer. A gene of particular interest in their laboratory is the tumor suppressor gene SOD2 that encodes the antioxidant enzyme superoxide dismutase. The lab is also assessing chromatin accessibility in the region of the SOD2 promoter in cells that differentially express the gene. They are currently using conditional knockout mice to study how the loss of SOD2 leads to various pathological conditions, particularly cancer. Future research directions will be aimed at
elucidating the role of cytosine methylation as a mechanism for inactivation of other genes involved in protection against oxidative damage as well as other classical tumor suppressor genes, and to elucidate the mechanism(s) by which CpG methylation can bring about these changes in gene expression.

Paloma Giangrande, PhD; Assistant Professor, Department of Internal Medicine (319-384-3242)  
http://www.int-medi.uiowa.edu/Divisions/HemOnc/Directory/PalomaGiangrande.html

The long-term research goals of the Giangrande laboratory are to develop RNA-based tools to modulate cellular pathways underlying pathological cell proliferation in the setting of cancer. Current efforts are focused on selecting RNA aptamers to receptors expressed on the surface of target cells with SELEX (Systematic Evolution of Ligands by Exponential Enrichment) for the purpose of (1) modulating receptor function and/or (2) delivering therapeutic molecules (e.g. siRNAs, antimirs, small molecule drugs) into specific cell types. Emerging interests include the development of diagnostic tools for imaging cancers and cardiovascular disease in vivo. The lab approaches these goals using both cell-based and animal models of disease progression and in collaboration with clinicians in the Pathology, Urology and Oncology Departments at the University of Iowa and other institutions. A major project in the lab is targeted therapy of prostate cancer using PSMA-guided aptamers.

Prabhat Goswami, PhD; Professor, Department of Radiation Oncology (319-384-4666)  
http://www.uiowa.edu/~frrbp/goswami.html

Dr. Goswami is an expert in the redox biology of the cell cycle research. He is well known for his innovative concept of a “redox cycle within the cell cycle”, linking oxidative metabolic processes to cell cycle regulatory processes. He demonstrated that a “ROS-Switch” regulates transitions between quiescent and proliferative growth states; a superoxide-signaling regulates proliferation and a hydrogen peroxide-signaling supports quiescence. Dr. Goswami is an active member of the Holden Comprehensive Cancer Center (HCCC) of The University of Iowa. He is the Co-director of the Radiation and Free Radical Research Core of the HCCC and he supervises the Radiation Core facility. Dr. Goswami has served as an ad hoc reviewer in ten NIH Study Sections including a P01 review. He has also served as a scientific reviewer for the DOD, DOE, NASA, RSNA, and Komen Breast Cancer Foundation. Dr. Goswami has published 68 peer reviewed publications and successfully trained 7 PhD graduate students and 3 postdoctoral fellows. Dr. Goswami is currently mentoring 2 PhD, 1 M2, and 2 undergraduate students. Dr. Goswami is a faculty member in the Interdisciplinary Molecular and Cellular Biology, and Human Toxicology Graduate Programs.

Michael Henry, PhD; Associate Professor, Department of Physiology & Biophysics (319-335-7886)  
http://www.physiology.uiowa.edu/henry.shtml?menu=1&tab=facultyTab

The long term research goals of the Henry laboratory are to understand the molecular and cellular basis of prostate cancer progression and metastasis in order to develop new methods for the diagnosis and treatment of this disease. Current efforts are focused on the role of a cell-matrix receptor dystroglycan and epithelial-mesenchymal transition in this process. The lab approaches this problem using both cell-based and animal models of disease progression. Emerging interests include how physiological and environmental components interact with central genetic pathways related to disease progression, including the influence of diet-induced obesity. Dr. Henry has extensive experience in basic mechanisms of cell signaling and cancer biology as well as drug discovery and development both in industry and academic settings. His expertise extends from elucidating basic signaling pathways related to cancer progression to various approaches for therapeutic intervention in these pathways including large molecule-targeted delivery of anticancer agents and discovery of small molecule drugs.

Yi Luo, MD, PhD; Associate Professor, Department of Urology (319-335-9835)  

A major research project in our laboratory is to develop a novel therapeutic strategy to cope with the limitations of the current modalities for prostate cancer treatment. We will use prostate-specific antigen (PSA), a protein known to be aberrantly expressed in prostate cancer, as a target for immunotherapy of prostate cancer. In fact, PSA has been demonstrated to be a useful immunotherapeutic target in clinical trials as well as in animal models. In addition, PSA has also been demonstrated to be antigenic and capable of inducing specific immune responses in both humans and mice. However, up to date, all currently available PSA-targeted immunotherapies have only demonstrated limited antitumor effects. To improve this immunotherapeutic approach, we will use both bacillus Calmette-Guérin (BCG, a bacterial vaccine strain) and adenovirus (Ad, a replication-defective strain) to deliver PSA for animal immunization. Both BCG and Ad microbes
have been demonstrated to be safe and effective for antigen delivery in humans and mice. Since these two microbes are known to be different in their infectious modes and host anti-infection responses, rationally combined use of BCG and Ad recombinants for vaccination will provide a synergistic/complementary immune induction and thus likely result in enhanced antitumor immunity. Indeed, we have previously observed a robust induction of PSA-specific T cell responses by vaccination with combined BCG-PSA (primer vaccine) and Ad-PSA (booster vaccine) in mice. In this study, we will further evaluate the effects of this vaccination method on preventing or treating experimental prostate tumors. The objective of this study is to provide a proof of principle that enhanced antitumor immunity can be achieved by combined vaccination with BCG and Ad recombinants.

Lyse Norian, PhD; Assistant Professor, Department of Urology (319-335-3013)  
http://www.medicine.uiowa.edu/dept_primary.aspx?appointment=Urology&id=569305

The Norian laboratory studies the causes of tumor-induced immune dysfunction in the presence and absence of obesity and the use of immunotherapies to treat cancers. Immunotherapy is a promising approach for the treatment of advanced solid tumors, but progress in this area is impeded by the fact that growing tumors suppress protective immunity in a variety of ways. Dr. Norian uses cellular and molecular techniques to explore the nature of tumor-derived dendritic cell (DC) and T cell functional deficiencies. Long-term goals are to develop novel, immune-based therapies for advanced solid tumors, using the knowledge we gain from our pre-clinical studies. Because her goal is to ultimately apply findings to the clinical setting, she is also interested in understanding how co-morbidities such as obesity impact protective immune responses in the presence and absence of tumor growth. Due to her affiliation with the Department of Urology, the laboratory has access to clinicians and human samples that can help translate murine studies into clinical application. Murine tumor models routinely used include: metastatic renal cell carcinoma (Rena), localized and metastatic prostate cancer (RM-11), spontaneous breast cancer (NeuT), metastatic breast cancer (4T1), and localized fibrosarcoma (CMS5). The use of multiple models helps to substantiate findings across multiple murine models.

Aliasger K. Salem, PhD; Associate Professor, Division of Pharmaceutics, College of Pharmacy (319-335-8810)  
http://www.pharmacy.uiowa.edu/pharmaceutics/people/Salem.htm

Dr. Salem's research interests are primarily focused on self-assembling systems, the rational design of novel drug and gene delivery systems and on the development of sophisticated scaffolds for tissue-specific regeneration. In tissue engineering, Dr. Salem's laboratory applies microfabrication techniques to novel biomaterials to provide spatial control over tissue formation and to integrate minimally invasive scaffold delivery strategies. In drug/gene delivery, he is currently exploring the synergistic application of degradable particle technology, CpG oligonucleotides and heat shock proteins for generating sustained immunotherapeutic responses against cancer. Dr. Salem's laboratory also collaborates with Dr. Lubaroff on the use of microparticles in association with cancer vaccines for the induction of strong anti-tumor immune responses and tumor destruction.

Michael Schultz, PhD; Assistant Professor, Department of Radiology (319-356-4159)  
http://www.medicine.uiowa.edu/Radiology/faculty-staff/faculty/schultz-michael.html

Dr. Schultz is a tenure track Assistant Professor at the University of Iowa in the Department of Radiology and a subject matter expert in the molecular design, organic synthesis, characterization, and radiolabeling of peptides and small molecules for small molecule cancer therapy, molecular imaging, and radionuclide therapy for cancer. He has participated in the Lincoln University program for three years and enjoys bringing the students into his lab and mentoring them for the summer session. Dr. Schultz feels that the students bring enthusiasm and provide an excellent opportunity for his graduate researchers to practice mentoring skills and begin to understand the process of teaching science. He has been very pleased with the contribution that the students make to the research efforts of his laboratory. Thus, he finds the program to be highly beneficial to his laboratory and looks forward to further opportunities to participate. The Schultz lab also works to identify key cell-surface receptor residues as targets for novel peptide- and aptamer-based receptor agonists and antagonists — and become proficient in manipulating the molecular characteristics of these targeting vectors in order to optimize their pharmacokinetic and biodistribution properties for imaging and therapy of cancer. An active collaboration exists between Drs. Schultz and Giangrande.
H2O2 was capable of inducing genomic instability and producing much greater levels of O2•- and H2O2, his lab also showed that tumor cell mitochondria were mediated by mitochondrial O2•- and H2O2. In this work cancer vs. normal cells by metabolic oxidative stress discover that glucose deprivation preferentially killed cancer therapy. His laboratory was also the first to cellular resistance to oxidative stress associated with gene amplification that resulted in a large increase chronic exposure of mammalian cells to O2•- and Dr. Spitz’s laboratory. Her research interests include metabolic oxidative stress in tumors and the role oxidative stress plays in signal transduction pathways. Her current interests focus on the EGFR/Pi3K/Akt signaling pathway and its involvement with NADPH oxidase activation, glucose metabolism and autophagy in cancer. Additionally she is interested in investigating novel combined modality therapies that target the EGFR/Pi3K/Akt pathway and how one can predict sensitivity to these therapies in cancer disease sites.

Dr. Simons-Burnett has been an active participant in the summer program, previously acting as a “big sister” to students while a member of Dr. Douglas Spitz’s laboratory. Her research interests include etiology of oncogenic diseases, focused on molecular epidemiology, HPV effects on the development of genital and other cancers; hormones and risk of HPV detection and replication; HPV and perinatal vertical transmission, head and neck cancers and reproductive diseases: HPV and vestibulitis; prostate cancer risk associated with pesticides and sex steroid hormone alterations.

Dr. Smith, a recent addition to our mentors, is a Professor of Epidemiology in the College of Public Health. She has a number of research interests that will benefit training of our summer students. These include etiology of oncogenic diseases, focused on molecular epidemiology, HPV effects on the development of genital and other cancers; hormones and risk of HPV detection and replication; HPV and perinatal vertical transmission, head and neck cancers and reproductive diseases: HPV and vestibulitis; prostate cancer risk associated with pesticides and sex steroid hormone alterations.

Dr. Spitz’s laboratory was the first to discover that chronic exposure of mammalian cells to O2•- and H2O2 was capable of inducing genomic instability and gene amplification that resulted in a large increase cellular resistance to oxidative stress associated with cancer therapy. His laboratory was also the first to discover that glucose deprivation preferentially killed cancer vs. normal cells by metabolic oxidative stress mediated by mitochondrial O2•- and H2O2. In this work his lab also showed that tumor cell mitochondria were producing much greater levels of O2•- and H2O2, relative to normal cells and this apparent defect in cancer cell mitochondrial metabolism could be exploited for therapeutic purposes. This work continues to have a significant impact on the field cancer biology and therapy using ketogenic diets to enhance cancer therapy based on these basic science observations. He has also collaborated on the discovery of the role that Sirt3 plays in maintenance of mitochondrial oxidative metabolism during stress leading to malignant transformation and the fact that MnSOD is a target for Sirt3 activation during ionizing radiation-induced injury relevant to transformation and normal tissue damage during radiotherapy. Dr. Spitz is also a well-established mentor for trainees and junior faculty. He serves as the director of the Biosciences Graduate Program and the Free Radical and Radiation Biology Graduate Program at the University of Iowa as well as the director of the Radiation and Free Radical Research Core Laboratory and the Free Radical Cancer Biology Program in the Holden Comprehensive Cancer Center.

Dr. Tracy is a Clinical Assistant Professor in the Department of Urology. He will be working as a faculty member in the mentoring of trainees in prostate cancer research. He has extensive experience with prostate cancer surgery as it is one of the main areas of his clinical expertise. Currently, he performs more prostate cancer surgery than any other physician in the Department of Urology. Additionally, he has worked on several research projects within the department that focus on prostate cancer including having helped with the development of a prospective study on outcomes after prostatectomy. Dr. Tracy has, in addition, contributed patients for study of circulating tumor cells before and after prostatectomy, and, more recently, helped to develop a prospective study of antibiotic prophylaxis for use in the peri-procedural period surrounding prostate biopsy. Dr. Tracy is a new mentor in the summer program.

The laboratory of Dr. George Weiner focuses on exploring methods to enhance the efficacy of monoclonal antibody therapy of cancer. Preclinical and clinical studies are exploring the relative role of various effector cells in antibody dependent cellular cytotoxicity, how complement impacts on the efficacy of monoclonal antibody therapy and how therapy can be improved. Dr. Weiner’s laboratory is also evaluating the use of other immunotherapy agents such as immunostimulatory CpG oligodeoxynucleotides (CpG ODN). He works
closely with Dr. Brian Link who leads the clinical research aspects of their collaborative research program. Dr. Weiner is the Director of the University of Iowa Holden Comprehensive Cancer Center, and of the Iowa/Mayo Clinic Specialized Program of Research Excellence (SPORE) in lymphoma. He is also the principal investigator of additional research grants from the National Cancer Institute and the Leukemia and Lymphoma Society in the field of immunotherapy of cancer.

**Michael Wright, PhD:** Assistant Professor, Department of Molecular Physiology & Biophysics (319-384-1764)
http://www.physiology.uiowa.edu/wright.shtml?menu=1&tab=facultyTab

The laboratory of Dr. Wright is applying cutting-edge quantitative mass spectrometry technologies to study cellular signaling at the molecular level in model systems of disease. They are developing novel experimental workflows to globally profile proteins and delineate protein complexes isolated from cells and tissues using directed and targeted mass spectrometry methods. Dr. Wright is particularly interested in identifying post-translational modifications on proteins and determining how these modifications control the function, stability, and localization of proteins implicated in human diseases. He is determining how androgen-signaling pathways influence the pathophysiology of prostate cancer by building quantitative models of androgen-signaling at the level of proteins to understand how molecular effectors influence AR function before and after binding androgenic ligands. The lab is elucidating androgen-signaling networks at three primary levels: 1) mapping androgen-sensitive protein pathways, 2) mapping androgen-sensitive kinase pathways, and 3) identifying androgen receptor-interacting protein complexes in model cellular systems of prostate cancer. The group is also interested in identifying plasma glycoprotein biomarkers to distinguish indolent and aggressive prostate cancer in patients with organ-confined disease. Overall, the long-term goal of Dr. Wright’s research program is to identify prognostic and therapeutic biomarkers in the management and treatment of prostate cancer.

**Nicholas Zavazava, MD, PhD:** Professor, Department of Internal Medicine (319-384-6577)
http://www.int-med.uiowa.edu/Divisions/Immunology/Directory/NicholasZavazava.html

The Zavazava laboratory has recently discovered a novel protein, Ym1 which abrogates tumor growth in multiple tumors. They are currently trying to understand the mechanism by which NK cells are activated by this protein. The student from Lincoln will be immersed in these studies. Dr. Zavazava proposes to extend these studies to prostate cancer and determine if this protein can be used as a novel therapeutic agent. This lab has trained many trainees who have moved on to be leaders at a number of institutions. Others have moved on into Pharmaceutical industry. The work in the laboratory has been recognized with several Young Investigator Awards from the American Transplantation Congress. One of our abstracts was rated the best of all abstracts submitted at the 2009 American Transplantation Congress meeting in Boston. Dr. Zavazava currently supervises 3 postdoctoral fellows, 3 graduate students,
Research Facilities - The research laboratories of the faculty mentors at the University of Iowa are located on the west side of Iowa City on the Health Sciences Campus. The facilities include the Medical Laboratories, Bowen Sciences Building, Pharmacy Building, UI General Hospital, Medical Education and Biomedical Research Facility, Carver Biomedical Research Building, and the Veterans Affairs Medical Center. Support for the research is provided by a large number of Shared Core Facilities that include the Gene Transfer Vector Core, DNA Core, Flow Cytometry Core, to name but a few. For research that includes laboratory animals, professional, humane veterinary care is provided by the Animal Care Facilities of the University of Iowa and the Veterans Affairs Medical Center.

Opportunities for Learning - Students will have a large number of opportunities to learn about research, prostate cancer, and cancer in general. These include meeting with other members of the HBCU SRT and mentors, joint laboratory meetings with other investigators collaborating with the mentor, journal clubs, and a six-week course designed to educate the students about prostate cancer, its origins, genetics, epidemiology, and treatment.

Living in Iowa City for the Summer

Housing and Meals - All students will be housed in the Mayflower Residence Hall on the Campus of the University of Iowa. It is conveniently located on the northern edge of the campus and is served by the free Cambus transportation system. The Mayflower has kitchen facilities and double air conditioned rooms. The living quarters are also across the Iowa River from the Iowa City Park.

Arrival and Welcome – For the 8 week program, students will be expected to arrive on Sunday, June 9, 2013. Flights by most major airlines are available to the Cedar Rapids Eastern Iowa Airport (CID). These include American, Delta, and United Airlines. A welcoming barbecue will be held on Sunday, June 9th with members of other summer research programs that include the Iowa Biosciences Advantage, and the Student Summer Research Opportunities Program.

Activities In and Around Iowa City - There are a number of activities in the Iowa City Area that students can find during the summer research program. These include, but are not limited to, the following:

Friday and Saturday Night Concert Series – Free musical concerts held each Friday and Saturday night from 6:30 to 9:30 pm on the downtown Pedestrian Mall.

Iowa City Jazz Festival – A free, three-day jazz concert featuring local, regional, and national jazz groups during the July 4th celebration. The festival will be held on the Pentacrest on the campus of the University of Iowa.

Thursday Night Concerts in Coralville – These musical concerts, held in Morrison Park in the adjacent town of Coralville, IA, are also free and open to the public.

Saturday Night Free Movies Series – This is the newest addition to Iowa City's long tradition of free, outdoor family-friendly entertainment that literally brings our community together. It is held outdoors on the Pentacrest from June through August.

Other Activities – There are a large number of indoor & outdoor activities that can be accessed through the Cities of Iowa City and Coralville and the University of Iowa. These include exercise facilities (running, tennis, basketball, volleyball, handball/racquetball, weights, biking, and swimming), local beaches, and museums (art, natural history, and sports). In addition, there are a large number of restaurants ranging from fast food to fine dining.

Application to the Program - Application forms, distributed with this brochure, must be completed and returned either to Dr. Swinton at Lincoln University or to Dr. Lubaroff at the University of Iowa. The deadline for submission is March 1, 2013. A committee composed of Dr. Swinton, Dr. Lubaroff, Dr. Heidger and two additional faculty from the University of Iowa will meet and make final decisions. Students will be notified of the decisions no later than March 15, 2013 pending prompt receipt of all applications.

Financial Support - The housing, meal, and transportation costs will be paid by the program. In addition, each student will be provided a stipend, the amount of which is currently being negotiated with the University of Iowa and Lincoln University.

For additional information please contact one of the following:

David Lubaroff, PhD, Department of Urology, University of Iowa, 375 Newton Road, 3210 MERF, Iowa City, IA 52242; 319-335-8423; david-lubaroff@uiowa.edu

Paul Heidger, PhD, Department of Anatomy & Cell Biology, University of Iowa, 51 Newton Road, Iowa City, IA 52242; 319-335-7722; paul-heidger@uiowa.edu.

Derrick Swinton, PhD, Department of Analytical Chemistry, Lincoln University, 1570 Baltimore Pike, Lincoln University, PA 19352; 610-932-8300, ext. 3470; dswinton@lincoln.edu

Diane Morman, Program Coordinator, Department of Urology, University of Iowa, 375 Newton Road, 3209 MERF, Iowa City, IA 52242; 319-335-8425; diane-morman@uiowa.edu