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The South Carolina Collaborative Undergraduate HBCU Student Summer Training Program

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Background: There is a critical need to increase the racial/ethnic diversity of prostate cancer researchers. The goal of the Training Program is to provide research training activities to **12** students over a 3-year period from three Historically Black Colleges and Universities (HBCUs) in South Carolina: Claflin University, South Carolina State University, and Voorhees College. The three **aims** of the Training Program are: Aim 1.) To provide training in the basics of research design and methods to 12 Student Fellows each year from the three HBCUs; Aim 2.) To immerse 4 Student Fellows per year in prostate cancer research; Aim 3.) To implement a unique dual-level research mentoring strategy for the students. **Results:** During the current reporting period, 4 Student Fellows were identified, recruited to participate in the program, and admitted to the DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program. The Student Fellows were matched with Research Mentors at MUSC, with whom they conducted research in the summer of 2013. Each Student Fellow prepared a scientific paper, gave a scientific presentation at the end of the summer program, and completed a 9-week Princeton Review Graduate Record Examination Test Preparation Course. In the summer of 2013, students at SCSU participated in summer program lectures via videoconference. **Conclusions:** State-of-the art comprehensive prostate cancer research education and training opportunities were provided to **4** Student Fellows from HBCUs in South Carolina. Each Student Fellow prepared a scientific paper and gave at least 1 scientific presentation. Nine Student Fellows gave scientific presentations, two of which were presented at national scientific meetings. A cadre of scientists who are well-prepared to conduct research spanning the continuum from basic science to clinical science to population-based research was developed.

15. SUBJECT TERMS

Prostate Cancer Research Training Program

Summer Undergraduate Research Program (SURP)

Student Fellows from Historically Black Colleges and Universities (HBCUs)

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Table of Contents

	<u>Page</u>
Introduction.....	5
Body.....	6
Key Research Accomplishments.....	8
Reportable Outcomes.....	22
Conclusions.....	23
References.....	N/A
Appendices A-D.....	25
Appendix A: Ernest E. Just Symposium Agenda.....	27
Appendix B: Ernest E Just Symposium Student Attendees.....	30
Appendix C: Summaries of Students' Abstracts.....	32
Appendix D: Academic Accomplishments to Date.....	172

INTRODUCTION

The Scientific Context of the Training Program

The South Carolina Collaborative Undergraduate HBCU Student Summer Training Program (referred to as the Training Program) will provide a biomedical research training experience to 12 students over a three-year period (2012-2015) from three Historically Black Colleges and Universities (HBCUs) – Claflin University (CU), South Carolina State University (SCSU), and Voorhees College (VC). Undergraduate students from the three HBCUs (defined as Student Fellows) will participate in research intensive summer internships in the laboratories/research units of senior prostate cancer research scientists at the Medical University of South Carolina Hollings Cancer Center (MUSC HCC). This new Training Program application builds upon the success of the previously funded Department of Defense (DOD) prostate cancer research training program (2009-2011) and the long standing NIH funded Summer Undergraduate Research Training Program at MUSC (1992-present). The inter-institutional leadership of these summer training efforts have carefully examined the formative and summative evaluations provided by previous Student Fellows, Mentors, and Advisors in order to maximize the ability of this new enhanced program proposal to reach its ultimate goal – to increase the racial and ethnic diversity of emerging scientists who may choose prostate cancer research careers in basic, clinical, and population sciences. In this new application, the Training Program has been improved with a built-in, dual-level research and career mentoring strategy involving current graduate students and post-doctoral trainees included on the mentoring team; the addition of a clinical shadowing experience in the MUSC/HCC multidisciplinary genitourinary clinics and tumor board; more year-round opportunities for which the Student Fellows will participate; and an opportunity for Training Program alumni to continue relationships with new trainees going forward. Measurable outcomes of the Training Program will include the number of Student Fellows who take the Graduate Record Examination (GRE), apply to graduate school, and give scientific presentations and publish their research results in peer-reviewed scientific journals based on their summer research experience. Efforts will be made to capture long term outcomes as well as to determine how many Student Fellows choose to pursue a medical or biomedical focused graduate and post graduate career.

The three Specific Aims are to:

- Aim 1. To provide training in the basics of research design and methods to 12 Student Fellows each year from the three HBCUs;
- Aim 2. To immerse 4 Student Fellows per year in prostate cancer research;
- Aim 3. To implement a unique dual-level research mentoring strategy for the students.

Program Director and Training Team

Dr. Marvella E. Ford is the Program Director. Drs. Omar Bagasra (CU), Judith Salley (SCSU), and Leroy Davis (VC) are Associate Directors. This four-person leadership team collaborates closely in the management and administration of the award, as well as the continued development and enhancement of the Training Program. The Program Director and Associate Directors share scientific interests in health disparities, serve in other leadership roles within their institutions, and meet frequently, both formally and informally. These individuals form the Executive Committee for the Training Program. Each institution has appointed Faculty Advisors consisting of Dr. Ewen McLean (CU), Dr. James B. Stukes (SCSU), and Mrs. Gayle Tyler Stukes (VC).

BODY

Statement of Work

Task 1. Identify and Recruit the Student Fellows

- (a) Identify the pool of potential Student Fellows (Year 2, months 1-3)
- (b) Interview the potential Student Fellows (Year 2, months 1-3)
- (c) Select the top Student Fellows (Year 2, months 1-3)
- (d) Match the Student Fellows with their Research Mentors at MUSC (Year 2, months 1-3)
- (e) Hold the Kickoff Intensive and Luncheon (Year 2, months 4-6)

Deliverables: Four Student Fellows per year were identified, recruited to participate in the program, and matched with senior prostate cancer research mentors at MUSC.

Task 2. Provide Training in Biomedical and Prostate Cancer Research

- (a) Conduct Aim 1: Training in the Basics of Research Design and Methods through participation in the MUSC Summer Undergraduate Research Program (Year 2, months 6-8)
- (b) Conduct Aim 2: Prostate Cancer Research Training (Year 2, months 6-8)
- (c) Sponsor the Student Fellows' Participation in a Graduate Record Examination (GRE) course (Year 2, months 6-8)

Deliverables: We provided state-of-the art comprehensive prostate cancer research education and training opportunities for 4 students from three of South Carolina's HBCUs. We have developed a cadre of scientists who are well-prepared to play a significant role in discovering and testing new prostate cancer biomarkers. These investigators will conduct research spanning the continuum from basic science to clinical science to population-based research. At least 75% of the Student Fellows will take the GRE and at least 75% of the Student Fellows will apply to graduate school.

Task 3. Prepare Tangible Scientific Products

- (a) Prepare and present scientific abstracts based on the Student Fellows' prostate cancer research (Year 2, months 10-12)
- (b) Prepare manuscripts that will be submitted to peer-reviewed journals (Year 2, months 10-12)

Deliverables: At least 4 scientific presentations will be conducted by Student Fellows. At least 2 peer reviewed publications will result.

Task 4. Evaluate the Training Program

- (a) Assess the number of applicants to the Training Program (Year 2, months 1-4)
- (b) Assess the number of Student Fellows who apply to graduate school (Year 2, months 1-12)
- (c) Assess the number of Student Fellows who are admitted to graduate school (Year 2, months 1-12)
- (d) Assess the number of graduate schools to which Student Fellows are admitted (Year 2, months 1-12)
- (e) Employ several tracking mechanisms to monitor the scientific progress of the students, including:
 - 1. Searching the MUSC graduate program databases to identify whether any of the students applied, were offered, or accepted positions at MUSC.
 - 2. Contacting the participating universities' alumni offices.

3. Employing other internet based search tools/communications (Google, MySpace, Facebook, and Historically Black College/University Connections, etc.) to identify students' current locations, contact information, and academic achievements (Year 2, months 10-12)
- (f) Identify the number of scientific abstracts presented and peer-reviewed publications that result (Year 2, months 10-12)

Deliverables: We will prepare a document assessing the tangible products that result from the Training Program.

KEY RESEARCH ACCOMPLISHMENTS

Task 1. Identify and Recruit the Student Fellows

(a) Identify the pool of potential Student Fellows (Year 2, months 1-3)

(b) Interview the potential Student Fellows (Year 2, months 1-3)

(c) Select the top Student Fellows (Year 2, months 1-3)

To accomplish Tasks 1(a) – 1(c), Dr. Ford, the Program Director worked with Associate Directors Dr. Rebecca Bullard-Dillard and her replacement upon leaving Claflin University, Dr. Omar Bagasra (Claflin University), Dr. Judith Salley (SC State University), and Dr. Leroy Davis (Voorhees College) as well as Faculty Advisors Dr. Ewen McLean (Claflin University), Dr. James Stukes (SC State University), and Mrs. Gayle Stukes (Voorhees College) to identify potential Student Fellows. The Associate Directors and Faculty Advisors issued a call for applicants to their student bodies and personally approached students whom they felt would be outstanding applicants for the summer research program. For example, Drs. Ford (Principal Investigator), Bagasra (Associate Director), Salley (Associate Director), and Davis (Associate Director) communicated via electronic mail to discuss the 2013 SURP application process and deadlines.

To cite another example, to broaden the pool of potential applicants, each Associate Director invited faculty and students from his/her institution to participate in the Ernest Just Symposium held on February 22, 2013 at MUSC. A total of 240 students participated, including 67 students from HBCUs in South Carolina (Table 1.). The 240 students represented 21 different high schools, colleges and universities. A total of 67 students from HBCUs in SC participated in the Symposium, as well as 75 students from HBCUs in other regions of the country. The agenda from the Symposium and the number of students from each institution are included in **Appendices A-B**. Dr. Salley was instrumental in recruiting HBCU students from across the U.S. The students who participated in the Symposium also received a tour of scientific research units at MUSC and met with MUSC faculty members who could become their future research mentors.

(d) Match the Student Fellows with Their Research Mentors at MUSC (Year 2, months 1-3)

In Year 2, the Student Fellows were matched with their Research Mentors at MUSC based on the expressed interests of the Student Fellows as stated in their written MUSC Summer Undergraduate Research Program (SURP) applications. The following tables show the names of the students who participated in the DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program, their Research Mentors at MUSC, and their research topics.

Summer 2013 DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program Students, Mentors, and Research Topics			
Student Name	Academic Institution	MUSC Research Mentor	Research Topic
Ms. Kiera Addison	SC State University	Dr. Danyelle Townsend	Redox Signaling is Deregulated in Cancer
Ms. Evelyn Martinez	SC State University	Dr. Steven Rosenzweig	Growth Factor Contribution to Epithelial Mesenchymal Transition
Ms. Tomesha Nesbitt	Voorhees College	Dr. Shikhar Mehrotra	The Effect of Vitamin D3 on T cell Activation and Death
Ms. Sadia Robinson	SC State University	Dr. David Turner	Examining the AGE-RAGE Signaling Axis as a Mechanism of Prostate Cancer Disparity

In addition to the students listed above, the Director and Associate Directors leveraged funding from two other grants to support an additional three students:

Summer 2013 DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program Additional Students, Mentors, Funding Sources, and Research Topics				
Student Name	Academic Institution	MUSC Research Mentor	Funding Source	Research Topic
Ms. Bobbie Blake	Claflin University	Dr. Jennifer Wu	DOD - Southeastern Virtual Institute for Health Equity and Wellness (PI: Slaughter; Project PI: Ford)	NKG2D Signaling Pathways Analysis
Ms. Franshawn Mack	SC State University	Dr. Marvella Ford	DOD - Southeastern Virtual Institute for Health Equity and Wellness (PI: Slaughter; Project PI: Ford)	Evaluating the Reliability of an Instrument Assessing Cancer Clinical Trial Perceptions in a Predominantly African American Sample in South Carolina
Ms. Jasmine Fox	SC State University	Dr. Victoria Findlay	NIH/NCI P20 South Carolina Cancer Disparities Research Center (PIs: Ford and Salley)	MiR-204 Negative Regulation of IGF2R as a Mechanism Driving Breast Cancer Disparity

(e) Hold the Kickoff Intensive and Luncheon (Year 2, months 4-6)

The Kickoff Intensive and Luncheon took place during the first meeting of the didactic training program in prostate cancer research. Dr. Debbie C. Bryant from the MUSC College of Nursing, who has a keen interest in working with summer undergraduate students, and Ms. Tonya Hazelton, who coordinates the DOD Training Program, gave an overview of the DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program.

Task 1 Deliverables: Four Student Fellows (plus an additional three students who were supported using leveraged funds) were identified, recruited to participate in the program, and admitted to the DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program. The Student Fellows were matched with Research Mentors at MUSC, with whom they conducted research in the summer of 2013.

Task 2. Provide Training in Biomedical and Prostate Cancer Research

(a) Conduct Aim 1: Training in the Basics of Research Design and Methods through participation in the MUSC Summer Undergraduate Research Program (Year 2, months 6-8)

The Student Fellows participated in an intensive training program in the Basics of Research Design and Methods through participation in the MUSC Summer Undergraduate Research Program (SURP). The following tables show the SURP curricula from 2013.

Summer Undergraduate Research Program Lecture Series

Summer 2013

Location: BE 112, 8:30-9:30 AM (unless otherwise noted)

(Absolutely no food or drinks allowed in BE 112)

<u>Date</u>	<u>Topic</u>	<u>Lecturer</u>
	<u>Responsible Conduct of Research – MANDATORY</u>	
May 28	The Development of a New Treatment and Diagnostic Test for Bladder Cancer: From Bench to Bedside	Perry Halushka, MD, PhD
May 29	Novel Therapies to Treat Acute Kidney Injury: From Bench to Bedside (*note: this lecture will be in BSB 302)	Rick Schnellmann, PhD
May 30	What is Translational Research?	Carol Wagner, MD
May 31	Human Subject Research Success Center: How Scientists Get Help Conducting Research/ Examples of Translational Research	Susan C. Sonne, PharmD Royce Sampson, MSN, RN
June 3	9-9:50am MANDATORY: Responsible Lab Citizenship & Mentoring (lecture/discussion) 9:50-10am - - - Break- - - 10-10:50am Data Management/Data Manipulation (lecture/case/study/discussion)	Ed Krug, PhD
June 4	8:30-9:30am MANDATORY: Public Perceptions of Scientific Research ("And the Band Played On") 9:30-9:40am - - -Break- - - 9:40-10:20am Questionable Research Practices (discussion of video)	Ed Krug, PhD
June 5	8:30-9:20am Mandatory: Moral Reasoning in Ethical Dilemmas (lecture/case study/discussion) 9:20-9:30am - - -Break- - - 9:30-10:20am Animal Use in Research (lecture & discussion)	Ed Krug, PhD Alison Smith, PhD
June 6	8:30-9:20am MANDATORY: Authorship and Plagiarism (lecture/case study/discussion) 9:20-9:30am - - -Break- - - 9:30-10:10am Research Misconduct/Whistleblower Protections (lecture/case study/discussion) 10:10-10:20am Closing Comments/Exit Evaluation	Ed Krug, PhD

Outside Assignment: Complete the University of Montana On-Line RCR training (link below) - you must score a minimum of 70% on all quizzes. Submit paper copies of quiz completion to Stephanie Brown-Guion (BE101F) no later than 4 PM Friday, June 15 (http://ori.dhhs.gov/education/products/montana_round1/research_ethics.html)

NOTE: The schedule on the following pages is color-coded. Lectures in the Black font are required of everyone. You must select a lecture track for the remainder of the summer. Your choices are **Cardiovascular** (blue font), **Cancer** (red font), **Craniofacial biology** (pink font), and **Neuroscience** (green font). If you are part of the OHH group, your lectures are attached at the end of this schedule.

Lecture Time: 8:30-9:30; Place: Bioengineering Building Room 112

<u>Date</u>	<u>Topic</u>	<u>Lecturer</u>
June 7	Hepatic Steatosis in a Growing World: The Impact On Transplantation	Kenneth Chavin, MD, PhD
June 10	Lipidomics	Ashley Cowart, PhD
June 11	(C) Kinds of Cancer	Robert Gemmill, PhD
June 12	Cell Biology – Tissue Ultrastructure	Debra Hazen-Martin, PhD
June 13	Developmental Biology	Michael Kern, PhD
June 14	Proteomics Technology	Lauren Ball, PhD
June 17	Recombinant DNA	David Kurtz, PhD
June 18	Transcription	Steven Kubalak, PhD
June 19	(H) The Heart	Perry Halushka, PhD, MD
June 19	(D) Tooth Development – Room BSB 451	Michael Kern, PhD
June 20	(C) Cancer Cell Cycle	Cynthia Wright, PhD
June 21	Confocal/Multiphoton Microscopy of Living Cells And Tissues	John Lemasters, MD, PhD
June 24	Microarray Analysis	Jeremy Barth, PhD
June 25	(H) Electrical Properties of the Heart	Rupak Mukherjee, PhD
June 26	(C) Cytogenetics	Daynna Wolff, PhD
June 27	(N) Retinoids & Vision	Masahiro Kono, PhD
June 27	(D) Salivary Diagnostics – Room BSB 451	V. Palanisamy, PhD
June 28	G Proteins	John Hildebrandt, PhD
July 1	Stem Cells	Amanda LaRue, PhD
July 2	(N) Dementia	Dr. Mark Kindy, PhD
July 3	(N) ADD/ADHD	Antonieta Lavin, PhD Jonathan Dilgen, PhD
July 5	(H) Arterial Pressure Control & High Blood Pressure	Perry Halulshka, PhD, MD
July 8	Receptors	Steven Rosenzweig, PhD
July 9	(N) Spinal Cord Injury	Narendra Banik, PhD
July 10	(H) Aspirin & NSAIDS	Perry Halushka, PhD, MD
July 10	(D) Temporomandibular Joint Biomechanics – BSB 451	Hai Yao, PhD
July 11	(C) Smoking & Cancer	Michael Cummings, PhD
July 11	(D) Periodontal Disease – BSB 451	Keith Kirkwood, DDS, PhD
July 12	(D) Oral Pharyngeal Cancer – BSB 451	Boyd Gillespie, MD
July 15	(C) Epidemiology of Cancer	Kristen Wallace, PhD

July 16	(H) Atherosclerosis	Perry V. Halushka, PhD, MD
July 17	(C) Cancer Chemotherapy	David Kurtz, PhD
July 17	(D) Oral Infections – BSB 451	Caroline Westwater, PhD
July 18	(N) Neuroimaging Lab Demonstration	Colleen Hanlon
July 18	(D) Craniofacial Anomalies – BSB 451	Carlos Salinas, DDS, DDM
July 19	(H) Renal Regulation of Homeostasis	Ed Soltis, PhD
July 22	(H) Imaging the Heart	Joseph Schoepf, MD
July 23	(N) Addiction & Alcohol	Corrigan Smothers, PhD
July 23	(C) Cancer Disparities	Marvella Ford, PhD
July 24	(N) Schizophrenia	Antonieta Lavin, PhD Jonathan Dilgen, PhD
July 24	(D) Oral Health Community Engagement – BSB 451	Renata Leite, DDS
July 25	(N) Addiction & Drugs	Patrick Mulholland, PhD

Key: Black – mandatory for everyone
 Red or (C) – Cancer track
 Blue or (H) – Cardiovascular track
 Green or (N) – Neuroscience track
 Pink (D) – Craniofacial Biology

Conduct Aim 2: Prostate Cancer Research Training (Year 2, months 6-8)

The Student Fellows participated in an intensive training 10-week program in Prostate Cancer Research. Lectures focused on population science, statistical methods in prostate cancer research, prostate cancer clinical research, and basic science research. Other lectures described funding opportunities available to the students, career development opportunities, qualitative research methods, perspectives of prostate cancer among community members, and tips for preparing graduate school applications. In addition, as prostate cancer is a hormone-related cancer and some of the biological mechanisms that impact the etiology and treatment of prostate cancer are also relevant to breast cancer, the curriculum included information pertaining to breast cancer as well.

The schedule also provided time for students to rehearse their research presentations and gain input from their mentors and other scientists at the HCC. Disparities research was a cross-cutting theme in all of the lectures.

The structure of the curriculum also provides the students with a better understanding of the different population groups that were included in their research. Therefore, cultural enrichment activities were added to the curriculum, such as the Gullah tour of Charleston, in order to expose the students to the local and historic culture of the Charleston population. The Sea Island (Gullah) population is a subpopulation of African Americans indigenous to the coastal regions of the eastern seaboard. They are the most genetically homogeneous group of blacks in the U.S. Their particularly low rate of European American genetic admixture makes this a unique population for basic, clinical and population-based research. The following tables show the Summer 2013 cancer research training curriculum.

**2013 BREAST AND PROSTATE CANCER
SUMMER UNDERGRADUATE RESEARCH TRAINING CURRICULUM
May 28, 2013-August 2, 2013
11:00a.m.-12:00p.m.**

Week	Topic	Potential Instructor	Location and Date
WEEK 1	Welcome and Overview of the Training Program	Leadership, Mentors and Planning Team	Tuesday, May 28, 2013
WEEK 1 (Clinical Science Research Lecture)	Anatomy and the Function of the Breast	Rita Kramer, M.D. Associate Professor Hematology / Oncology	Wednesday, May 29, 2013 BE 402
WEEK 2 (Clinical Science Research Lecture)	Controversies in Breast Cancer Screening	Madelene Lewis, M.D. Assistant Professor Radiology	Tuesday, June 4, 2013 BE 402
WEEK 2 (HCC Outreach Lecture)	Hollings Cancer Center Outreach Mobile Unit & Community Compass	Melanie Slan, MS Juanita Brunson, MS Outreach Coordinators	Thursday, June 6, 2013 BE 402
WEEK 3 (Clinical Science Research Lecture)	Anatomy and the Function of the Prostate	Harry S. Clarke, M.D.,Ph.D. Professor Urology Services	Monday , June 10, 2013 3-4pm BE402
WEEK 3 (Academic Planning Lecture)	Funding Opportunities for Underrepresented Minority Scholars	Joann F. Sullivan, Ph.D. Assistant Dean for Extramural Program Development	Tuesday June 11, 2013 BE 402
WEEK 3 (Population Science/Epidemiologic Research Lecture)	Epidemiologic Issues in Prostate Cancer Research	Anthony Alberg, Ph.D. Professor Cancer Prevention & Control Program	Thursday, June 13, 2013 BE 402
WEEK 3 (Clinical Science Research Lecture)	Controversies in Prostate Cancer Screening	Jonathan Picard, M.D. Assistant Professor Urology Services	Tuesday, June 18, 2013 BE 402
WEEK 3	Cultural Enrichment Event	Cultural Enrichment Event	Wednesday, June 19, 2013
WEEK 4 (Population Science/Epidemiologic Research Lecture)	Epidemiologic Issues in Breast Cancer Research	Joan Cunningham, Ph.D, Research Assistant Professor Public Health Sciences	Thursday, June 20, 2013 BE402
WEEK 4 (Biostatistical Methods Lecture)	Biostatistical Issues in Breast and Prostate Cancer Research	Elizabeth Garrett-Mayer, Ph.D Professor Public Health Sciences	Tuesday, June 25, 2013 BE 402
WEEK 5 (Population Science Research Lecture)	Community-based genetic research project among the Sea Islanders (Gullahs) in SC	Ida J. Spruill, Ph.D Assistant Professor College of Nursing	Thursday, June 27, 2013 BE402
WEEK 5 (Tips for Preparing Graduate School Applications)	Improving Graduate School Admission Rates	Cynthia F. Wright, Ph.D. Associate Dean for Admissions and Career Development	Monday , July 1, 2013 BE402
WEEK 5 (Population Science Research Lecture)	Qualitative Research Methods	Charlene Pope, Ph.D. Associate Professor College of Nursing	Tuesday, July 2, 2013 BE 402
WEEK 6 (Clinical Research Lecture)	Vitamin D and Prostate Cancer	Sebastiano Gattoni-Celli, M.D. Professor Radiation Oncology	Tuesday, July 9, 2013 BE 402
WEEK 7 (Basic Science Lecture)	Genetic Basis of Cancer	Dennis Watson, Ph.D. Professor Pathology & Laboratory Medicine	Thursday, July 11, 2013 BE402
WEEK 7 Cultural Event	"Receptor crosstalk leading to cancer cell invasion"	Steven Rosenzweig,Ph.D Professor Pharmacology	Tuesday, July 16, 2013 BE402



CORE COURSE



BREAST CANCER COURSE



PROSTATE CANCER COURSE

WEEK 8	Cultural Enrichment Event	Cultural Enrichment Event	Thursday, July 18, 2013
WEEK 8	Research Presentation Rehearsals	All Research Students and mentors	Tuesday, July 23, 2013 BE402
WEEK 9 (Rehearsals)	Research Presentation Rehearsals	All Research Students and mentors	Thursday, July 25, 2013 BE402
WEEK 9 (Rehearsals)	Research Presentation Rehearsals	All Research Students and mentors	Tuesday, July 30, 2013 BE402
WEEK 10 (Rehearsals and Evaluations)	Evaluations and Closeout Program	All Research Student and Staff	Wednesday, July 31, 2013



CORE COURSE



BREAST CANCER COURSE



PROSTATE CANCER COURSE

**(c) Sponsor the Student Fellows' Participation in a Graduate Record Examination (GRE) course
(Year 2, months 6-8)**

In 2013, all four Student Fellows took the 10-week Princeton Review GRE Test Preparation Course. The Princeton Review is a standardized test preparation company. The course met on Wednesday evenings from 5:30 pm – 8:30 p.m. The course seamlessly adjusts classwork and homework to the skill level of each student. This is accomplished by focusing on the areas where each student needs the most improvement. The course provides instruction in test-taking skills, and provides opportunities for dynamic group discussions and collaborative drills.

Task 2 Deliverables: In 2013, state-of-the art comprehensive prostate cancer research education and training opportunities were provided for 4 students from two of South Carolina's HBCUs. Funds were leveraged from other federally funded training grants to provide the same level of education and training to an additional 3 students from HBCUs in South Carolina. We are developing a cadre of scientists who are were-prepared to play a significant role in discovering and testing new prostate cancer biomarkers. In the future, these investigators will likely conduct research spanning the continuum from basic science to clinical science to population-based research.

Task 3. Prepare Tangible Scientific Products

(a) Prepare and present scientific abstracts based on the Student Fellows' prostate cancer research (Year 2, months 10-12)

(b) Prepare manuscripts that will be submitted to peer-reviewed journals (Year 2, months 10-12)

(c) Develop manuscripts to describe the scope and outcomes of the project (Year 2, months 9-12)

In 2013, each Student Fellow prepared a scientific research paper that will form the basis of a peer-reviewed publication. The Student Fellows are completing manuscripts with their research mentors. Each Student Fellow gave a scientific presentation based on the results of his or her work.

In addition, Ms. Franshawn Mack gave a presentation on November 15, 2013 at the Southeast Regional Research Conference in Little Rock, AR. The title of her presentation was "Evaluating the Reliability of an Instrument Assessing Cancer Clinical Trial Perceptions in a Predominantly African American Sample in South Carolina." She was also a co-author of the following presentation:

- Ford ME, Burshell DR, Mack F, Wei W, Garrett-Mayer E. Evaluating the Reliability of an Instrument Assessing Cancer Clinical Trial Perceptions in a Predominantly African American Sample. Poster presented at the Sixth American Association for Cancer Research Conference: The Science of Cancer Health Disparities in Ethnic Minorities and the Medically Underserved, December 6-11, 2013, Atlanta, GA.

Summaries of each Student Fellows' research projects are included in **Appendix C**. A manuscript describing the scope and outcomes of the Training Program will be initiated in the spring of 2013.

Deliverables: A total of 9 scientific presentations were made by the Student Fellows, including two presentations at national scientific meetings.

Task 4. Evaluate the Training Program

(a) Assess the number of applicants to the Training Program (Year 2, months 1-4)

In the spring of 2013, 16 students from South Carolina's HBCUs applied to the DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program. As planned, four Student Fellows were selected who were funded through the DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program enrolled in the Training Program in the summer of 2013. An additional three Student Fellows were selected. Their participation in the Training Program was supported through leveraged funds from a DOD Southeastern Virtual Institute for Health Equity and Wellness grant and an NIH/NCI P20 South Carolina Cancer Disparities Research Center grant.

(b) Assess the number of Student Fellows who apply to graduate school (Year 2, months 1-12)

The Student Fellows who participated in the 2013 DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program were rising sophomores through seniors. As described below, we are employing several strategies to monitor the Student Fellows' progression through their academic careers.

(c) Assess the number of Student Fellows who are admitted to graduate school (Year 2, months 1-12) and (d) Assess the number of graduate schools to which Student Fellows are admitted (Year 2, months 1-12)

We are actively keeping track of the progress of the Student Fellows using the strategies that are described below.

(e) Employ several tracking mechanisms to monitor the scientific progress of the students, including:

- 1. Searching the MUSC graduate program databases to identify whether any of the students applied, were offered, or accepted positions at MUSC.**
- 2. Contacting the participating universities' alumni offices.**
- 3. Employing other internet based search tools/communications (Google, MySpace, Facebook, and Historically Black College/University Connections, etc.) to identify students' current locations, contact information, and academic achievements (Years 2, 3, and beyond)**

We have implemented several steps for tracking student scientific progress. Communication and assistance from the Associate Directors and Faculty Advisors have proved to be very effective. Additionally, social media tools such as Facebook have also been useful for engaging the students and opening a venue for communication. Another method we have found useful is text messaging. We have found that students respond more quickly to text messages than to emails and telephone calls. We will utilize and build upon these methods to improve continued student tracking. These multiple tracking strategies will be used to update the table that is included in **Appendix D**, which lists the academic accomplishments of the Student Fellows.

(f) Identify the number of scientific abstracts presented and peer-reviewed publications that result (Year 2, months 10-12)

The Student Fellows gave a total of 9 scientific presentations, including two presentations at national scientific meetings. The mentors of the Student Fellows have confirmed that manuscripts that include some of the Student Fellows as co-authors are underway.

Deliverables: The Student Fellows are completing their sophomore and junior years of college and will apply to graduate or professional schools. The Student Fellows gave a total of 9 scientific presentations, two of which were made at two national scientific meetings. Also, each year, we ask the Student Fellows to evaluate the Training Program. The results from the 2013 Student Fellows are presented in the following table.

SUMMARY RESULTS OF STUDENTS EVALUATIONS 2013 (n=7)

Survey Item	Strongly Disagree		Disagree		Not Sure		Agree		Strongly Agree	
	N	%	N	%	N	%	N	%	N	%
1. Overall, the summer program was a good research experience.	0	0.0	0	0.0	0	0.0	0	0.0	7	100%
2. The summer program helped me learn the fundamentals of breast and prostate cancer and research.	0	0.0	0	0.0	0	0.0	0	0.0	7	100%
3. The Princeton Review Graduate Record Examination (GRE) Course was effective in helping me to learn GRE test preparation strategies.	0	0.0	0	0.0	0	0.0	1	14%	6	86%
4. The seminar schedule was convenient.	0	0.0	0	0.0	0	0.0	3	43%	4	57%
5. The seminar topics were of interest to me.	0	0.0	1	14%	0	0.0	3	43%	3	43%
6. Participating in the program helped to strengthen my desire for a career in cancer research.	0	0.0	0	0.0	2	28.5%	3	43%	2	28.5%
7. The Program Assistant (Ms. Hazelton) was accessible and assisted me when needed.	0	0.0	0	0.0	0	0.0	0	0.0	7	100%
8. My research mentor was accessible and assisted me when needed.	1	14%	0	0.0	1	14%	1	14%	4	57%
9. I would recommend this program to other students at my college/university.	0	0.0	0	0.0	0	0.0	1	14%	6	86%

REPORTABLE OUTCOMES

Student Summer Research Summaries

Each Student Fellow prepared a research paper and gave a scientific presentation to their peers, mentors and other faculty at MUSC. Details regarding the manuscripts and scientific presentations developed by the Student Fellows are included in **Appendix C**.

CONCLUSIONS

During past year of funding of the DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program, the tasks outlined in the Statement of Work were successfully met. Twelve Student Fellows were recruited from Claflin University, SC State University, and Voorhees College. Each Student Fellow conducted research and prepared a research paper that was presented at the conclusion of the program. The Student Fellows also presented their work at national conferences and were included as co-authors on peer-reviewed scientific publications, based on their summer research.

As shown in the following tables, two additional students participated in the DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program using funds leveraged from another DOD grant that was funded in 2010 (DOD Grant Number W81XWH-10-2-0057, Southeastern Virtual Institute for Health Equity and Wellness). The DOD SE VIEW grant provided funding for two additional students per year beginning in 2010.

2010 DOD SE VIEW Grant Funded Students				
Student's Name	Institution	MUSC Research Mentor	Research Title	Research Summary
Janielle Samuel	Voorhees College	Dr. Marvella E. Ford	Testing protein glutathionylation levels In MCF7 breast cancer cells expressing glutathione S-transferase Pi Isoforms	GSTpi has been implicated in the forward reaction of S-glutathionylation. Therefore, we are interested in understanding how polymorphism may alter cellular responses for both oxidative and nitrosative stress. As such, the four alleles of GSTpi have been transfected into MCF7 breast cancer cells and we are testing the rate and extend the S-Glutathionylation via western blot analysis.
Edward McMorris	Voorhees College	Dr. Christina Voelkel-Johnson	Acid ceramidase overexpression and its role in the activation of and addiction to Akt signaling in prostate cancer	Previous studies have demonstrated the role of the ceramide metabolizing enzyme acid ceramidase in promoting an aggressive cancer phenotype in prostate cancer cell lines. In addition, it has been found that greater than 80% of prostate tumors overexpress acid ceramidase, suggesting that acid ceramidase may be an important mediator of development and progression of prostate cancer. In this study, we demonstrate that the increased rate of proliferation in acid ceramidase overexpressing cells is dependent on signaling through the oncogenic PI3K/Akt pathway. In addition, we found that acid ceramidase overexpressing cells are more sensitive to Akt inhibition than control cells, suggesting that acid ceramidase overexpressing tumors are addicted to Akt signaling. These findings highlight the importance of investigating the Akt pathway as a potential therapeutic target in acid ceramidase overexpressing tumors.

2011 DOD SE VIEW Grant Funded Students (Continued)

Student's Name	Institution	MUSC Research Mentor	Research Title	Research Summary
CoDanielle Green	SC State University	Dr. Marvella E. Ford	Evaluating an intervention to increase cancer knowledge in racially diverse communities in South Carolina; as well as, the increase in cancer knowledge's effect on cancer prevention activities.	To conduct a cancer education intervention with racially diverse communities in South Carolina. Then, to assess the impact that the cancer knowledge intervention is having on the cancer prevention activities of the residents.
De'Angelo Dinkins	SC State University	Dr. Christina Voelkel-Johnson	Thioredoxin 1 as a Therapeutic Target in Advanced Prostate Cancer	Prostate cancer is the 2nd leading cancer in men after lung cancer. Indolent disease can be treated fairly well and progresses slowly. However, the more aggressive form of prostate cancer spreads though out the body and there are no curative treatments. We tested the hypothesis that increased expression of redox proteins is an underlying cause for the aggressive, therapy-resistant prostate cancer phenotype. In our project we looked at the expression of redox proteins and susceptibility to chemotherapy in ARCaPe and ARCaPm cells.

2013 Annual Report Appendices

Appendix A: Ernest E. Just Symposium Agenda

Ernest Just Scientific Symposium
February 22, 2013

Located in the James E. Clyburn Research Center Auditorium

Part I: Introduction

8:00-9:00 am Registration and Breakfast - Entrance to Auditorium
Opening: Stephen Lanier, Ph.D.
Associate Provost for Research
Professor of Pharmacology, Medical University of South Carolina

9:00-9:10 am Etta D. Pisano, M.D., Dean, College of Medicine
Vice President for Medical Affairs, Medical University of South Carolina

9:10 - 9:40 am **Greeting:** Perry V. Halushka, Ph.D., M.D.
Professor, Pharmacology and Medicine
Dean, College of Graduate Studies, Medical University of South Carolina
Title: "The Creativity of Ernest Everett Just"
William McDade, M.D., Ph.D.
Deputy Provost for Research and Minority Issues
Office of the Provost
University of Chicago



Part II: Role Models

9:40-10:10 am **Title:** *"Finding it in ALL Academic Medicine"*
Samantha E. Kaplan, M.D., MPH
Assistant Professor of Obstetrics & Gynecology
Assistant Dean for Diversity & Multicultural Affairs
Director, Early Medical School Selection Program
Boston University School of Medicine



10:10-10:30 am Break
Just Symposium
Keynote

10:35-11:15am **Title:** *"Science: A Powerful Tool for Justice"*
Griffin P. Rodgers, M.D.
Director, National Institute of Diabetes & Digestive & Kidney Diseases
National Institutes of Health



Graduate Presenter

11:20-11:30am **Title:** *"What's Wrong with my Heart? Improving left ventricular function following Myocardial Infarction"*
Presenter: **Denise Kimbrough, PhD candidate**
Medical University of South Carolina
Molecular and Cellular Biology & Pathobiology
Department of Cardiology
Gazes Cardiac Research Institute



**Undergraduate
Presenter**

Title: *"Paralysis Due to Caffeine at the Neuromuscular Junction"*
Presenter: Ms. Melissa Carr-Reynolds
Spelman College

11:45-12:55 pm

BREAKOUT SESSIONS/Lunch

Campus tour for visiting students, Undergraduate Advisors meet with MUSC College Admissions Officers (Drug Discovery Bldg. Rm 111)

Part III Science

1:00-1:50 pm

Title: *"The role of iRhom2/ADAM17 in EGFR receptor signaling and TNF-dependent pathologies"*
Carl Blobel, M.D., Ph.D.

Professor: Departments of Medicine & Physiology & Biophysics
Center for Vascular Biology
Weill Cornell Medical College



2:00-2:50 pm

Title: *"Creating the Optimal Environment: Biomaterials in Regenerative Medicine"*
Jennifer Elisseeff, Ph.D.

Professor of Ophthalmology and Biomedical Engineering
Director, Translational Tissue Engineering Center (TTEC)
Wilmer Eye Institute and Department of Biomedical Engineering
John Hopkins University



3:00-3:50 pm

Title: *"CANCER - The Close Cousin of Wound Healing"*
Kapil Mehta, Ph.D.

Professor of Experimental Therapeutics Cancer Medicine
(Biochemistry) The University of Texas MD Anderson Cancer Center



Appendix B: Ernest E Just Symposium Student Attendees

Name of School	# Students Who Participated in the February 22, 2013 Ernest E. Just Symposium at MUSC
Anderson University	18
Benedict College	40
Bowie High School	1
Charles Herbet Flowers High School	11
Claflin University	14
Clark Atlanta University	23
Clemson University	6
Coastal Carolina University	6
Fayetteville State University	21
Gwynn Park High School	13
Lowcountry AHEC	7
Morehouse College	7
Savannah State University	6
Spelman	18
The Citadel	2
UMBC	4
Upstate AHEC	17
USC Aiken	4
USC Upstate	6
Voorhees	13
Winthrop University	3
TOTAL	240

	HBCU in SC
	HBCU in a Geographic Region Outside of SC

Appendix C: Summaries of Students' Abstracts from the 2013 Summer Research Program

Keira Addison

Redox Signaling is deregulated in Breast Cancer

Dr. Danyelle Townsend, PhD

Abstract

Reactive Oxygen Species (ROS) releases oxidative stress in cells which disturbs cellular immunity in the body leading to an unbalanced cellular environment and cancer. Factors that influence ROS are radiation, UV exposure, other environmental factors and the mitochondria in cells. When cells have high levels of oxidative stress, there are antibodies that are released to detoxify the cells, balancing out the cellular environment. Redox signaling is the process of reducing oxidative stress through the release of antibodies and the opening of different signaling pathways. In this work we studied the differential expression of antibodies (Thioredoxin, Sulfiredoxin, GST π and Peroxiredoxin) in breast cancer (MCF-7) and normal breast cells (MCF-10) by western blots. Our results show that the antibodies are expressed more in normal cells than breast cancer cells. According to these preliminary results, redox signaling is deregulated in breast cancer cells.

Redox Signaling is Deregulated in Breast Cancer

Keira Addison

Mentor: Danyelle Townsend, Ph.D.

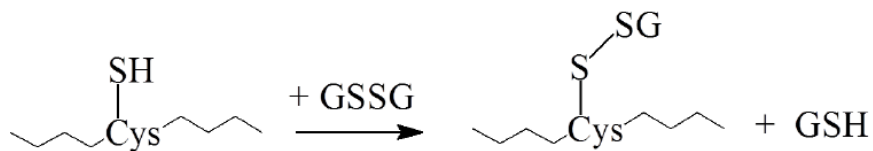
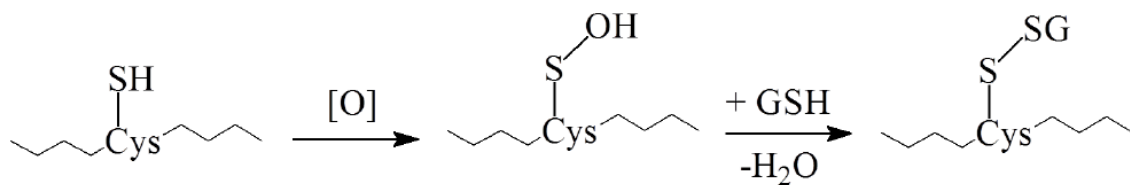
Summer Undergraduate Research Program

What is Redox Signaling ?

- Reactive Oxygen Species are high levels of oxygen that can pose cancerous risks to cells
- When a cellular environment has high levels of reactive oxygen species, it triggers the redox signaling process
- Redox signaling is the reduction of oxidative stress by the activation of antioxidants that work to provide a balanced cellular environment

S-Glutathionylation

- Post-translational modification on cysteine residues that alters structure / function / subcellular localization in response to oxidative or nitrosative stress



Hypothesis

- Redox signaling is deregulated in breast cancer.
- Aim
 - Evaluate the enzymes involved in redox signaling in normal and breast cancer cell models

GST π , Sulfiredoxin, Peroxiredoxin, Thioredoxin

- **GST π** (Glutathione S-transferase)
 - Catalyzes S-glutathionylation reactions
- **Sulfiredoxin (Srx)**
 - Catalyzes S-deglutathionylation of proteins
 - Catalyzes reversal of sulfinic acid residues (Prdx)
- **Peroxiredoxin (Prdx)**
 - Protects cells from oxidative stress by reducing hydrogen peroxide
 - Regulates cell proliferation
- **Thioredoxin (Trx)**
 - Plays a role in de-glutathionylation and de-nitrosylation of cysteine residues
 - Inhibitor of apoptosis

Cell Model of Normal and Cancer Breast Cancer Patients ~ 75% ER +

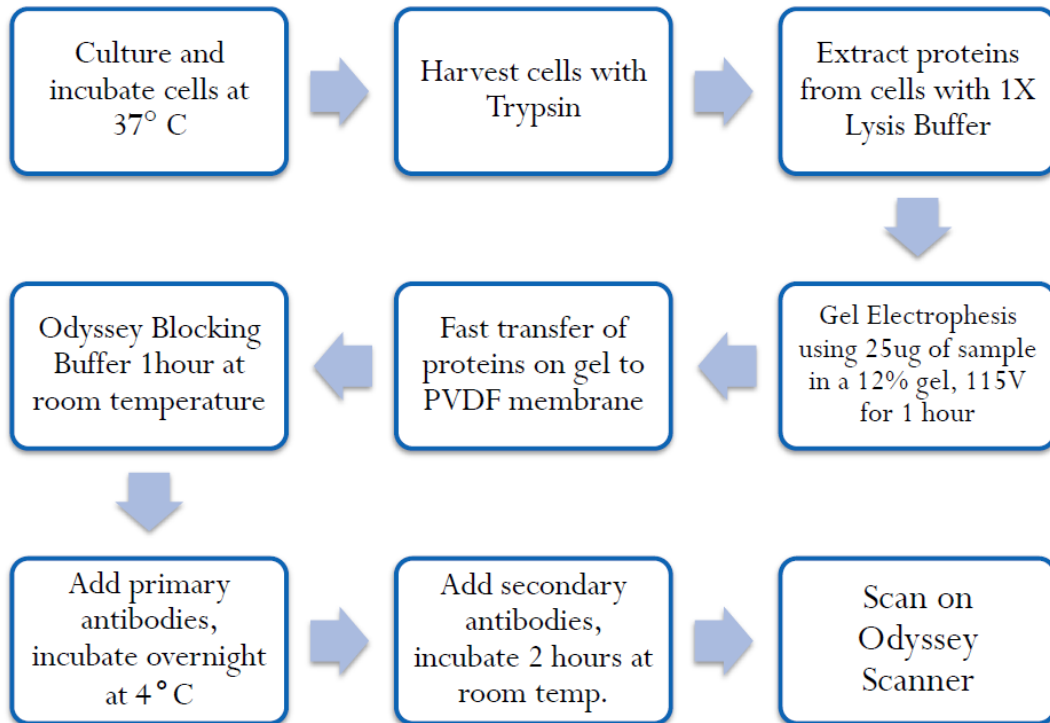
MCF-7

- Breast Cancer cells by the Michigan Cancer Foundation
- Expresses estrogen receptors and responds to anti-estrogen therapy

MCF-10

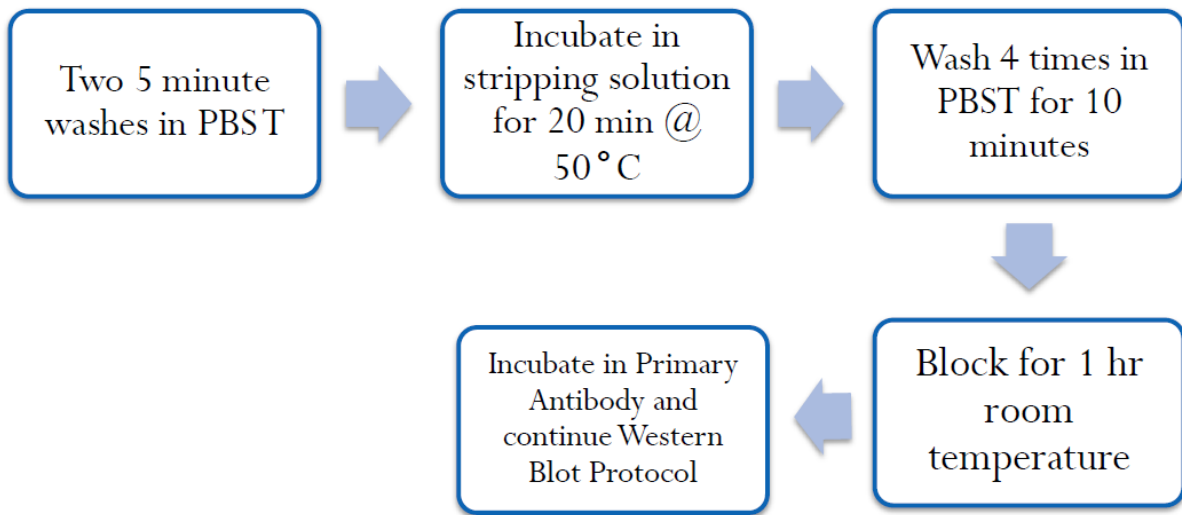
- Normal breast cells
- No estrogen receptors present

Materials & Methods

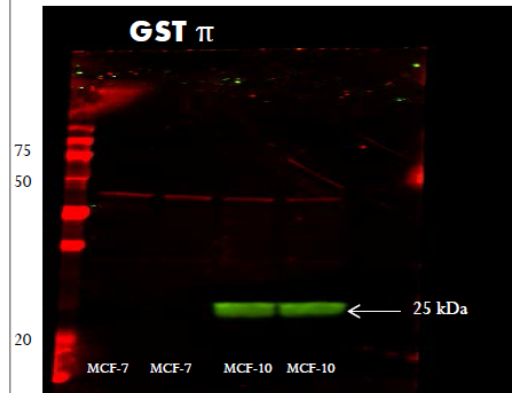


Materials & Methods

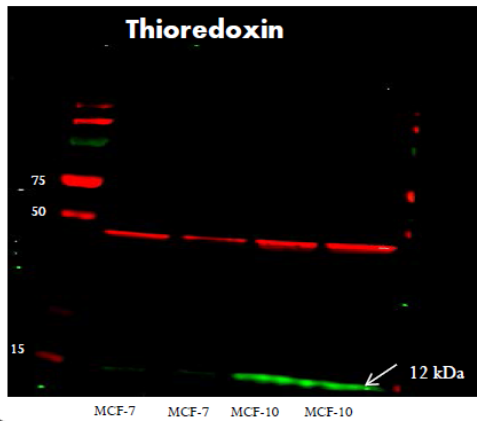
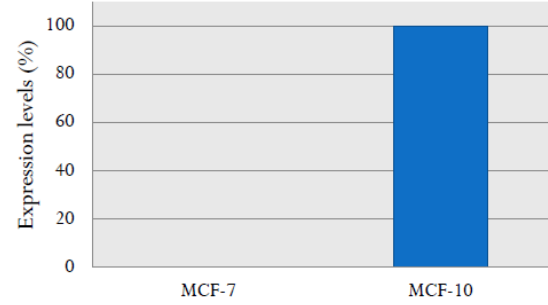
Stripping Membrane



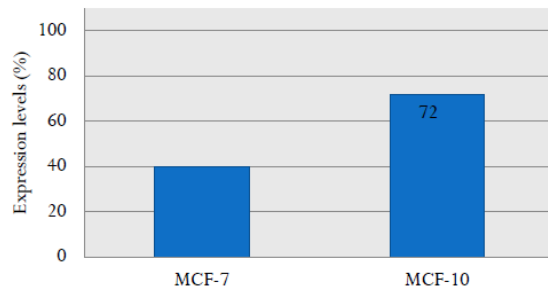
Results



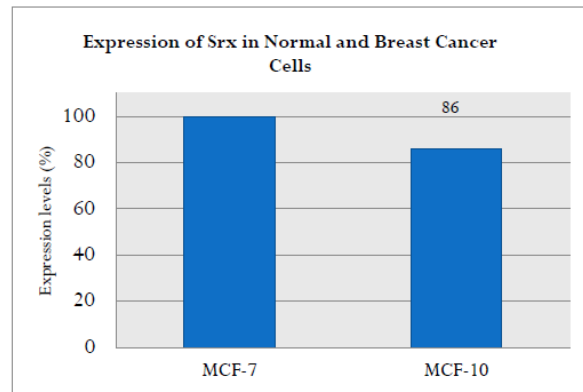
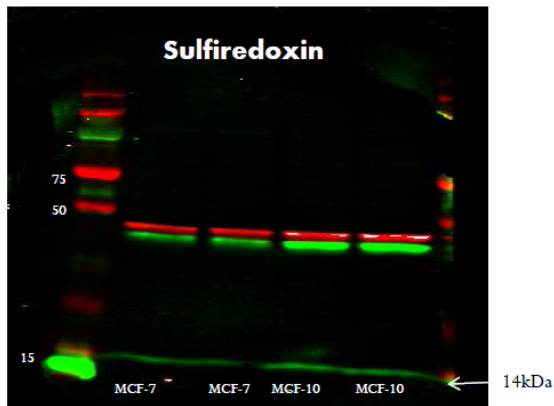
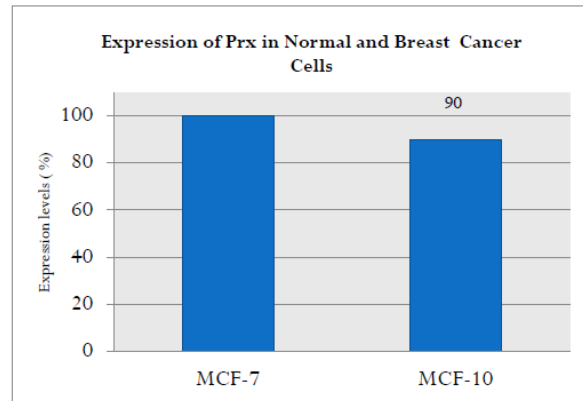
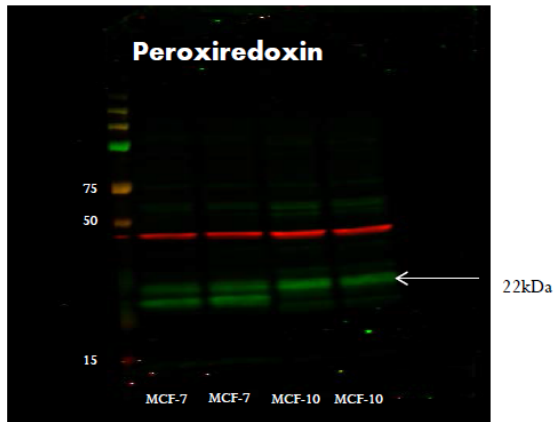
Expression of GST π in Normal and Breast Cancer Cells



Expression of Trx in Normal and Breast Cancer Cells



Results



Conclusions

- MCF7 breast cancer cells do not express detectable levels of GSTP where as “normal” MCF10 have high levels
 - MCF7 cells are likely to have diminished enzyme mediated S-glutathionylation reactions
- MCF7 breast cancer cells have significantly lower levels of Thioredoxin relative to normal
 - De-nitrosylation / glutathionylation is potentially impaired
- Sulfiredoxin and Peroxiredoxin levels are not changed in MCF7 breast cancer cells
- ** Enzymes involved in the S-glutathionylation signaling pathway are blunted in MCF7 breast cancer cells **

Acknowledgements

- Dr. Danyelle Townsend and Leticia Reyes, Lab Manager
- Dr.'s Townsend, Tew and Uys lab members
- Dr. Marvella Ford
- Ms. Tonya Hazelton
- Ms. Juanita Brunson
- Ms. Brown-Guion
- MUSC's Summer Undergraduate Research Program
- Department of Defense- South Carolina Collaborative Undergraduate HBCU Student Summer Training Program

Evelyn Martinez

Cancer Research

Dr. Rosenzweig

Introduction

Head and Neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide, with over 600,000 new cases each year. In the United States alone, HNSCC accounts for 10,000 cancer related deaths per year ("All About Head & Neck Cancer," n.d.). Anatomically, head and neck cancers are found above the collar bone in the oral cavity, pharynx, mouth, and tongue (Rothenberg & Ellisen, 2012). Squamous cell carcinoma accounts for 90 percent of the malignant tumors found in the head and neck region, starting as a malignancy of the squamous cells which are the flat cells found in the upper layers of the skin like the lining of the nose, mouth, and throat. Environmental factors such as chronic tobacco use and excessive alcohol consumption are known to induce HNSCC. Evidence also shows that Human Papilloma Virus (HPV), particularly type 16 and 18 are linked to oropharyngeal cancer ("Squamous Cell Carcinoma," 2012). Prognosis variables of HNSCC include the presence of distant metastases and presence of lymph node metastases. Although there are multiple aggressive treatments for HNSCC such as surgery, chemotherapy, and radiation therapy, nearly 50 percent of patients with advanced disease have reoccurrences (Chung et al., 2004).

Epithelial-mesenchymal transition (EMT) has been associated with therapeutic resistance and contributes to tumor growth, invasion, and metastases (Krisanaprakornkit & Iamaroon, 2012). It is a process in which epithelial cells lose their cell to cell adhesion, restructure the cytoskeleton, and take on a mesenchymal phenotype. Epithelial cells line the human body and are characterized as closely packed cells connected together by cell junctions and play a role in diffusion and secretion (Ananth, 2013). Mesenchymal cells are spindle-shaped cells that only interact with each other through focal points.

Epithelial cells express a high level of E-cadherin while mesenchymal cells express N-cadherin. As epithelial cells undergo EMT there is a loss in E-cadherin and an increase in N-cadherin known as “cadherin switching.” This gives transformed epithelial cells mesenchymal-traits such as loss of cell adhesion, allowing them to more effectively invade nearby structures.

Vascular endothelial growth factor (VEGF) and endothelial growth factor (EGF) have been suggested to stimulate EMT in oral squamous cell carcinoma (OSCC). VEGF is a signaling protein that stimulates vasculogenesis, blood vessel formation during embryonic development, and angiogenesis. Because cancers cannot grow without an adequate blood supply, cancers that overexpress VEGF are able to grow and metastasize (Lucas et al., 2010). VEGF binds to and activates a receptor tyrosine kinase (VEGFR) through transphosphorylation (“VEGF Signaling Pathway,” nd). Once activated, the VEGFR induces processes common to growth factor receptors including cell migration and proliferation.

Many articles state that VEGF and EGF have been widely accepted to stimulate migration and metastasis in pancreatic and colon cancer. In this study, we hypothesized that VEGF and EGF stimulate EMT in OSCC in order to initiate metastasis. Cells from human tongue oral cancer cell lines (SCC9) and laryngeal cancer cell lines (SCC22A) were treated with VEGF and EGF. Western blot analyses were used to determine changes in the expression of the molecular markers, E-cadherin and N-cadherin, of EMT after growth factor treatment.

Growth Factor Contribution to Epithelial Mesenchymal Transition

Evelyn Martinez

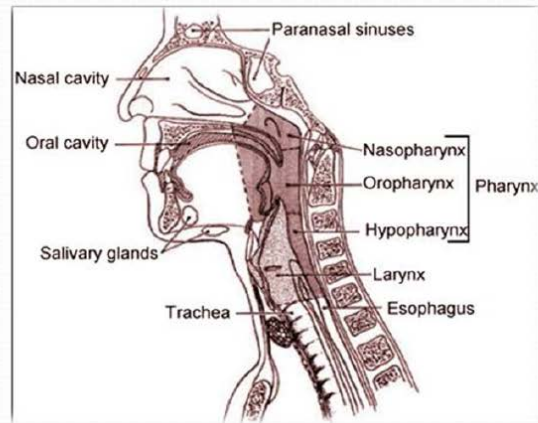
Mentor: Dr. Rosenzweig

Department of Pharmacology

SURP 2013

Head and Neck Squamous Cell Carcinoma (HNSCC)

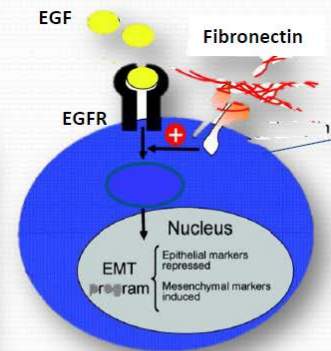
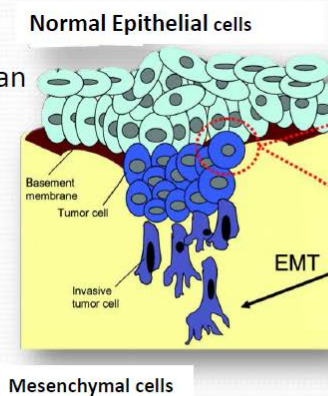
- 6th most prevalent cancer worldwide – 600,000 new cases each year
- What is squamous cell carcinoma?
- Etiologic factors:
 - Chronic tobacco smoking
 - Excessive alcohol consumption
 - HPV-type 16 and 18



Epithelial-Mesenchymal Transition (EMT)

- EMT: process in which epithelial cells lose their cell to cell adhesion
→ restructure the cytoskeleton → take on a mesenchymal phenotype

- Epithelial Cells –
 - Closely packed cells connected by cell junctions that line the human body
- Mesenchymal Cells-
 - Spindle-shaped cells that only interact with each other through focal points



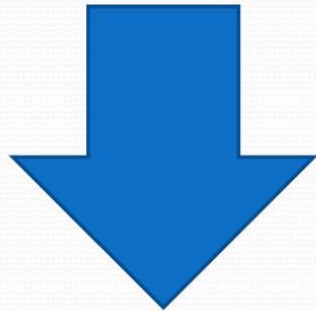
clincancerres.aacrjournals.org

Cadherin Switching



N-cadherin

- Cell adhesion molecule that induces
- scattered morphology
- higher motility, invasion, & metastasis

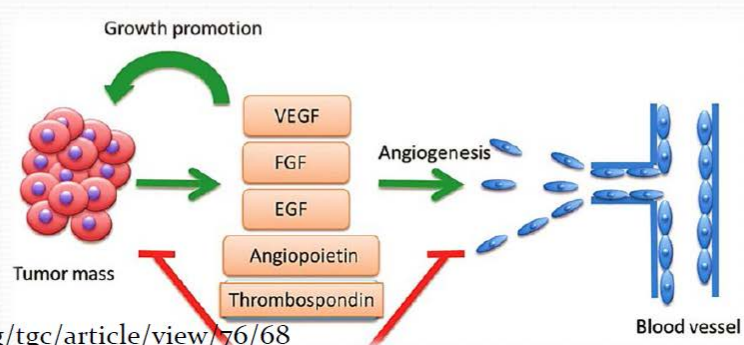


E-cadherin

- Cell adhesion molecule involved in
- regulating cell-cell adhesion
- mobility
- proliferation of epithelial cells

GROWTH FACTORS

- Biological factors
 - Regulate the division and proliferation of cells
 - Influence growth rate of some cancers
- Vascular Endothelial Growth Factor (VEGF)
- Epithelial Growth Factor (EGF)



<http://www.amepc.org/tgc/article/view/76/68>

Hypothesis

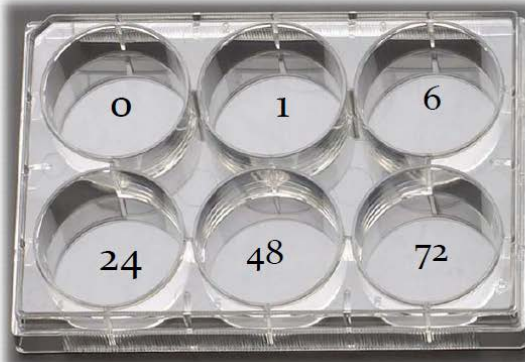
- To determine if VEGF and EGF stimulate EMT in oral squamous cell carcinoma (OSCC) in order to initiate metastasis
- Specific Aim:
 - To identify changes in the expression of the molecular markers of EMT after growth factor treatment using Western blot analyses

Methods

Cells from human tongue oral cancer cell line (SCC9) and laryngeal cancer cell line (UM-SCC22A) were split into a 6-well plate



Treated with 100 ng/mL of VEGF and EGF at 6 different time points



Extraction of protein

Lysis buffer → Sonicate cells → Protein assay

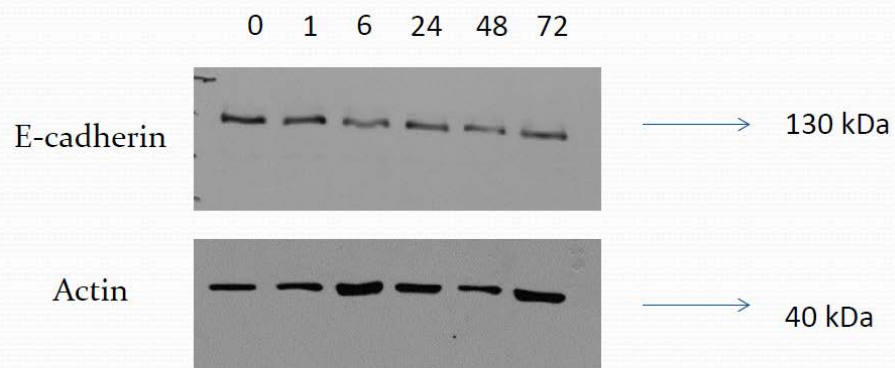


Western Blot

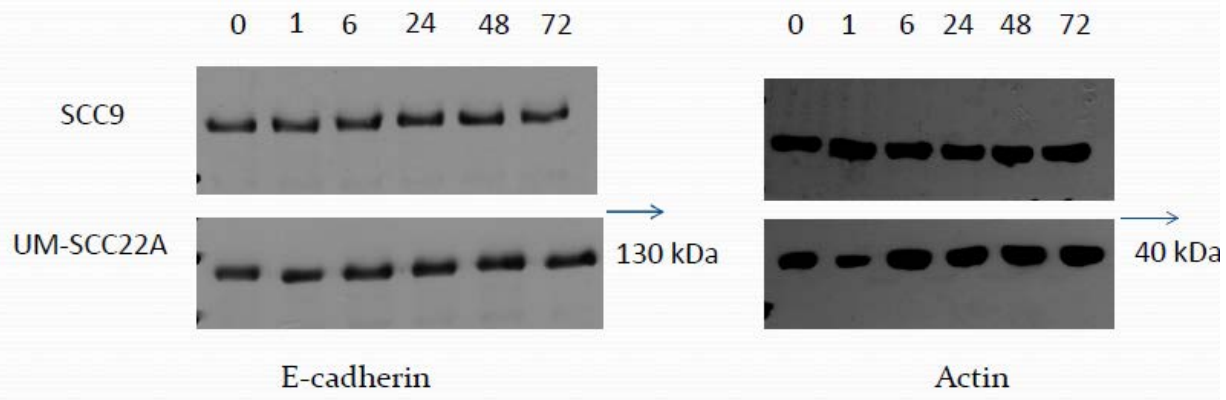
1. Load 40 mg of protein
2. Run gel
3. Transfer onto membrane
4. Block with 5% milk TBST
5. Probe with primary, incubate overnight
6. Wash
7. Probe with secondary
8. Expose blots
9. Strip and repeat steps 4-8 for N-cadherin and Actin

Results-VEGF

SCC9



Results-EGF





Conclusion & Discussion

- VEGF and EGF did not stimulate EMT and induce migration in our oral cancer cell lines
- Literature states VEGF and EGF stimulate migration and metastasis
 - Concentration of VEGF and time points were the same as literature
- Variables:
 - Cell density too high/too low
 - Contamination we didn't catch

Future Direction

- Snail, a transcription factor, has been involved in the progression of tumors by regulating E-cadherin
 - Suppresses expression of E-cadherin



Membranes could be probed with snail to possibly stimulate EMT

Acknowledgements

- Dr. Rosenzweig



- Casey Holmes and the Rosenzweig lab





Acknowledgements (cont...)

- Summer Undergraduate Research Program at MUSC
 - Dr. Ford
 - Ms. Brown-Guion

The Effect of Vitamin D3 on T cell Activation and Death

Name: Tomesha Nesbitt

MUSC Summer Undergraduate
Research Program

Mentor: Dr. Mehrotra

Date: July 31, 2013

Abstract: Vitamin D plays an important role in the human body. It helps the body absorb the calcium and phosphate needed. In humans, the most important compounds in this group are vitamin D3 also known as cholecalciferol and vitamin D2, which is also known as ergocalciferol. Vitamin D3 stops the growth of T cells. Active T cells up regulate vitamin D and non-active T cells do not. In T cells, vitamin D expression is triggered through engagement of T cell receptor leading to activation of an mitogen- activated protein kinase pathway, and the expression of vitamin D in T cells correlates with greater T cell responsiveness. Up regulation of vitamin D, like CD69 is an early response to stimulation that occurs in T cells. Vitamin D3 stops the growth of T cells; vitamin D3 also has the ability to decrease T cell activation. Vitamin D regulates the expression of more than 900 genes involved in a wide array of physiology functions.



The Effect of Vitamin D3 on T Cell Activation and Death

Name: Tomesha Nesbitt

Program: Student Undergraduate Research

Mentor: Dr. Mehrotra

Date: July 31, 2013



Introduction

- **Vitamin D3 ,also known as cholecaliferol is one of the most important compounds in humans.** [Hollick et.al., Mayo Clinic Proc., March 2006)
- **Vitamin D3 inhibits differentiation, maturation, and functions of dendritic cells leading to impaired immune responses.** [Song et.al., The Journal of vitamins and hormones, 3, 1 May 2003, Pages 235-247]
- **Vitamin D3 exerts a marked inhibitory effect on adaptive immune cells.** [UK essays, Immunomodulatory Effects Of Vitamin D Health Essay, 2003-2013]
- **Potential efficacy of vitamin D3 supplementation at 4000 international units (IU) per day for one year in subjects diagnosed with early stage, low-risk prostate cancer.** [Hollis et.al.,The journal of steroid biochemistry and molecular biology, 2013 Jul;136:233-7. doi: 10.1016/j.jsbmb.2012.11.012. Epub 2012 Dec 7]



Introduction Continue

- **Vitamin D3 (VD3), the most physiologically relevant form of vitamin D, is synthesized in the skin from 7-dehydrocholesterol, a process which depends on sunlight.** [Mora et.al., The Journal of Nat Rev Immunology, 2008 September; 8]
- **Vitamin D3 inhibiting cell growth of the leukemic cell lines.** [Defacque et.al. The Journal of Pharmacological and experimental Therapeutic, 1994 Oct;271(1):193-9]



Experimental Aim

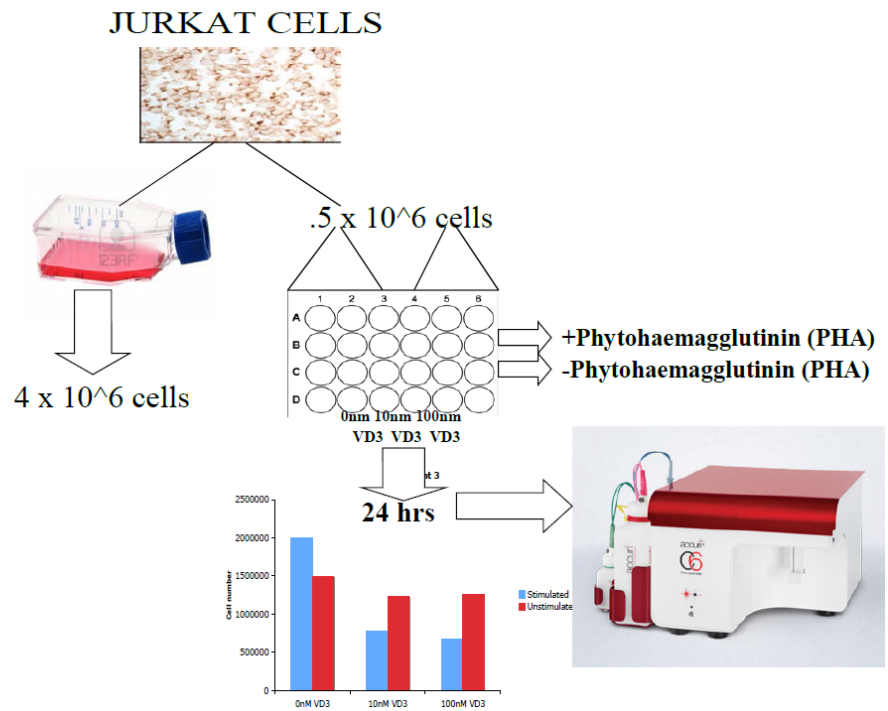
- To elucidate the effect of vitamin D3 on the T cells activation and death by using various cellular assays.



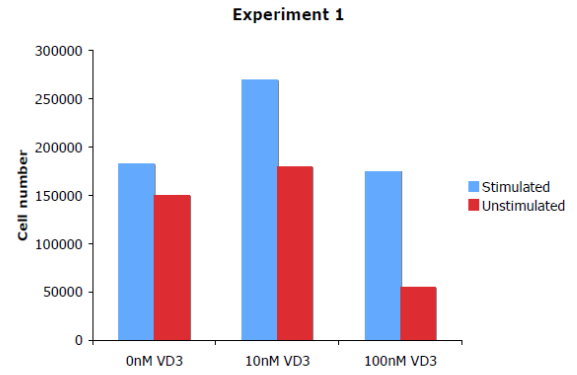
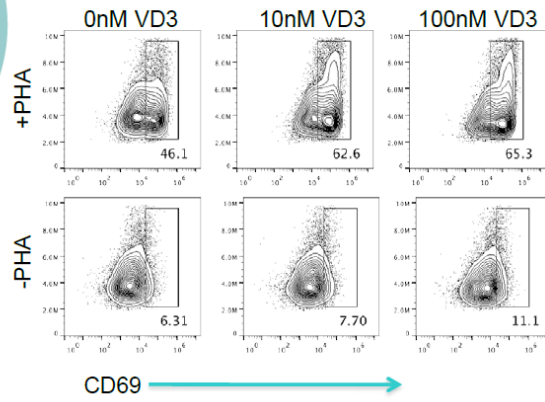
Hypothesis

- Vitamin D3 will suppress T cell activation.
- Vitamin D3 will enhance the death of T cells.

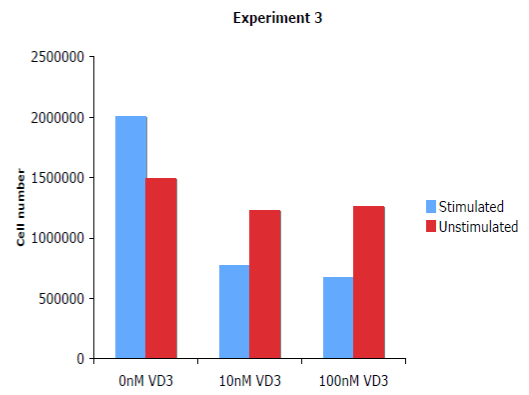
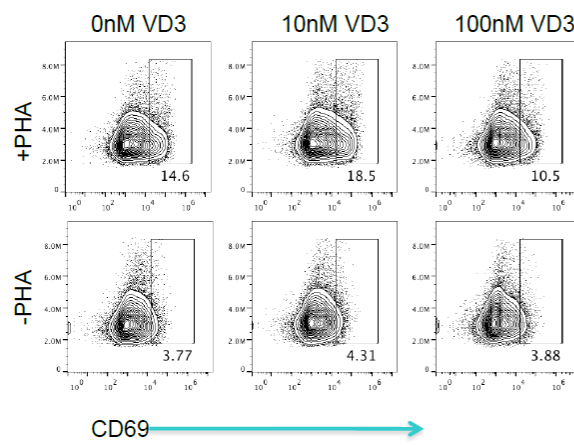
Methods and Materials



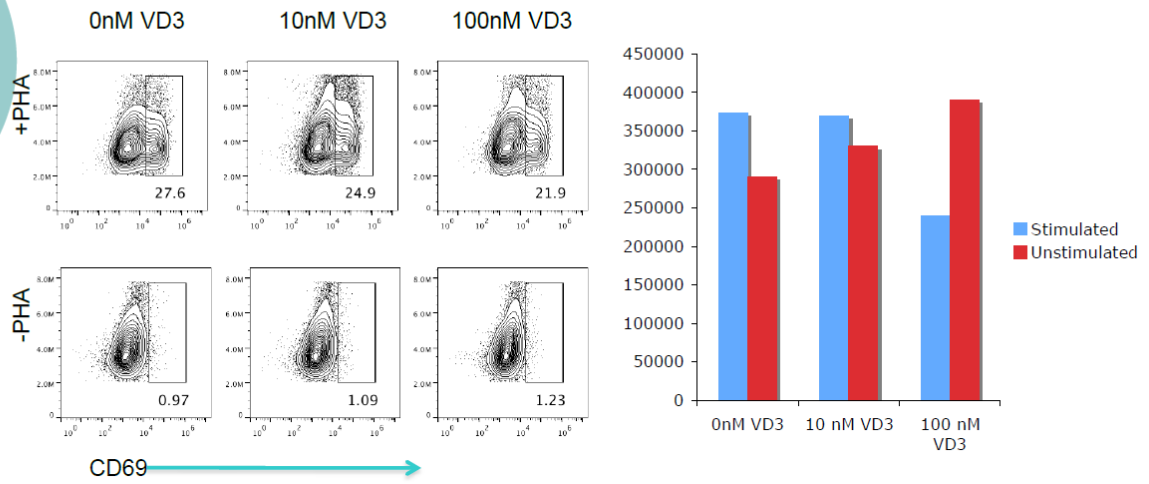
Experiment 1



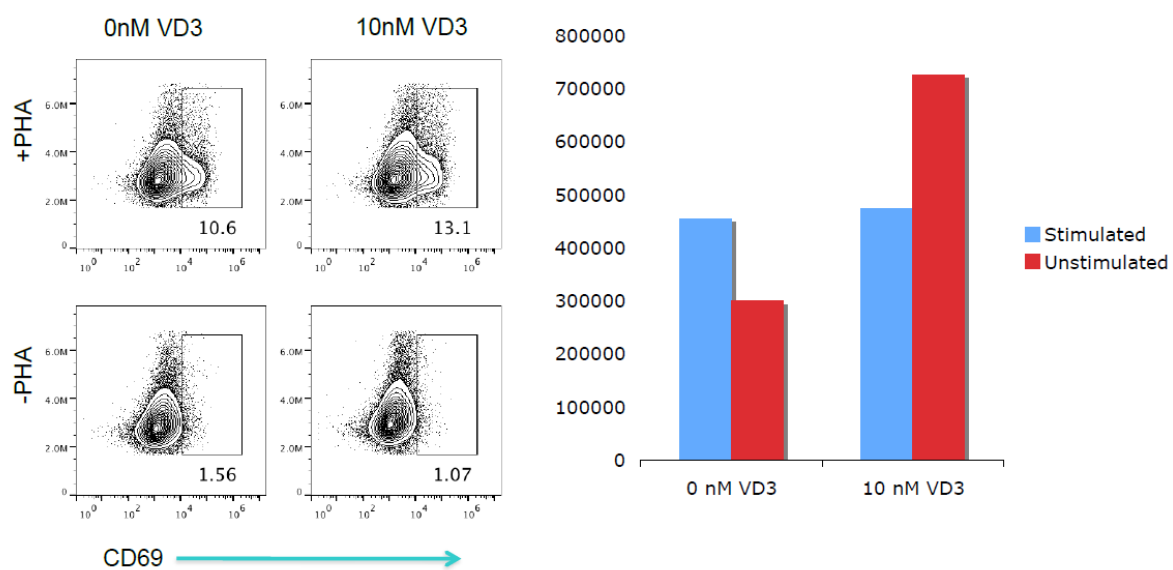
Experiment 2



Experiment 3



Experiment 4





Results

- Vitamin D3 enhanced the up-regulation of Cluster of Differentiation 69 (CD69) in activated T cells.
- Vitamin D3 caused a reduction in cell number of activated T cells at higher doses.



Conclusion

- Vitamin D3 does not suppress T cell activation.
- Vitamin D3 enhances death in activated T cells.



Summary

- The study helped me understand the regulation of T cell activation and death by Vitamin D3.



Acknowledgements

- Dr. Shikhar Mehrotra
- Dr. Krishnamurthy Thyagarajan (TK)
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- Dr. Marvella Ford
- Ms. Tonya Hazelton
- Ms. Juanita Brunson
- All the lab techs

Examining the AGE-RAGE Signaling Axis as a Mechanism of Prostate Cancer Disparity

Sadia M. Robinson, Dion Foster, David P. Turner

Department of Pathology & Laboratory Medicine

Abstract

Nationally, African American prostate cancer patients are two and a half times more likely to die of prostate cancer than their European counterparts. However in the State of South Carolina, minority African Americans are three times more likely to die from prostate cancer. It is now apparent that a racial disparity in cancers exists due to molecular variances in tumor biology as well as consequence of stress, socioeconomic and environmental problems.

Glycation is the non enzymatic glycosylation of sugar moieties to macromolecules which produces vastly reactive metabolites known as advanced glycation end products (AGE's). Elevated AGE levels drive the serious complications observed in diabetes and Alzheimer's patients and AGE's are now emerging as possible intermediaries of cancer. Cancer and dietary sugars are possible mechanisms of cancer health disparities because of associated biological and socioeconomic links. Research studies have been found that lack of exercise and high fat and sugar filled diets aid greatly to the aid of AGE pools. Foods containing abundant AGE's promote obesity and men who are obese are more likely to die because of prostate cancer than thinner men. A higher proportion of African American are overweight or obese and do not exercise compared to European American men.

Harmful effects of AGE's are facilitated in part through its transmembrane receptor RAGE (receptor for advanced glycation end products) which can activate signaling cascades promoting signaling pathways such as NFkB and AKT. This increases excretion of pro-inflammatory cytokines and increases oxidative stress which both promote aggressive cancer.

EXAMINING THE AGE-RAGE SIGNALING AXIS AS A MECHANISM OF PROSTATE CANCER DISPARITY

By: Sadia Robinson

Mentors: Dr. David Turner and Dion Foster

**Department of Pathology & Laboratory
Medicine**

August 1 , 2013

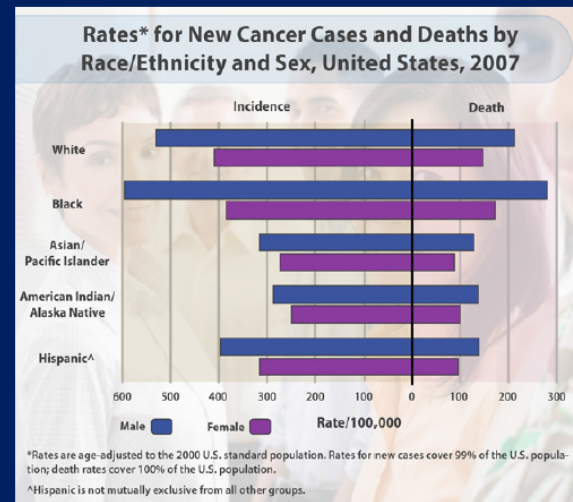
Health Disparity

“The difference in the incidence, prevalence, mortality, and burden of disease and other adverse health conditions that exists among specific population groups”



Cancer Health Disparities

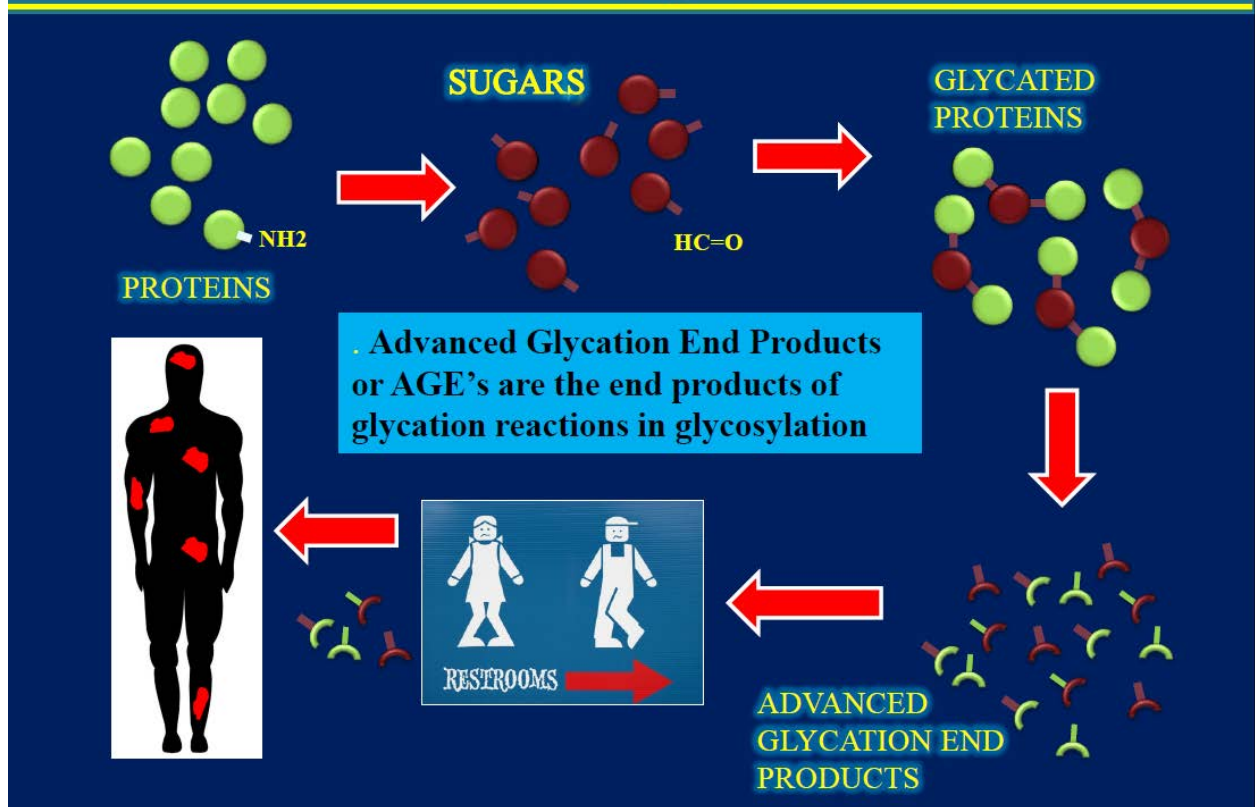
- Overall, African Americans are more likely to develop and die from cancer than any other racial or ethnic group
- In South Carolina African American men are at the highest risk to be diagnosed and die of prostate cancer in America



What are Advanced Glycation End Products ?

- ▣ Endogenous AGE's are reactive metabolites produced during natural metabolism via glycosylation
- ▣ Exogenous AGE's are derived from our diet, and environmental factors such as tobacco smoke
- ▣ High levels of AGEs are implicated in many chronic diseases

What is Glycation?



AGE's are in our Food

Exogenous AGEs are also accumulated in the body through the ingestion of food, smoke and alcohol



High fat foods



Heavily cooked foods



Smoking

Sugary foods



Alcoholic Beverages



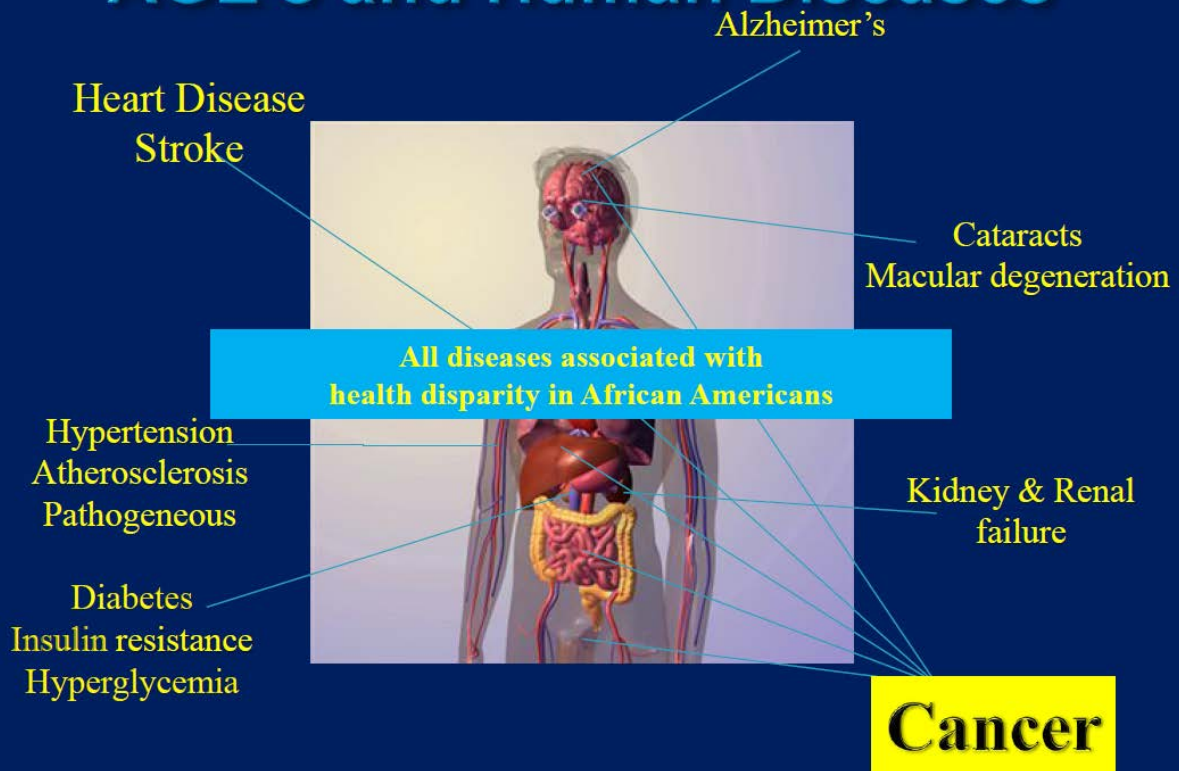
Red Meats



AGE content in western diets has steadily increased over the last 50 years

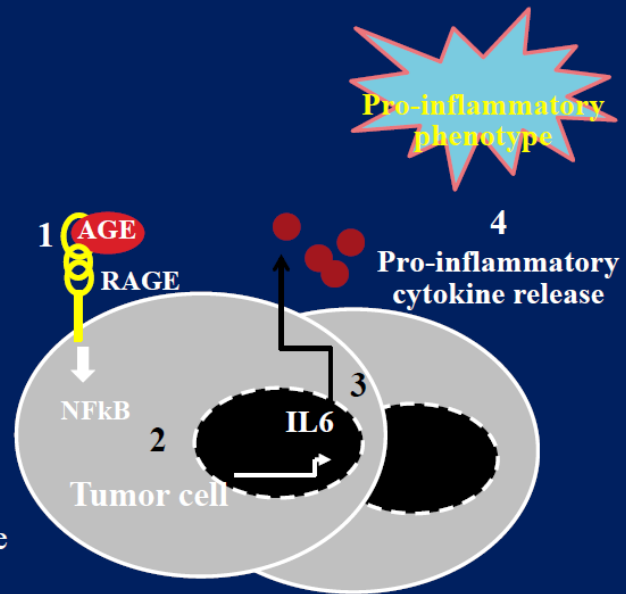


AGE's and Human Diseases



What is RAGE ?

- AGE metabolites are ligands for the RAGE receptor resulting in the activation of signaling pathways
- RAGE is a 35kDa polypeptide transmembrane receptor of the immunoglobulin superfamily
- Increased expression of RAGE is known to promote multiple cancer types ie: Breast Cancer, Prostate Cancer



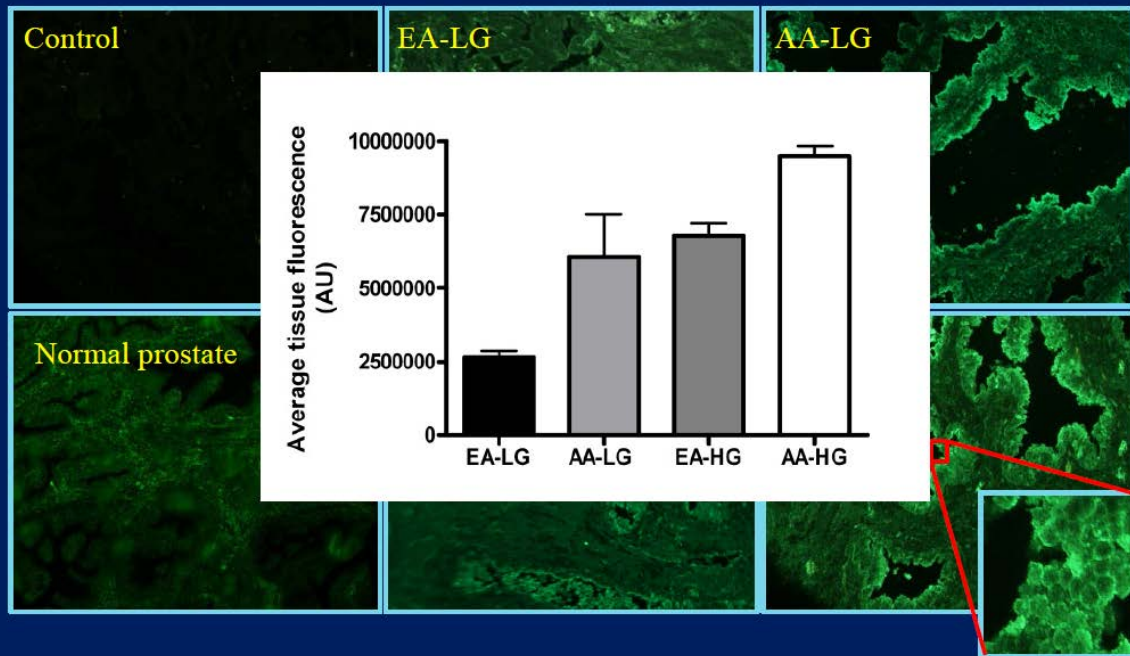
Hypothesis

Increased RAGE activation is a consequence of elevated AGE levels and is a biological mechanism promoting prostate cancer disparity

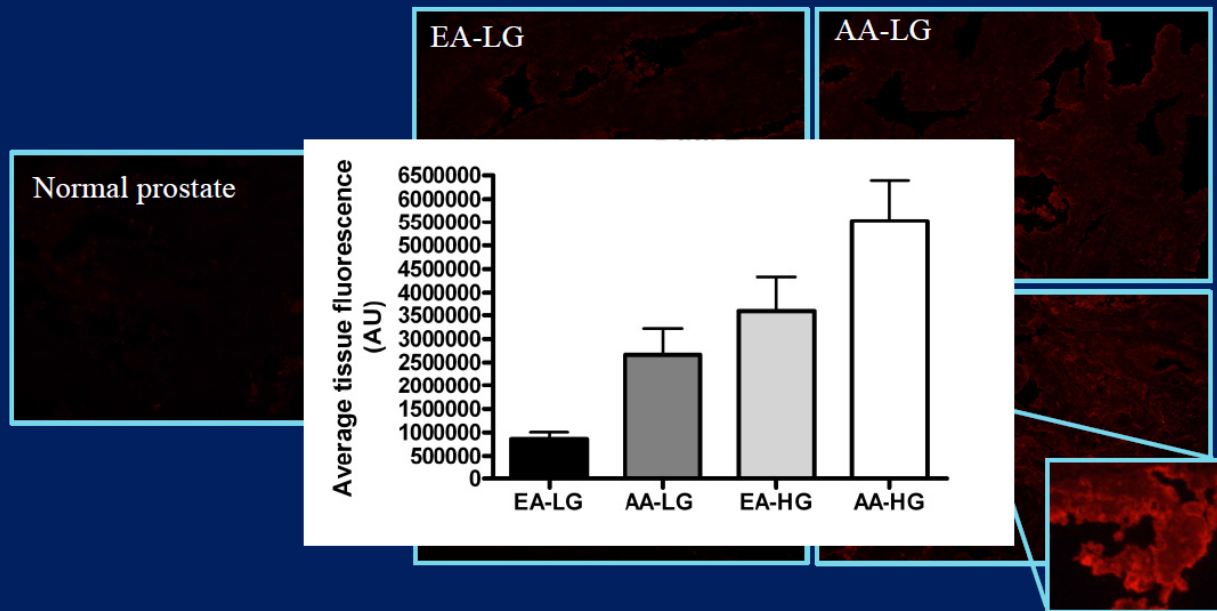
Specific Aims

- ▣ Develop molecular models with which to target RAGE expression in prostate cancer
- ▣ Examine the effects of targeting RAGE expression on cancer associated pathways
- ▣ Examine the effect of AGE treatment on cancer associated pathways

Tumor AGE assessment



Tumor RAGE assessment



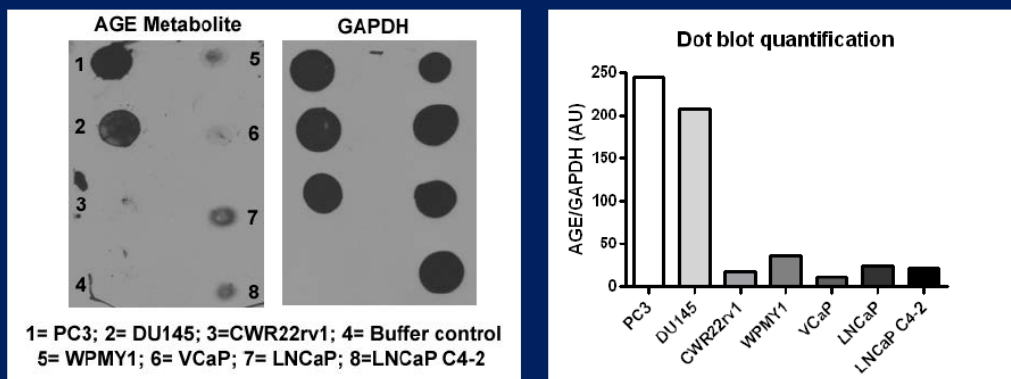
Methods- to assess AGE & RAGE in cell lines

- a) Dot Blot experimentation used to examine cell lines DU145 and PC3
- b) shRNA used to reduce RAGE expression levels
- c) Mammalian expression vectors to increase RAGE expression in prostate cancer cell lines
- d) To assess RAGE protein reduction and increased expression, western blot analysis

Methods – to examine cancer associated pathways

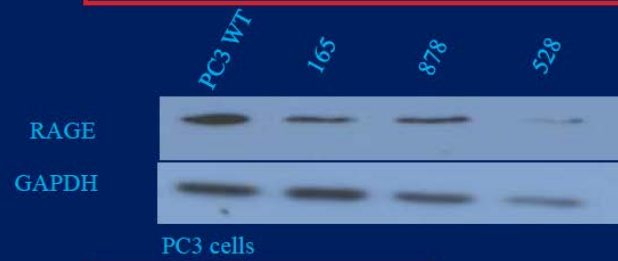
- a.) Sulforhodamine B (SRB) proliferation assays were used to assess cell growth
- b.) Transwell assays will be used to assess cell migration

Dot Blot Results

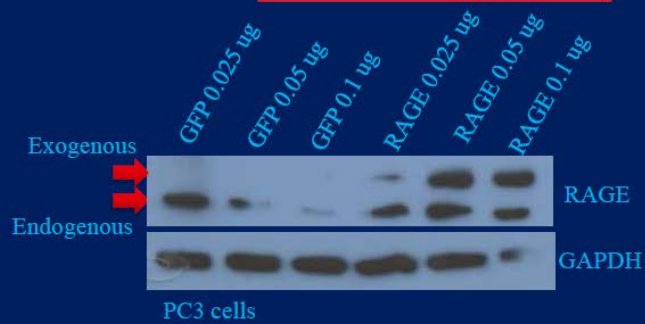


Targeting RAGE Expression

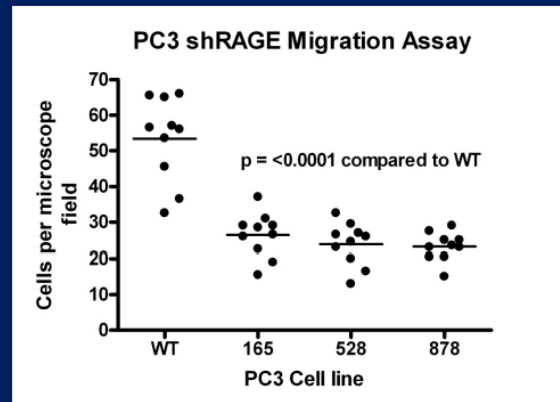
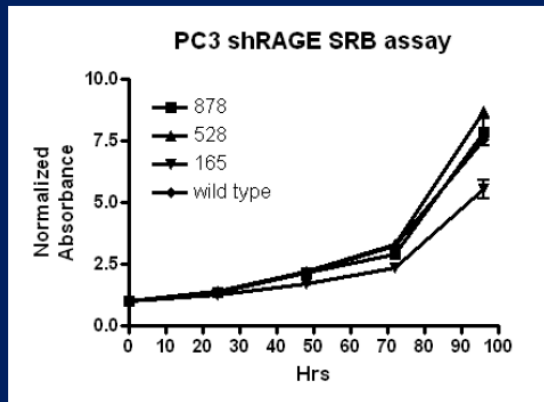
RAGE shRNA mediated knockdown



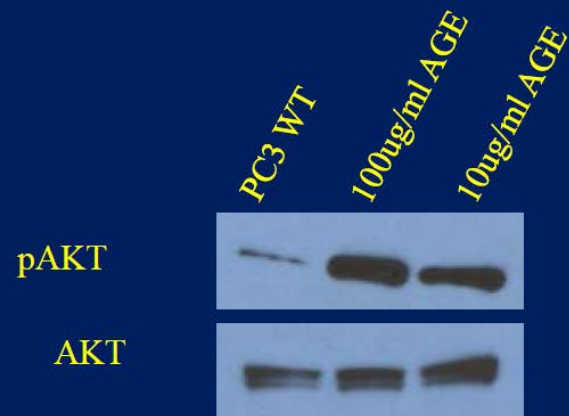
RAGE overexpression



Cell growth & migration assays



AGE treatment



Summary

- 1) **AGE's are reactive metabolites that accumulate in our organs and tissues as we grow older**
- 2) **They accumulate endogenously during normal metabolism and exogenously through the foods we eat**
- 3) **AGE accumulation is associated with diseases associated with growing older**
- 4) **Due to Western diets, dietary AGE's now contribute significantly to the accumulation pool and therefore disease phenotypes**
- 5) **Our work shows that:**
 - **AGE levels are elevated in cancer tissue and cell-lines**
 - **Highest AGE levels are observed in African American cancer patients**
 - **RAGE promotes cancer associated processes**

Conclusion

- ▣ The AGE-RAGE interaction is important in prostate cancer development, and inhibition of this interaction has potential as a new molecular target for cancer therapy or prevention.
- ▣ As AGE and RAGE levels are highest in African American cancer patients, the AGE-RAGE signaling axis may be a mechanism of cancer disparity

AGE Reduction= Disease Prevention



Raw chicken
800 AGE kU/100g



Poached chicken
1,000 AGE kU/100g



Fried chicken
8,000 AGE kU/100g



Big Mac
7,801 AGE kU/100g



Bacon, fried 5min, no oil
91,577 AGE kU/100g



Chicken Nuggets
8,627 AGE kU/100g

Acknowledgements

- ▣ Dr. Marvella Ford
- ▣ Dr. David Turner
- ▣ Dion Foster
- ▣ Dr. Stephanie Brown-Guion
- ▣ Ms. Tonya Hazelton
- ▣ Summer Undergraduate Research Program
- ▣ South Carolina State University

Bobbi Blake

Mentor: Dr. Jennifer Wu

**Funding Source: DOD Southeastern Virtual Institute for Health
Equity and Wellness (PI: Slaughter; Project PI: Ford)**

NKG2D Signaling Pathways Analysis

Hypothesis

Stimulation of NK cell lines with purified soluble MIC will lead to NK cell activation in a dose-dependent manner as measured by pAKT and DAP10/12 expression.

Introduction

The response of natural killer cells are initiated by cellular surface receptors and regulated by signaling pathways that function in activation or inhibition. The balances between the signals are the difference between cytokine production or immune escape. Activation of NK cells occurs through the interaction of NKG2D receptor and MIC molecules. NK cell kill cells that lack MIC “self-recognition” receptors (Lanie, 2003).

Previous studies have shown positive correlation of patients with different tumors and high level of soluble MIC in serum samples (Roda-Navarro & Reyburn, 2009). This relation suggests the occurrence of immune evasion.

Two targets, pAKT and DAP10/12 have been identified to indicate cell proliferation. pAKT, protein kinase b is a main factor in cellular survival pathways in which it has the ability to inhibit apoptosis and promote the production of growth factors. DAP10/12 is an adaptor on the NKG2D receptor that aids in costimulation and enhances activation (Jiang, Zhong, & Ritchey, 2002).

In this study, NK cells are exposed to soluble MIC cells and pAKT and DAP10/12 expression is examined. The impact of soluble MIC molecules on positive and negative signaling in NK cells is a promising area in understanding the mechanisms of NK cell homeostasis.

NKG2D Signaling Pathways Analysis

Bobbie Blake

Mentor : Dr. Jennifer Wu

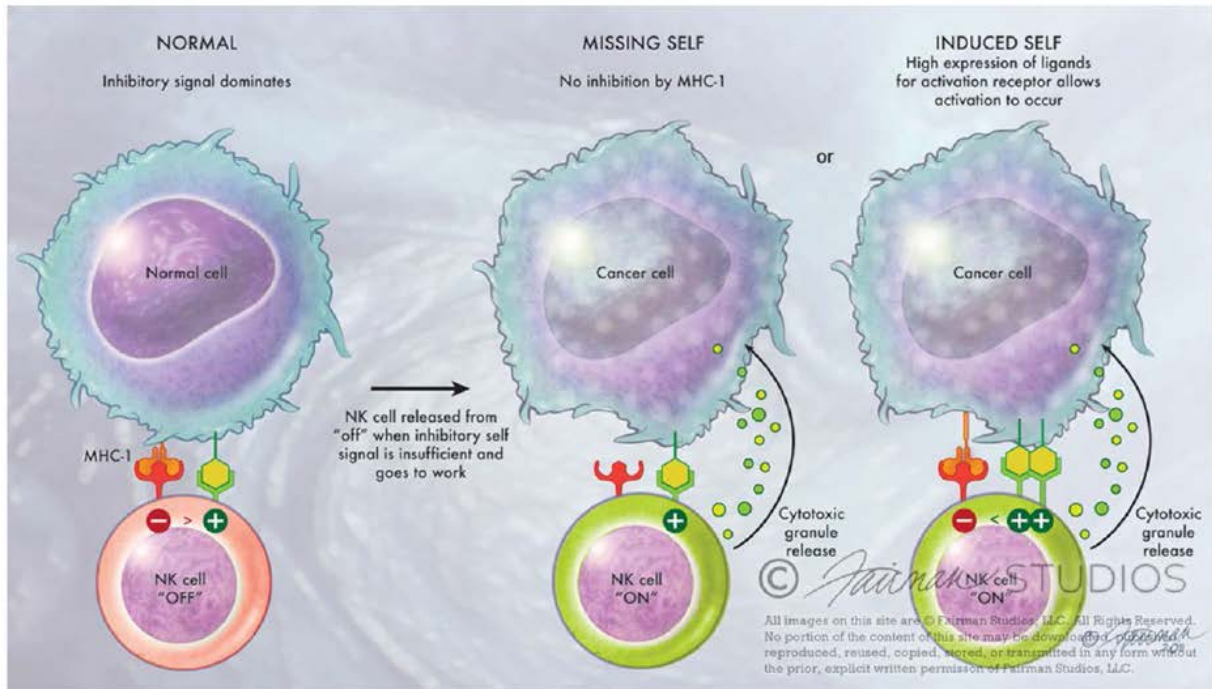
Summer Undergraduate Research Program

Natural Killer (NK) Cell

- Cytotoxic lymphocytes in the immune system
- Antibody-dependent cell-mediated cytotoxicity
- Cytolytic granule mediated cell apoptosis
- Missing 'self' hypothesis
 - NK cells recognize the lack of self-ligands on infected cells or cells undergoing other types of stress

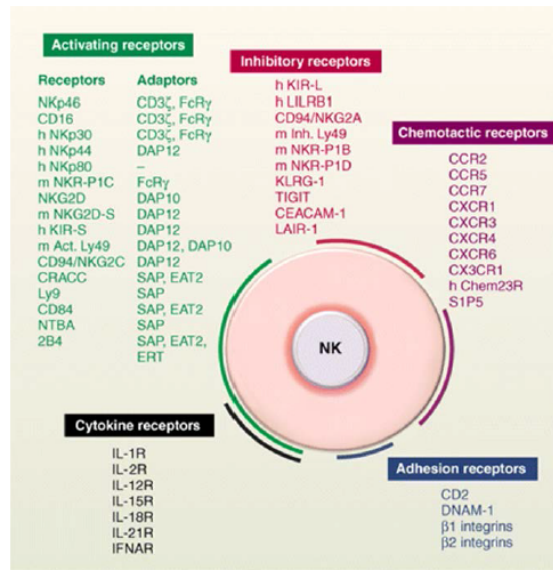
Tumor cell surveillance

NK Cell Function



NK Cell Receptors

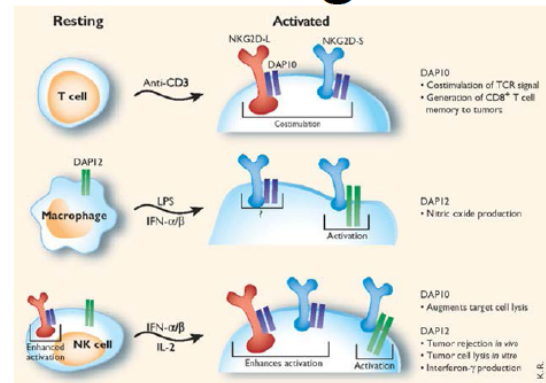
- NKG2D receptor activates NK cells after engaging ligands induced by cellular stress



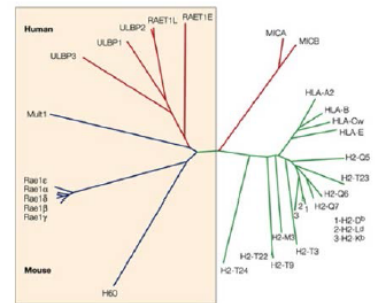
Vivier et al., Science Jan 2011

NKG2D Receptor and MIC Ligand

- Activating receptor expressed by
 - All NK cells
 - Most NKT cells
 - Certain subsets of $\gamma\delta$ T cells
 - All human CD8+ cells
 - Activated mouse CD8+ cells
 - Activated macrophages
 - IFN-producing killer DCs



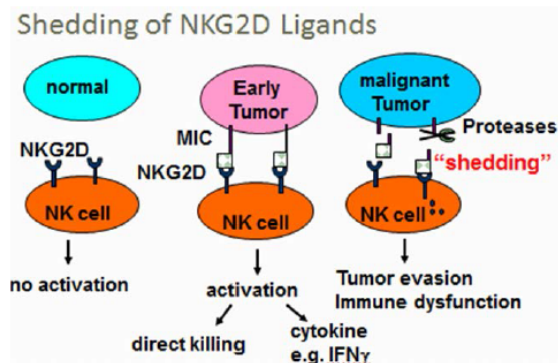
- Distinct ligands and signaling adaptors (DAP10/12) for human and mouse
- NKG2D receptor binds to MIC ligands
- MICA - MHC class I related polypeptide sequence A



Nature Reviews | Immunology

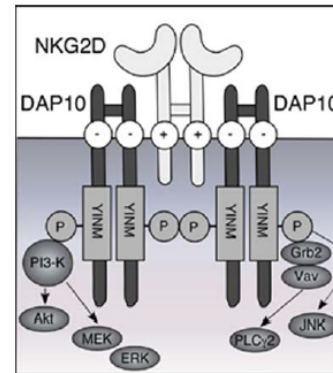
Soluble MIC in Cancer

- Cancers adopt diverse strategies for immune evasion to ensure their survival.
- Epithelial tumors shed soluble MIC in later stages of cancer
- Shedded MIC= serum sMIC



Signal Pathway of NKG2D

- Proteins of Interest
 - DAP10-adaptor proteins, which activate signaling pathways for cytotoxicity and cytokine production
 - AKT-pAKT, protein kinase b is a main factor in cellular survival pathways in which it has the ability to inhibit apoptosis and promote the production of growth factors.



Hypothesis and Specific Aims

- Hypothesis
 - Stimulation of NK cell lines with purified soluble MIC will lead to NK cell activation in a dose-dependent manner as measured by pAKT and DAP10/12 expression.
- Specific Aim 1: Determine whether sMIC lead to AKT phosphorylation in NK cell lines NKL and NK-92MI
- Specific Aim 2: Determine if changes in AKT phosphorylation occur through the NKG2D signaling protein DAP10/12

Methods

- Cell Culture – NKL and NK-92MI cell line will be cultured in a 1×10^6 x 1 ml per well, 24 well plate
 - NKL and NK-92 cells were cultured in the presence of IL-2 and during the experiment IL-2 was removed.
- Cell Harvest- Cells were exposed to soluble MIC at the concentrations 0, 50, 100 ng/ml and harvested at 1, 4, 24 and 48 hour time points.
 - Cells were lysed for proteins in the presence of protease and phosphatase inhibitors
- BCA Protein Assay- Quantify protein concentrations
- Western Blotting- Quantify expression of AKT and DAP10 proteins at varied time points of exposure to sMIC

Expected Results

DAP10 Proteins

- Increase expression of proteins with increase in sMIC concentration and time

Akt Proteins

- Decrease in expression of phospho Akt protein with an increase in sMIC concentration and time.

Future Directions

- The current study involves NK cell interacting with soluble ligand
- Future studies will involve NK cell interacting with tumor cell expressing soluble ligand.

Acknowledgements

- Dr. Ford
- Dr. Jennifer Wu, Mentor
- Fahmin Basher , MD/PhD student
- Ms. Tonya Hazleton
- Summer Undergraduate Research Program
- MUSC Hollings Cancer Center

Franshawn Mack

Mentor: Dr. Marvella Ford

**Funding Source: DOD Southeastern Virtual Institute for Health
Equity and Wellness (PI: Slaughter; Project PI: Ford)**

Evaluating the Reliability of an Instrument Assessing Cancer Clinical Trial Perceptions in Predominantly African American Populations in South Carolina

Franshawn Mack

Dr. Marvella E. Ford

Dana Burshell

Wei Wei

Dr. Elizabeth Garrett-Mayer

July 19, 2013

Background: African Americans (AA) are disproportionately affected by cancer mortality compared to their European American (EA) counterparts. While greater participation in cancer clinical trials among AA could help to reduce this disparity, negative perceptions of trials may play a role in negatively impacting trial participation in this population.

Objective: To evaluate the reliability of the Attitudes towards Randomized Trial Questionnaire (ARTQ) in assessing perceptions of cancer clinical trials in predominantly AA populations in South Carolina (SC). The ARTQ was developed in Europe and has not yet been tested for use in an AA sample.

Methods: Principal Component Analysis and Cronbach's alpha estimates were used to assess the reliability of the ARTQ in a convenience sample of 315 participants (81.4% AA), from 2008 to 2013, who lived in SC counties with high racial disparities in cancer mortality rates.

Results: Slightly more than half of the participants had at least a college diploma (60.8%), 84.8% were female, and 53.4 % had an annual income of \$40,000 or more. In this study, Cronbach's alpha for the ARTQ was 0.86.

Conclusion: The ARTQ displayed strong evidence of high statistical reliability. This analysis has great implications for future research because it represents the first test of reliability of the ARTQ in a predominantly African American sample and lays the groundwork for use of the ARTQ in future studies in diverse populations.

Evaluating the Reliability of an Instrument Assessing Cancer Clinical Trial Perceptions in a Predominantly African American Sample in South Carolina



Franshawn Mack, Rising Sophomore,
South Carolina State University
2013 MUSC Summer Undergraduate Research Program

Funding Source



- ✧ Mentor: Dr. Marvella Ford
- ✧ Grant: Department of Defense- Southeastern Virtual Institute for Health Equity and Wellness (DOD-SE VIEW)

Presentation Outline



- ❧ Introduction
 - ❧ Statement of Problem
 - ❧ Purpose of Study
- ❧ Methods
 - ❧ Study Sample
 - ❧ Measures
 - ❧ Analysis
- ❧ Results
 - ❧ Demographic Characteristics
 - ❧ Instrument Responses
 - ❧ Reliability Analysis
- ❧ Discussion
- ❧ Conclusions
- ❧ Acknowledgements

Introduction



Introduction (continued)



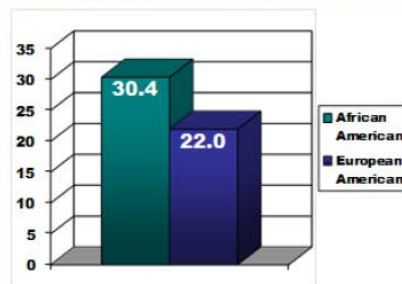
- ❧ For the majority of cancer types African Americans (AA) have the highest cancer mortality rate of any other racial or ethnic group in the United States. This is also true in South Carolina.

Cancer Mortality For South Carolina

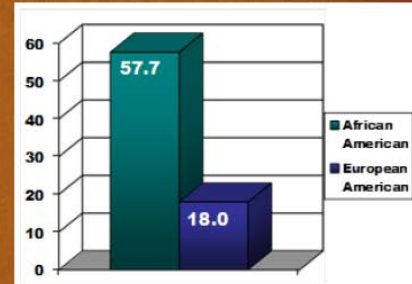
Age Adjusted Rates: 2000 US Standard Population

County: All Counties In South Carolina, 2008

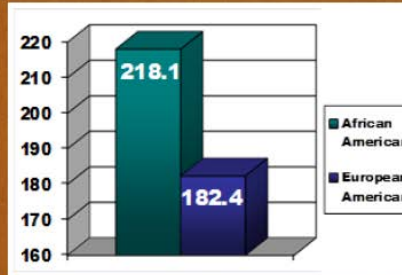
Breast Cancer



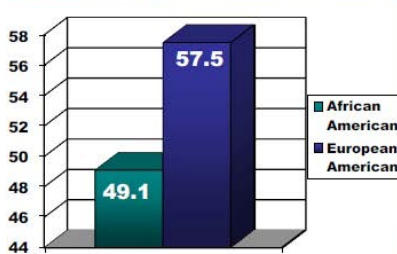
Prostate Cancer



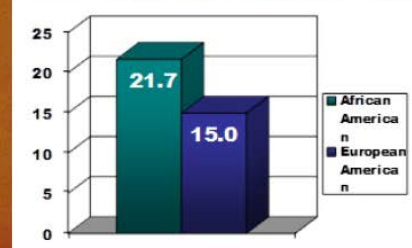
All Cancers



Lung Cancer



Colorectal Cancer

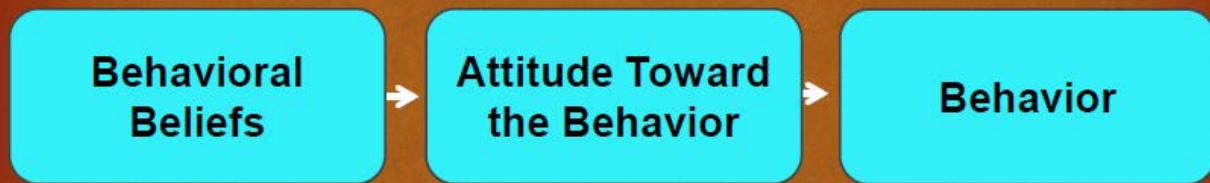


Statement of the Problem



- ❧ Despite being disproportionately impacted by cancer, AA participate in cancer clinical trials less frequently than European Americans (EA)
- ❧ Negative perceptions of clinical trials could affect AA participation

Conceptual Framework



Ajzen I, Fishbein M. Attitudinal and normative variables as predictors of specific behavior. *Journal of Personality and Social Psychology* 1973;27:41-57.

Botosaneanu A, Alexander JA, Banaszak-Holl J. To test or not to test? The role of attitudes, knowledge, and religious involvement among U.S. adults on intent-to-obtain adult genetic testing. *Health Education & Behavior* 2011; 38:617-628.

Statement of Problem (continued)



- ❧ In order for health disparities research to be conducted in a meaningful manner, it is important to determine first whether measures developed among nonminority populations perform in the same way when applied to minority populations (Ramirez et. al 2005)

Statement of Problem

(continued)



- ❧ The Attitudes to Randomized Trial Questionnaire (ARTQ) is widely used in Europe to assess perceptions of trials
- ❧ However, the reliability of this instrument has never before been tested in an AA sample, so its applicability in this population is unclear

Statement of Problem (continued)



- ❧ Reliability in this context refers to the repeated use of an instrument, over time, with consistent results

Purpose of the Study



- ❧ **Purpose:** To evaluate the reliability of the ARTQ in a predominantly AA sample. This is the first study to do so
- ❧ **Hypothesis:** The ARTQ will show evidence of high statistical reliability

Methods



Study Sample



- ❧ Study participants were residents in South Carolina communities with high racial disparities in cancer mortality rates
 - ❧ 17 sites in 11 counties
 - ❧ Majority of counties along the I-95 Corridor
- ❧ Male or female
- ❧ Any race or ethnicity
- ❧ Ages 21 years or older

Study Sample (continued)



- ❧ The study sample participated in an educational program using a National Institutes of Health PowerPoint presentation that describes cancer clinical trials
 - ❧ 30-minute presentation focusing on cancer clinical trials information
- ❧ The study investigators modified the NIH presentation to make it more culturally appropriate:
 - ❧ Inclusion of lay language
 - ❧ Use of images with ethnically/racially diverse people
 - ❧ Review of previous atrocities (Tuskegee Syphilis study)
 - ❧ Description of safeguards developed to protect trial participants

Study Sample (continued)



- ❧ The clinical trial education program was part of a larger evidence-based, 4-Hour Cancer Education Program developed by the South Carolina Cancer Alliance
- ❧ Incorporated a Train the Trainer Design and a Pre-Test/Post-Test Design

Measures



- ❧ Pre-test data, interviewer-administered
 - ❧ General sociodemographic information
 - ❧ Age, race, education level, income
 - ❧ 7-Item Attitudes to Randomized Trial Questionnaire (ARTQ) (Fallowfield et al. 1998)
 - ❧ Responses include Yes, No, DK

Measures (continued)



Fallowfield Study (1998): Development of the ARTQ

- ❧ Seven-item instrument used to assess perceptions of cancer clinical trials
 - ❧ Consecutive sample of 323 patients with cancer in the United Kingdom (UK)
 - ❧ 315 patients completed the ARTQ, unassisted

Measures (continued)



Summary of the 7-item ARTQ Questions:

Response Categories: Yes, No, Don't Know

1. Do you think patients should be asked to take part in medical research?

Would you be prepared to take part in a study:

2. comparing different treatments?

3. where the treatment was chosen at random?

Measures (continued)



Would you be encouraged to take part in a randomized study:

4. where either treatment would be suitable for you?
5. if you could leave the study if the treatment was not suitable for you?
6. if before you agreed to participate, your doctor would tell you all about both treatments being compared?

Measures (continued)



7. If you knew all of the following things were taken into account, would you change your mind and agree to take part in the study?

- ❧ Both treatments were completely suitable
- ❧ You could leave the study if the treatment did not suit you
- ❧ There was plenty of information before the random choice was made

Analysis



Reliability Analysis

- ❧ Principal Component Analysis (PCA) was used to evaluate the dimensionality of the ARTQ
- ❧ Cronbach's alpha was used to measure internal consistency, indicating survey reliability

Results



Demographic Characteristics (N=315)



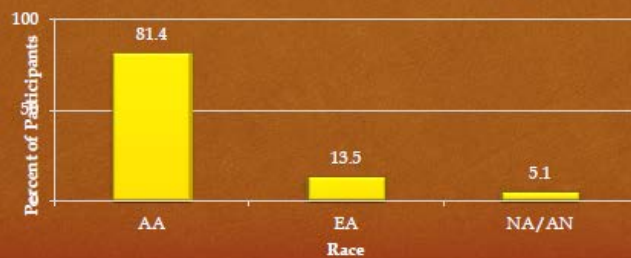
Gender* (n=211)

- Majority of the study participants were female (84.8%)

Race* (n=296)

- Most participants were African American (81.4%)
- Compared to the state population of 0.5% Native American/Alaskan Native (NA/AN), our study included a significant population of NA/AN (5.1%)

Racial Distribution of Participants*



*= missing data

Demographic Characteristics (N=315)

Education* (n=298)

- More than half of the study participants had at least a college degree (77.9%)

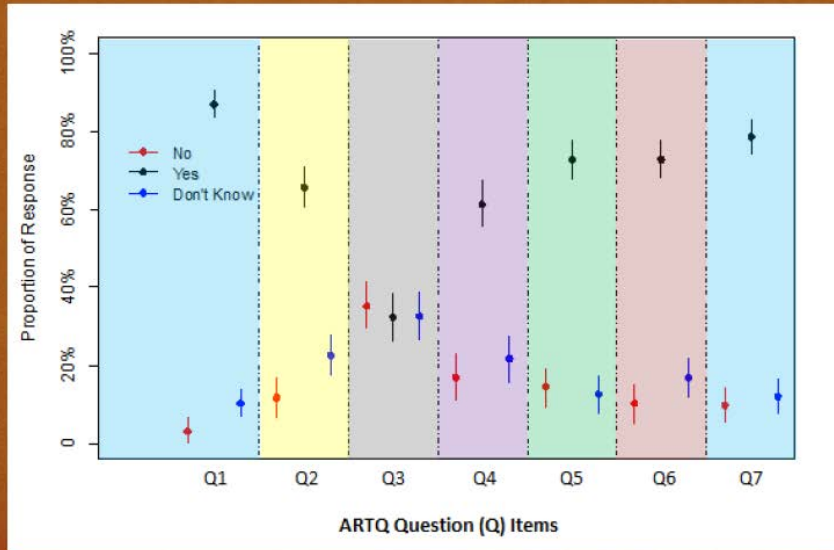
Income* (n=286)

- Slightly more than half had an annual household income equal to or greater than \$40,000 (53.1%)

Survey Responses



Proportion of Participants Who Responded Yes/No/Don't Know for the Seven Items in the Attitudes to Randomized Trial Questionnaire



Statistical Tests

- PCA confirmed unidimensionality of the ARTQ
- Cronbach's $\alpha=0.86$

Cronbach's alpha	Internal consistency
$\alpha \geq 0.9$	Excellent (High-Stakes testing)
$0.8 \leq \alpha < 0.9$	Good (Low-Stakes testing)
$0.7 \leq \alpha < 0.8$	Acceptable (Surveys)
$0.6 \leq \alpha < 0.7$	Questionable
$0.5 \leq \alpha < 0.6$	Poor
$\alpha < 0.5$	Unacceptable

Discussion



Discussion



Study results show the ARTQ to be reliable in this predominantly AA South Carolina sample

Conclusions



- ✎ This is the first study to employ the ARTQ to evaluate perceptions of trials in a predominantly AA sample- the majority of studies using the ARTQ were conducted in Europe with primarily EA samples

Conclusions (continued)



- ❧ Additional testing of the ARTQ is required in other samples of diverse population groups from different geographic regions of the US to confirm the reliability of the instrument in these groups:
 - ❧ Male vs. Female
 - ❧ Low Education Level vs. Higher Education Level
 - ❧ Low income Level vs. Higher Income Level
 - ❧ Subgroups of AA (e.g., Sea Islands, Haitians, Nigerians)
 - ❧ Latinos/Hispanics
 - ❧ Non-English speaking populations in the U.S. who have low trial participation rates

Acknowledgements



- ❧ Dr. Marvella Ford
- ❧ Ms. Dana Burshell
- ❧ Mr. Wei Wei
- ❧ Dr. Elizabeth Garrett-Mayer
- ❧ Mrs. Tonya Hazelton
- ❧ Ms. Juanita Brunson
- ❧ Mrs. Stephanie Brown-Guion
- ❧ MUSC Summer Undergraduate Research Program

Jasmine Fox

Mentor: Dr. Victoria Findlay

**Funding Source: NIH/NCI P20 South Carolina Cancer Disparities Research
Center (PIs: Ford and Salley)**

MiR-204 Negative Regulation of IGF2R as a Mechanism Driving Breast Cancer Disparity

Jasmine Fox, South Carolina State University

Victoria Findlay, Ph.D., Mentor

2013 MUSC Summer Undergraduate Research Program (SURP)

Abstract

Breast cancer accounts for 22.9% of all cancers in women in the world (<http://breastcancersymptoms.net>). Approximately 1 in 8 women will develop breast cancer, and it causes 13.7% of cancer death in women. In the US, African American (AA) women have a significantly higher rate of mortality due to BC compared to Caucasian American (CA) women.

MicroRNAs are small non-coding RNAs that function to silence gene expression by translational repression or mRNA target degradation (2). The microRNA of interest in this study is miR-204; we identified the Insulin Growth Factor 2 Receptor (IGF2R) as a direct target of miR-204. The IGF-2R is a multifunctional receptor that binds IGF-II resulting in its internalization and degradation via lysosomes. The IGF-2R does not have tyrosine kinase/signaling activity, instead it functions to sequester IGF-II away from the IGF1R signaling pathway, resulting in its proposed role as a tumor suppressor.

Studies have shown that the levels of IGF2R are lower in AA women compared to CA women with breast cancer. To assess whether miR-204 levels are disparate in AA women with breast cancer, we performed real time PCR in serum samples from 20 patients; 10 AA and 10 CA. Our analysis shows that there is a significant increase in the levels of miR-204 in the AA breast cancer patients when compared to the CA patient samples. We have previously shown that miR-204 over-expression results in an increase in migration and invasion. Therefore, to assess whether this miR-204 mediated increase is through the negative regulation of the IGF2R we transfected miR-204 expressing and scrambled control breast cells with the IGF2R ORF. IGF2R levels were confirmed by western blot analysis. We found that expression of exogenous IGF2R was able to restore invasive levels of the cells back to control level. We also performed immunofluorescence to demonstrate that IGF2R when exogenously expressed was localized to the cell membrane. These studies are being optimized.

MIR-204 NEGATIVE REGULATION OF IGF2R AS A MECHANISM DRIVING BREAST CANCER DISPARITY

Jasmine Fox

Mentor: Victoria Findlay, Ph.D.

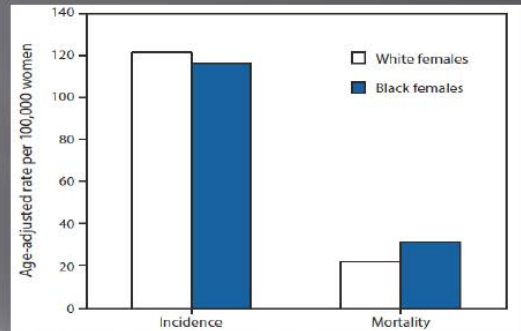
Summer Undergraduate Research Program
(SURP) 2013

Breast Cancer Overview

- ▣ Breast Cancer (BC), is the development of cancerous tumors in the breast tissue that arise from epithelial cells
- ▣ Breast cancer accounts for 22.9% of all cancers in women in the world
- ▣ Approximately 1 in 8 women will develop breast cancer
- ▣ BC causes 13.7% of cancer death in women

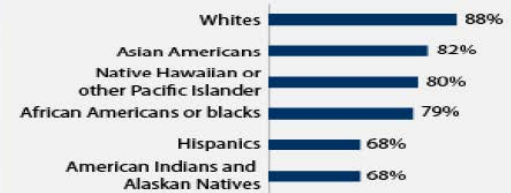
Breast Cancer Disparities

- AA women have the highest BC death rates of all races and ethnic groups
- EA women have the highest incidence rate for BC, but AA are most likely to die from BC
- AA women often have fewer socioeconomic resources than other women such as:
 - Lack of medical coverage
 - Barriers to early detection/screening



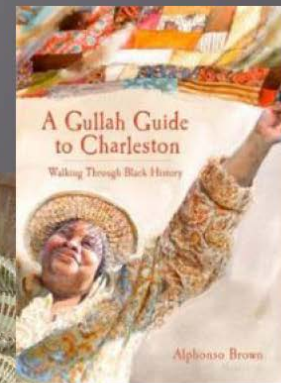
Who has health coverage?

Percent of Americans with health coverage, by race



Note: Percentages for Native Hawaiian or other Pacific Islander and American Indian and Alaskan Natives is based on 2005–2007 data, all other percentages based on 2009 data.

The Sea Island Population of SC



- African Americans from the Sea Islands of SC are direct descendants of blacks from the “rice or windward coast” of West Africa
- The Sea Island descendants are primarily from the country of Sierra Leone
- The Sea Island population is genetically and culturally distinct due to previous geographic isolation and low rates of genetic admixture
- The low rates of admixture in the Sea Island population makes them uniquely positioned to allow genetic studies

MicroRNAs (miR-204)

Background

- ▣ MicroRNAs are small non-coding RNAs that function to silence gene expression by translational repression or mRNA target degradation
- ▣ The microRNA of particular interest in this study is MicroRNA 204 or miR-204
- ▣ miR-204 is a novel oncomir
- ▣ Over-expression of miR-204 in immortalized non-transformed and non-invasive breast cancer cell lines results in increased migration, invasion, and cellular transformation

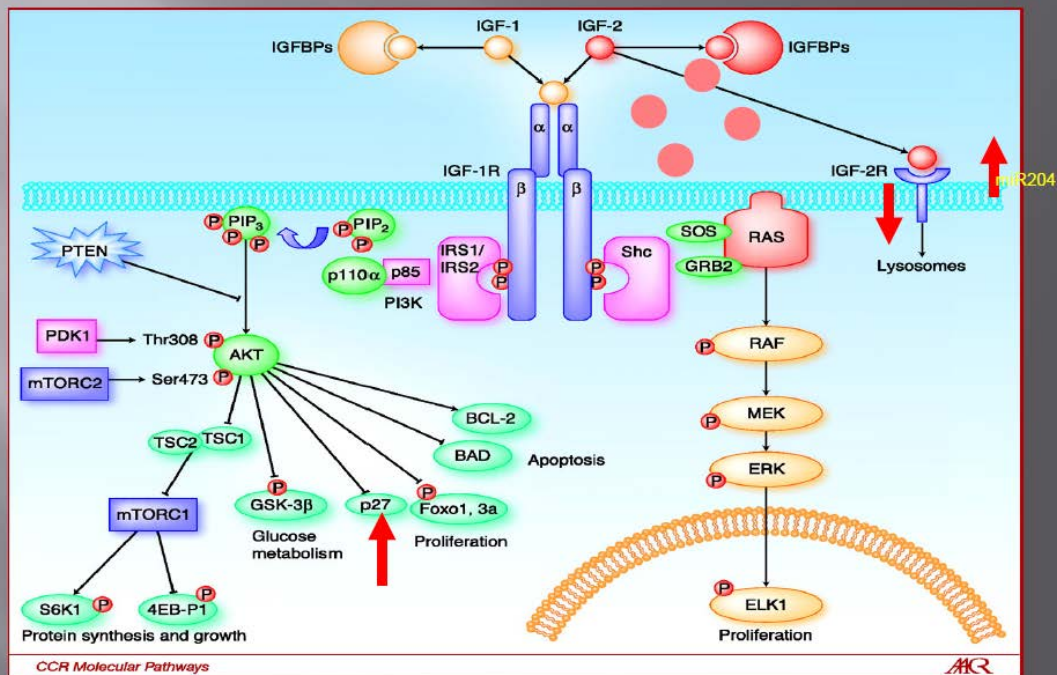
IGF2 and IGF2R Background

- ▣ Insulin Growth Factor 2 Receptor (IGF2R) has been identified as a novel direct target of miR-204
- ▣ Insulin growth Factor 2 receptor (IGF2R) is a transmembrane receptor that binds IGF-2, resulting in its degradation via internalization and transport to lysosomes
- ▣ IGF-II is a mitogenic and anti-apoptotic peptide
- ▣ IGF-II influences the proliferation of various cell types including normal and transformed breast epithelial cells

IGF2R in Cancer

- ▣ Low levels of IGF2R expression were shown to correlate with poor patient prognosis in breast cancer patients and a recent study showed significantly higher levels of IGF2R in EA compared to AA tumor samples

Key components of the IGF-1R pathway.



Zha J, Lackner M R Clin Cancer Res 2010;16:2512-2517

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ACR Clinical Cancer Research

Hypothesis

- ▣ We hypothesize that miR-204 mediated negative regulation of the IGF2R is a mechanism promoting breast cancer disparity.

Specific Aims

- ▣ 1) To evaluate the levels of miR-204 in serum samples from AA and EA women with breast cancer
- ▣ 2) To demonstrate that miR-204 mediated increase in migration is through the negative regulation of the IGF2R

Specific Aim 1 - Methodology

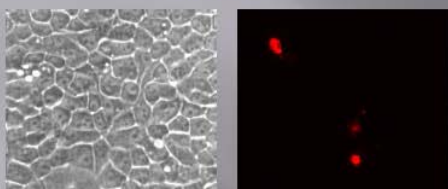
- ▣ Transfection with different ratios of Transfection Reagent:IGF2R plasmids
- ▣ Transfection in MCF10A cells stably transfected with scrambled and miR-204
- ▣ Protein extractions using RIPA buffer to lyse the cells and run on western blot:
 - ▣ - the levels of IGF2R using protein specific antibody
- ▣ RNA Extraction, Reverse Transcription and Real Time PCR
- ▣ Migration assay
- ▣ Immunofluorescence assay - localization

MCF10A Transfection Optimization

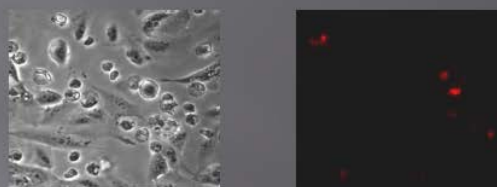
Screening of TransFection Reagent , Ratio= μl Reagent: μg DNA

DNA= pmiR-EV (cherry)

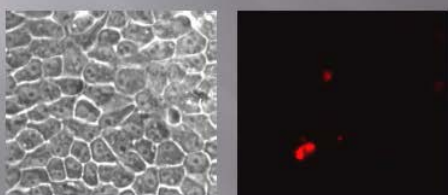
Ratio 1:1



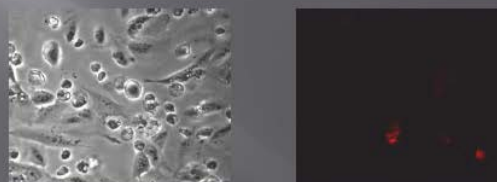
Ratio 4:1



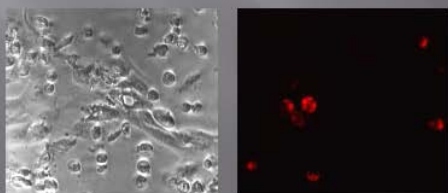
Ratio 2:1



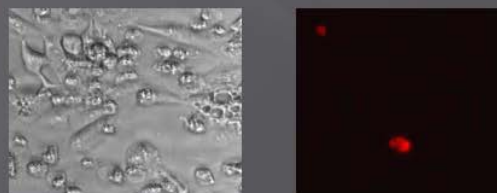
Ratio 5:1



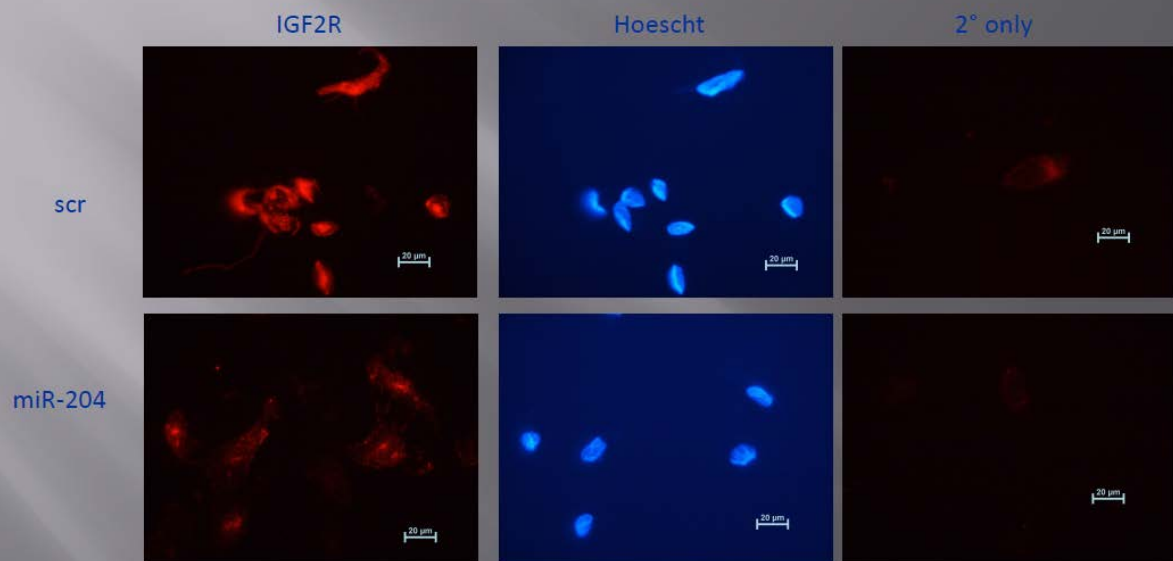
Ratio 3:1



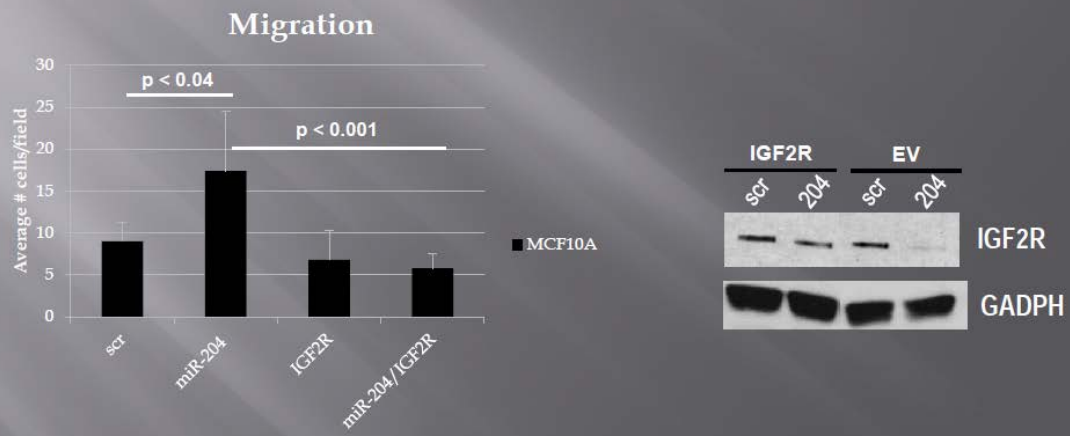
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MCF12A stables



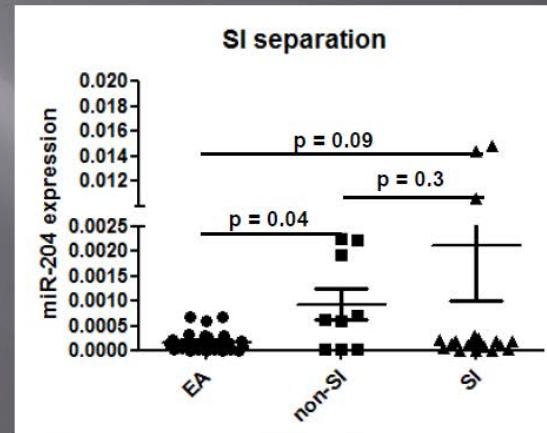
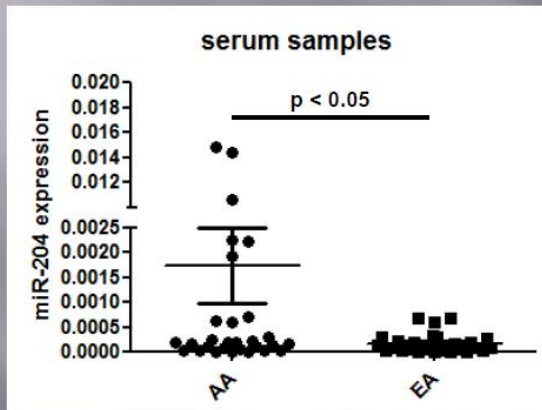
IGF2R “Rescue”



Specific Aim 2 Methodology

- ▣ Serum samples were obtained from the HCC tissue Biorepository
- ▣ 10 EA & 10 AA (3 non-SI & 7 SI)
- ▣ RNA extraction from serum samples using Trizol
- ▣ miR reverse transcription
- ▣ Real Time PCR assay

miR-204 levels are disparate in serum from breast cancer patients



non-SI:SI
3:7

CONCLUSIONS

- ▣ We demonstrated that miR-204 increases migration via direct negative regulation of IGF2R
- ▣ We showed that levels of miR-204 expression in serum samples were higher in AA women than EA women
- ▣ This decrease in IGF2R expression may contribute to the increase risk of malignant transformation in AA breast cancer patients

Acknowledgements

- ▣ Victoria Findlay, Ph.D., mentor
- ▣ Lourdes Nogueira
- ▣ Qi Guo
- ▣ Dr. Marvella Ford
- ▣ MUSC's Summer Undergraduate Research Program (SURP)
- ▣ Hollings Cancer Center

Appendix D: Academic Accomplishments to Date of the 2013 Student Fellows

Year of Program Participation: 2013

❖ These are Student Fellows who participated in the 2013 DOD South Carolina Collaborative Undergraduate HBCU Student Summer Training Program. Therefore it is too early to report additional accomplishments at this time. Many accomplishments are expected to occur during the course of the next few years following their participation.

Student Name	Summer Research Project	Funding Source	Publications, Presentations and Honors	GRE Status	Graduate School Admission
Ms. Jasmine Fox SC State University	Mentor: Dr. Victoria Findlay Research Project: MiR-204 Negative Regulation of IGF2R as a Mechanism Driving Breast Cancer Disparity	National Institutes of Health/ National Cancer Institute	Publication: No publications to date Presentation: 2013 MUSC Summer Undergraduate Research Program	Has not taken the GRE.	Still enrolled at SC State University.
Ms. Sadia Robinson SC State University	Mentor: Dr. Dave Turner Research Project: Examining the AGE-RAGE Signaling Axis as a Mechanism of Prostate Cancer Disparity	Department of Defense (HBCU)	Publication: No publications to date Presentation: 2013 MUSC Summer Undergraduate Research Program	Has not taken the GRE.	Still enrolled at SC State University.
Ms. Tomesha Nesbitt Voorhees College	Mentor: Dr. Shikhar Mehrotra Research Project: The Effect of Vitamin D3 on T cell Activation and Death	Department of Defense (HBCU)	Publication: No publications to date Presentation: 2013 MUSC Summer Undergraduate Research Program	Has not taken the GRE.	Still enrolled at Voorhees College.
Ms. Keira Addison SC State University	Mentor: Dr. Danyelle Townsend Research Project: Redox Signaling is deregulated in Breast Cancer	Department of Defense (HBCU)	Publication: No publications to date Presentation: 2013 MUSC Summer Undergraduate Research Program	Has not taken the GRE.	Still enrolled at SC State University.
Ms. Franshawn Mack SC State University	Mentor: Dr. Marvella E. Ford Research Project: Evaluating the Reliability of an Instrument Assessing Cancer Clinical Trial Perceptions in a Predominantly African American Sample in South Carolina	Department of Defense (SE VIEW)	Publication: No publications to date Presentation: 2013 MUSC Summer Undergraduate Research Program •Ford ME, Burshell DR, Mack F , Wei W, Garrett-Mayer E. Evaluating the Reliability of an Instrument Assessing Cancer Clinical Trial Perceptions in a Predominantly African American Sample. Poster presented at the Sixth American Association for Cancer Research Conference: The Science of Cancer Health Disparities in Ethnic Minorities and the Medically Underserved, December 6-11, 2013, Atlanta, GA. Southeast Regional Research Conference in Little Rock, Arkansas on November 15-17, 2013 (oral presentation)	Has not taken the GRE.	Still enrolled at SC State University.
Ms. Bobbie Blake Claflin University	Mentor: Dr. Jennifer Wu Research Project: NKG2D Signaling Pathways Analysis	Department of Defense (SE VIEW)	Publication: No publications to date Presentation: 2013 MUSC Summer Undergraduate Research Program	Has not taken the GRE	Still enrolled at Claflin University
Ms. Evelyn Martinez SC State University	Mentor: Dr. Rosenzweig Research Project: Growth Factor Contribution to Epithelial Mesenchymal Transition	Department of Defense (HBCU)	Publication: No publications to date Presentation: 2013 MUSC Summer Undergraduate Research Program	Has not taken the GRE	Still enrolled at SC State University.