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TITLE: Project INSPIRE-HBCU Undergraduate Collaborative Summer Training Program to Inspire Students in Prostate Cancer Research

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14. ABSTRACT The overall goal of Project INSPIRE is to provide continuum of opportunities including didactic and meaningful research experience and training in basic, biomedical, clinical and/or population sciences research for promising undergraduate students enrolled at Florida A & M University (FAMU), who are at an important career-decision-making point, in a host institution such as the Moffitt Cancer Center (MCC), with an established record of achievement in prostate cancer research, that will lead to attracting this group into careers that focus on prostate cancer research. The objectives outlined for this project will be completed in three years. As proposed, we recruited 4 students from FAMU during the summer of 2007, which were matched with their mentors and all completed the program as proposed. Four pilot projects and research reports were completed by the interns in the program and 2 scholarly abstracts were presented at a National scientific meeting. All 4 students have demonstrated interest in graduate study to continue their work with prostate cancer and efforts continue to enable this endeavor.					
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I. Introduction:

It is estimated that 232,090 new cases of prostate cancer (CaP) will be diagnosed in the US in 2005 and 30,350 men will die of this disease making CaP the second leading cause of cancer deaths in American men. This is more so in the African American population, where an estimated 30,770 cases of prostate cancer are expected to occur in 2005 accounting for over 42% of all cancers in this population and 5,050 will die from this disease (ACS 2007) ¹. Between 1997-2001, the prostate cancer incidence rate was on an average 60% higher and the death rate 2.4 times higher in African American men than in white men. For AA men with a family history of hereditary CaP, the increased risk is even greater ². Autopsy studies and clinical findings support the argument that CaP exhibits more aggressive biological behavior in AA men than that observed in other populations. As recognized by the U.S. Department of Defense (DOD), to successfully address these challenges of disparities in prostate cancer incidence, mortality and morbidity, the number of Historically Black Colleges and Universities (HBCU) scientists who are trained as prostate cancer researchers need to increase. This is because, HBCU scientists, due to the mission of HBCU institutions, focus their health care research on disparities experienced by the minority population. More importantly, minorities traditionally trust HBCU researchers and are more likely to cooperate with them in addressing health issues in their community. In spite of recommendations to increase African American scientists in this field of research, with several training and career development programs established by the National Institute of Health (NIH) and DOD to increase the number of minority scientists, there is a gap in the early phases of the training pipeline, including the current prostate cancer education, training and research activities for undergraduate students at Florida A&M University (FAMU), a Historically Black Colleges/Universities (HBCU). There is thus a critical need to inspire and increase the number of young scientists from underserved groups and create a cadre of culturally sensitive well-trained scientists to improve research and ultimately contribute to reducing this disproportionate burden of prostate cancer incidence and mortality in African American men. Project INSPIRE will begin to address this weakness.

The overall goal of Project INSPIRE is to provide continuum of opportunities including didactic and meaningful research experience and training in basic, biomedical, clinical and/or population sciences research for promising undergraduate students enrolled at Florida A & M University (FAMU), who are at an important career-decision-making point, in a host institution such as the Moffitt Cancer Center (MCC), with an established record of achievement in prostate cancer research, that will lead to attracting this group into careers that focus on prostate cancer research. The objectives outlined for this project will be completed in three years.

II. BODY:

The proposed undergraduate training program, Project INSPIRE, was designed to create and nurture opportunities and promote careers in prostate cancer research for aspiring and promising undergraduate students from FAMU, a HBCU. The program has created links between established scientists and aspiring undergraduate students at the junior level at FAMU, and will provide didactic and research experiences and training in basic, biomedical, clinical and population sciences research, specific to prostate cancer. Under the direction of Moffitt research faculty, students have worked in an area of study such as basic research or cancer control, and learn research skills while being exposed to an enriching scientific environment. Working with experienced investigators, scientists and physicians, the students planned, conducted and record scientific observations and studies, gaining experience in daily research and learning to function independently as well as part of a team. Students attended seminars and interacted with the current members of internship programs – in Project LINK and SPARK, in addition to graduate and postdoctoral fellows. Because an important goal of the program was to facilitate students' connections to the next steps in a cancer research career, we made available and continue to keep students informed about career opportunities in conjunction with NCI's CURE program, graduate programs, other internships that will prepare them for graduate studies. Project INSPIRE office has served as a clearinghouse of information. We expect students to remain in contact with Moffitt Cancer Center and the CURE program for continued career opportunity enhancements.

There were no major technical difficulties encountered during the summer internship program pertaining to neither student conduct nor completion of the requirements of curriculum proposed or from the faculty. Although these were summer months and a time when faculty take their vacations, we paired several of the faculty members with co-mentors that permitted continuous mentoring of interns during the entire summer.

AT THE END OF THE SUMMER 2007, WE CONDUCTED AN EVALUATION OF THE STUDENTS AND FACULTY OF PROJECT INSPIRE CLASS OF SUMMER 2007.

MAJOR RECOMMENDATIONS FROM STUDENTS:

Provide more specific guidelines as to the scope of their work during the summer at Moffitt. Access to other faculty members were made during the internship program without the primary mentor's approval. This had implication as to the time commitment and conduct and focus on the summer research project.

Changes made in Year 3 of the Summer 2008 internship:

- Will develop guidelines that will be communicated to the interns during the summer of 2008 to ensure that while interactions with and mentorship by several

faculty at the Cancer Center was encouraged, these activities must be communicated to the primary mentor.

MAJOR RECOMMENDATIONS FROM FACULTY:

-PREFER TO SELECT STUDENTS FROM A LARGER POOL OF STUDENTS

Changes made in Year 3 of the Summer 2008 internship:

We have communicated this issue to the collaborating faculty, Dr. Folake Odedina. In addition to the PI at Moffitt and the program coordinator at FAMU, we have now included the Summer Internship Program Project INSPIRE alumni students in marketing the program during the campus visit to FAMU to recruit interns for FY 2008.

III. Key Research Accomplishments:

Based on the goals of Project INSPIRE, the following objectives were developed and met during this period:

a) Developed a didactic and research training program that specifically inspires, creates opportunities and promotes careers in prostate cancer research for aspiring undergraduate students drawing on the elements of mentoring, collaboration and networking;

TASKS:

Months 1-2: Faculty met and outlined content of Didactic curriculum
Assigned content areas to experts in the field
Finalized didactic training curriculum & evaluation
Content of modules due in project office and evaluation at the end of 6 weeks (Appendix 1)
Sent letters to faculty actively involved in prostate cancer research at Moffitt Cancer Center to invite participation as mentors for the summer training and internship program
Finalized a minimum of 4-6 mentors for the year 2006-2007
Met with Advisory Committee for final approval of curriculum and list of mentors.

Mentors Selected:

(a) Nagi Kumar, Ph.D. (Program Director)

Director, Department of Nutrition Research
Associate Professor, Department of Interdisciplinary Oncology,
Division of Cancer Prevention and Control
University of South Florida College of Medicine

(b) Paul Jacobsen, Ph.D.

Program Leader, Health Outcomes & Behavior
Professor, University of South Florida,
Department of Interdisciplinary Oncology, College of Medicine,
Division of Cancer Prevention and Control

(c) Cathy D. Meade Ph.D, R.N., F.A.A.N.,

Professor, University of South Florida

Department of Interdisciplinary Oncology, College of Medicine,
Division of Cancer Prevention and Control
Director of the Education Program at the H. Lee Moffitt Cancer
Center & Research Institute

(d) **Dr. Clement Gwede, Ph.D.**

Assistant Professor, Department of Interdisciplinary Oncology,
College of Medicine, Division of Cancer Prevention and Control
Cancer Control

(e) **Dr. Brian Rivers, Ph.D.,**

Assistant Professor in the Health Outcomes and Behavior Program
at H. Lee Moffitt Cancer Center

(f) **Dr. Aslam Kazi, Ph.D./Dr. Said Sebti, Ph.D.**

Professor, University of South Florida,
Department of Interdisciplinary Oncology, College of Medicine Drug
Discovery Program

Met & Oriented mentor/faculty from Moffitt and Faculty Advisor from
FAMU

Curriculum

Program Content

Location of interns at MCC/phone/e-mail/Housing

Assignment/Calendar

(b) Placed 4 undergraduate students during the months of June –August 2007
summer in a peer-reviewed funded research environment designed to foster
learning, provide positive researcher/student interactions, and cultivate an
interest in a prostate cancer research career.

TASKS:

Months 1-5 Publicized/Marketed Summer Internship Program at FAMU by PI
from Moffitt Cancer center and Coordinator from FAMU meeting with potential
students at FAMU campus and publicizing the program opportunity. Content
covered:

Program philosophy, goal and objectives

Application Requirements

Reviewed Applications

Interviewed potential students

Selected students & matched with mentors

Finalized and informed candidates by a formal letter

Received acknowledgement of acceptance from students

Sent information package to students

Dates-orientation/program

Mentor/contact information

Accommodation information and contracts signed

Tampa city/MCC/University campus information mailed to
students

Table: 1 The Following Candidates were selected from FAMU to participate as the Class of Summer 2006 in Project INSPIRE and matched with mentors/Research Topics:

FAMU Student Interns	Moffitt Faculty Mentors	Research Topic
Lori Gordon	Cathy D. Meade Ph.D, R.N., F.A.A.N.,	It Takes Two: Beauty and the beHOLDen This exploratory study assesses the feasibility of using African American beauty salons to promote prostate cancer education and awareness
Maclin Williams	Dr. Aslam Kazi, Ph.D. and Dr. Nagi Kumar, Ph.D. Dr. Said Sebti's Lab	Mechanisms of Cellular Apoptotic Induction Caused by Polyphenon E in Prostate Cancer Cell Lines.
Olivia Marks	Dr. Clement Gwede, Ph.D.	Racial and Geographical Differences in the Quality of Life (QOL) in Men Treated for Localized Prostate Cancer
Andrew Dixon	Dr. Aslam Kazi, Ph.D. and Dr. Nagi Kumar, Ph.D. Dr. Said Sebti's Lab	Polyphenon E potently inhibits proteasome activity in human Multiple Myeloma cells, increases p27 and induces cell cycle arrest.

Month 6-8 Summer Internship/Training Program Completed

Orientation- badges, e-mail addresses, introduction to mentor/policies & procedures
 Input student information into the tracking system
 Begin research experience
 Begin monthly seminars
 Begin didactic session on-line

Complete pilot study
 Presentation on Research day
 Complete on-line exam /evaluation for completion of didactic session

Table 3: FORMAL FAMU INTRODUCTORY DIDACTIC TRAINING SESSION

Module #	Module Title	Moffitt Instructor
1	Fundamental and Principles of Prostate Cancer Prevention	Dr. Nagi Kumar
2	Fundamental and Principles of Prostate Cancer Prevention	Dr. Clement Gwede
3	Socio-psychological factors related to Prostate Cancer – Implications in screening, prevention and treatment	Dr. Susan Thomas Vadaparampil
4	Diagnosis and Treatment of Prostate Cancer	Dr. Meyer Fishman
5	Cancer, Culture and Literacy: Implications in the African American Population	Dr. Cathy Meade
6	Genetic Markers and Polymorphisms in Prostate Cancer	Dr. Wenlong Bai
7	Fundamental and Principles of Prostate Cancer Treatment	Dr. Julio PowSang
8	Molecular Targets – Prostate Cancer Biology	Dr. Linda Mora-Diaz
9	Ethical Issues in Research/Research Designs/Methods	Dr. Nagi Kumar/ Dr. Craig Beam
10	Preparing Successful Grant Applications	Dr. Nagi Kumar

(c) Create a series of support networks/activities to assist both students and mentors in their role by utilizing cancer center, university, community and national resources.

TASKS:

- Month 9
- Conduct on-going evaluation-
 - FAMU students
 - Program
 - Mentor evaluation
 - Monitor & track students
 - Provide information regarding follow up
 - Seminar presentation of pilot study
 - Report in peer-review journals
 - Other presentations and publications
- Month 10-12
- Review and report findings of evaluation to Advisory committee
 - Review and revise program/curriculum
 - Continue to track students- monthly e-mails/provide information on pertinent seminar/continuing education information.
 - Access to seminars and lectures at Moffitt Cancer Center
 - Invite Alumni to participate in Research day annually

Newsletter regarding accomplishments of participants and progress in prostate cancer research

IV. Reportable Outcomes:

The reportable outcomes of Project INSPIRE for year 2006-2007 were as follows:

(1) We have increased interest in prostate cancer research and the problems of health disparities as indicated by increase in the number of interested students each year to be admitted to this program.

(2) Since the first group completed the internship in August 2006, the interest at FAMU among undergraduate and graduate students has increased significantly. Dr. Kumar completed 6 information sessions at FAMU in January 2007 on FAMU campus focusing on several majors- biology, chemistry, pharmacy, social sciences, nursing and environmental sciences programs.

(3)As proposed, we recruited 4 students from FAMU during the summer of 2007, which were matched with their mentors and all completed the program as proposed. (Table 1).

(4) Four (4) pilot projects completed by the interns in the program (Appendix I- Presentations) have contributed to all the 4 research programs and the ongoing studies in this area and were presented at the Moffitt cancer center's research Day on August 3, 2007 as follows:

(a) Mechanisms of Cellular Apoptotic Induction Caused by Polyphenon E in Prostate Cancer Cell Lines. Maclin Williams, Project INSPIRE intern
Mentor: Dr. A. Kazi. Research Day, Moffitt Cancer Center at the University of South Florida College of Medicine, August 3, 2007.

(b). Polyphenon E potently inhibits proteasome activity in human Multiple Myeloma cells, increases p27 and induces cell cycle arrest. Andrew Dixon, Mentors: Dr. A. Kazi & Dr. N. Kumar. Research Day, Moffitt Cancer Center at the University of South Florida College of Medicine, August 3, 2007.

(c) Racial and Geographical Differences in the Quality of Life (QOL) in Men Treated for Localized Prostate Cancer, Olivia Marks, Research Day, Moffitt Cancer Center at the University of South Florida College of Medicine, August 3, 2007.

(d) It Takes Two: Beauty and the beholden. Lori Gordon. Research Day, Moffitt Cancer Center at the University of South Florida College of Medicine, August 3, 2007.

(5) Four full research reports of the work completed by the interns are enclosed. (Appendix II)

(6) Thus far, we have had 2 poster presentations that have been presented at a National Meetings by 2 of our 4 summer interns:

(a). Racial and Geographical Differences in the Quality of Life (QOL) in Men Treated for Localized Prostate Cancer, Presented by: Olivia Marks, IMPaCT: Innovative Minds in Prostate Cancer Today, Atlanta, GA, 2007.

(b). It Takes Two: Beauty and the beholden. Presented by: Lori Gordon. IMPaCT: Innovative Minds in Prostate Cancer Today, Atlanta, GA, 2007.

(7) Thus far, we have 2 manuscripts in preparations that will be submitted for publication in referred journal by the intern in collaboration with their mentors.

(a). Aslam Kazi, Maclin Williams & Nagi Kumar. Mechanisms of Cellular Apoptotic Induction Caused by Polyphenon E in Prostate Cancer Cell Lines.

(b). Polyphenon E potently inhibits proteasome activity in human Multiple Myeloma cells, increases p27 and induces cell cycle arrest. Aslam Kazi, Andrew Dixon & Nagi Kumar,

(8) All 4 students who completed the internship have continued to engage in networking with accomplished prostate cancer researchers and leaders at MCC.

(9) All 4 students have demonstrated interest in graduate study to continue their work with prostate cancer by applying to enroll in graduate studies. (Table 3)
As proposed, we are continuing to assist further progress of the class of 2007 to obtain placement in graduate programs or internships.

Table 3: Current Status of Summer 2007 Interns;

FAMU Student Interns	Mentors	Current Status, January 2007
Maclin Williams	Aslam Kazi, Ph.D, Drug Discovery	Graduate Student in Molecular & Cellular Biology
Andrew Dixon	Aslam Kazi, Ph.D & Nagi Kumar, Ph.D. Chemoprevention/Drug Discovery.	Applying for Master's program Currently-Senior: Biochemistry
Olivia Marks	Clement Gwede, Ph.D.	Graduate student , Major: Economic, Social, and Administrative Pharmacy
Lori Gordon	Cathy Meade, Ph.D.	Pharm D. Program

We will continue to track Research Presentations/ student scientific presentations, papers, projects and refereed publications of students/mentors in collaboration. We will also determine the number of students who actually continue in a science field and progress through to a prostate cancer research career. We will continue to track students even after they leave our program to assess and assist with their career path. Each student will receive yearly updates about the program via an electronic newsletter. Additionally, all past participants will be invited to annual research celebration events to further share in their progress and success. In sum, we will use both quantitative and qualitative data to provide further evidence of Project INSPIRE 's positive effects.

There was a significant public interest in the program, which was widely covered by the media.

V. Conclusions:

There continues to be a disproportionately high burden of prostate cancer incidence mortality and morbidity in African American men. In order to address the disparities of prostate cancer occurrence and survival among medically underserved minorities, we have designed the Project INSPIRE research-training program for FAMU undergraduate students. Theory and empirical evidence suggest that the development of a focused training program grounded in mentoring, collaboration and networking will assist in career development of aspiring scientists. Our mission at the Cancer Center is to create and perpetuate an environment that supports diversity and equity so that we may better serve our community in addressing their needs for cancer care and education. Thus, Project INSPIRE represents a strong response to an urgent need to achieve parity in the number of underserved cancer scientists in the training pipeline of prostate cancer research. The already established training and research collaboration between MCC and FAMU, coupled with the expanding research programs and resources of the Moffitt Cancer Center, will create an exciting synergy and environment that should make Project INSPIRE continue to thrive. The career trajectory of minority students and the research capacity of faculty and students at both institutions can be influenced significantly through this collaboration.

VI. References: None.

Appendix I
Presentations by Project INSPIRE
Summer 2007

Slide 1

It Takes Two: Beauty and the beHOLDen

An exploratory study to assess the feasibility of using African American beauty salons to promote prostate cancer education and awareness

Lori Gordon, PharmD Candidate
Principal Investigator: Dr. Cathy Meade, PhD, FAAN, RN

Project INSPIRE

August 3, 2007

Slide 2

Background/Significance- Prostate Cancer Burden in the African Americans

From: *Am J Epidemiol*, 2006

Table 5. Comparison of Cancer Death Rates Between African Americans and Whites, US, 2000-2002

Cancer	African Americans			Whites		
	Rate*	Absolute Rate†	Rate Ratio‡	Rate*	Absolute Rate†	Rate Ratio‡
Prostate	68.7	28.2	2.8	6.2	1.2	2.2

*Note: *Rate per 100,000 per year; †Rate per 100,000 per year; ‡Rate ratio (95% CI).*

Figure 1. Age-Specific Prostate Cancer Death Rates by Race and Year, 1975-2002

Figure 2. Age-Adjusted Prostate Cancer Death Rates by Race and Year, 1975-2002

Slide 3

Background/Significance- Causes of these Health Disparities

OUTSIDE PRESSURES

- Race
- Low SES
 - Low awareness
 - Less healthcare access and availability
 - High mortality
- Ineffective health information dissemination
 - Culturally insensitive
 - High literacy level
- Stagnant growth as a group

CULTURAL FACTORS

- Lack of trust of medical community
- Low level of participation in health promotion activities
- Preference for folk treatment vs. formalized health care
- Fear and uncertainty about prostate cancer and male sexuality

Slide 4

Background/Significance- Beauty Salons: the Potential Solution

- Why use the beauty salon to educate African American women about prostate cancer?
 - Previous paradigm: beauty salons for women's health topics; barbershops for men's health topics.
 - Laura Linnan, North Carolina BEAUTY & CUTS
 - promote physical activity and healthy eating
 - promote and encourage use of 1-800-4-CANCER
 - Women are the "gatekeeper" of the health of the family



Slide 5

Background/Significance- Beauty Salons: the Potential Solution

- Combating each barrier
 - Historically & currently a symbol of sovereignty, progression, and independence
 - Comfortable setting
 - Socially & culturally important to the African American community
 - Accessible and frequented by women of all socioeconomic statuses
 - Oral communication is present and prized
 - Intimate relationships
 - Lifetime reinforcement



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graph TD; A[SALON STYLIST] --- B[SALON VISITORS]; A --- C[SALON CLIENTS]; A --- D[SIGNIFICANT OTHERS];
```

Slide 6

Research Aims

- To assess the current level of prostate cancer awareness among African American women
- To explore the feasibility of utilizing beauty salons as an innovative community-based venue to communicate prostate cancer information



Slide 7

Research Methods- Interested Demographic



US Census Bureau, 2000
Hillsborough County African American population

Data Classes

Persons
0 - 500
500 - 1000
1000 - 2000
2000 - 3000
3000 - 4000
4000 - 5000
5000 - 6000

- African American beauty salons
 - Active Florida state license (Department of Business and Professional Regulation)
 - Located where large number of African Americans reside
 - Proximity to Moffitt Cancer Center
- Stylists & Clients
 - Self-identified Black/African American
 - Aged 18 or older
 - At least one "Significant Other Reach"

Slide 8

Research Methods- Instruments



- Orally administered survey to stylists and clients
 - T/F, Scale, Open-Ended
- Field notes
 - Observations of salon atmosphere
 - Natural conversation
 - Physicality
 - Print/media available
 - Visitors!!!
- Demographic Information
 - Age, (Gender), Ethnicity, "Significant Other Reach", Family History of Cancer
 - Marital Status, Education level, Household Income Level
- Awareness Instrument (8 questions)
 - Impact of prostate cancer on the African American male population
 - Familiarity with terminology and symptoms
- Feasibility Instrument (≈20 questions)
 - Communication
 - Interest
 - Preferred intervention methods
 - Novel method: live theatrical presentation
 - Transfer to men
 - Follow-up education with stylist

Slide 9

Progress Report




- Approved by Moffitt SRC
- Currently being reviewed by USF IRB
 - Once approved, serve as a foundation for further study in this area
- Positive Community Feedback
- Future Directions: Expand & Implement Project
 - Increased awareness and education
 - Increased intervention implemented by African American women (i.e. diet)
 - Different approaches depending on the significant other attempting to reach
 - Other potent locations
- How to INSPIRE a student researcher...
 - Interest in African American health disparities
 - Achieving EQUITY
 - Can they be addressed broadly vs. a specific disease state, like prostate cancer?
 - Community Partnerships: Outreach & Education
 - TB-CCN
 - Proposals & Protocols Processes
 - Pharmacy & Research

Slide 10



Acknowledgements

- American Cancer Society
- Department of Defense
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- Florida A & M University
 - Jarrod Carol, BS
- H Lee Moffitt Cancer Center & Research Institute
 - Cancer Education & Outreach Department
- National Cancer Institute
- National Institutes of Health
- Saunders Foundation

Research Mentors

- Nagi Kumar, PhD, RD, FADA
- Gatty Meade, PhD, FAAN, RN
- Brian Rivers, PhD, MPH
- Clement Gwede, PhD, MPH, RN
- B. Lee Green Jr., PhD, MEd
- Juan Luque, PhD
- Dina Martinez, MA, MPH
- Maria Cabrera, MPH, CHES
- LaShonda Coulbertson, MPH, CHES
- Shalewa Noel-Thomas, MPH
- Linda Paige-Honeywell

FLORIDA A&M UNIVERSITY H. LEE MOFFITT CANCER CENTER & RESEARCH INSTITUTE

Slide 1

Racial and Geographical Differences in the Quality of Life (QOL) in Men Treated for Localized Prostate Cancer

Presented by: Olivia Marks
Project INSPIRE
August 3, 2007

Advisor/Mentor: Dr. Clement Gwede

Slide 2

Burden of Prostate Cancer

- American Cancer Society estimates about 218,890 new cases of prostate cancer in the United States in 2007. (American Cancer Society 2007)
- African American men are 1.6 times more likely to get prostate cancer than Caucasian men. (American Cancer Society 2007)
- Mortality is 2.4 times greater for African Americans than Caucasians. (American Cancer Society 2007)
- Prostate specific antigen (PSA) test screening has played a major role in detecting early stage prostate cancer which can reduce mortality rates

Slide 3

Issues in Prostate Cancer Research

- Quality of life has become a major topic in prostate cancer research.
- Research has shown that patients experience a decline in QOL after treatment. [Hinderson et al 2009, 15\(10\):422-429](#)
- Studies have also shown that African Americans have poorer treatment outcomes than Caucasians after treatment. [Labadarios 2009, 15\(10\):422-429](#)
- Knowledge about differences in QOL between African Americans and Caucasians is still limited.

Slide 4

Study Objectives

- Objective 1: To examine racial differences in quality of life between African Americans and Caucasians after treatment for localized prostate cancer in CaPSURE – a longitudinal database
 - Hypothesis: African American men will have poorer QOL outcomes compared to Caucasians
- Objective 2: To assess whether there are geographical differences in quality of life after treatment for localized prostate cancer

Slide 5

Study Significance

- First study to assess geographical differences
- First study to use longitudinal data to examine geographical differences
- Study may yield new information on racial and geographical differences and improve understanding of health disparities in QOL outcomes for localized prostate cancer

Slide 6

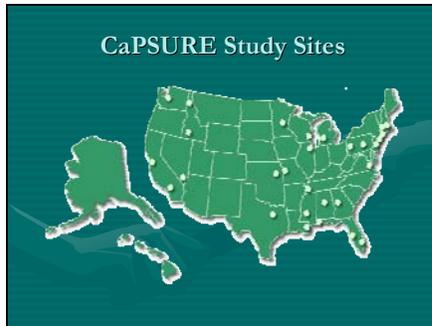
Research Methods

- Data from Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE)
 - longitudinal, observational database
- AA and Caucasians with localized prostate cancer
- Examine patients at pretreatment, 6 and 12 months posttreatment
- RAND SF-36
- UCLA-PCI (University of California, Los Angeles, Prostate Cancer Index)
- Regional breakdown is based on census regions (e.g., South vs all other).

Slide 7



Slide 8



Slide 9

Statistical Analysis

- Descriptive statistics (frequencies, means, standard deviations)
- Inferential statistical analyses (correlational and multiple regression)
- These analyses will
 - Assess racial differences
 - Document the magnitude of changes in QOL over time
 - Explore geographic differences

Slide 10

Future Plan

- CaPSURE data request is pending
- Analyze data for Master's Thesis
- Present concept at Innovative Minds in Prostate Cancer Today (IMPACT) conference on September 5-8, 2007
- Publish research in a peer reviewed journal

Slide 11

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- Dr. Brian Rivers (Moffitt)
- Dr. Hong Xiao (FAMU)
- Dr. Folakemi Odedina (FAMU)

Slide 1



Mechanisms of cellular apoptotic induction caused by Polyphenon E in Prostate Cancer Cell Lines

Presented By:
Maclin Williams
Project INSPIRE intern
Mentor: Dr. A Kazi
Research done in Dr. Sebtli's Lab

Slide 2



INTRODUCTION

- Polyphenon E characteristics
- Prostate Cancer Cell Lines
 - LNCap
 - DU-145
 - C7 and C7 KRAS (Pancreatic Cells)
- Mechanisms for Apoptosis

Slide 3



SPECIFIC AIMS

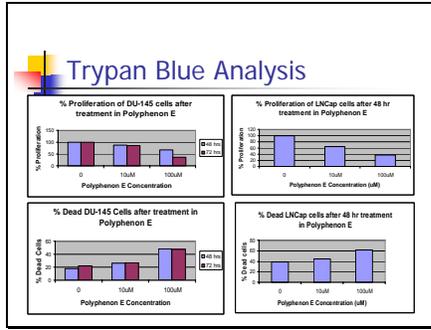
- To explore the mechanisms by which Polyphenon E induces apoptosis in various prostate cancer cell lines
- To compare the effect of Polyphenon E on cancer cells compared to normal cells

Slide 4

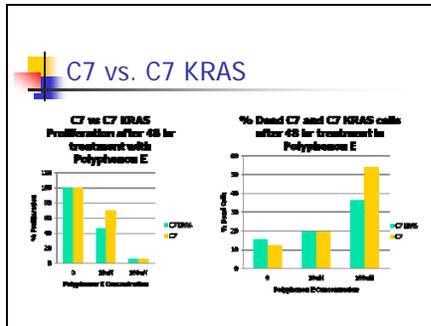
Methods

- Trypan Blue Analysis
 - 48 and 72 hr treatments
- MTT Analysis
 - 48 hr treatments
- Soft Agar Assay
- Western Blot Analysis

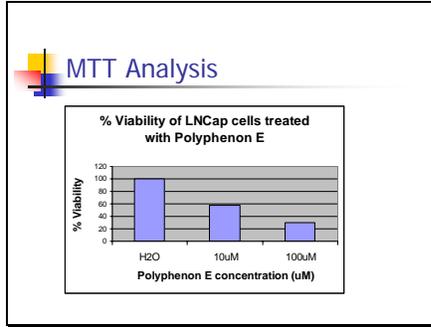
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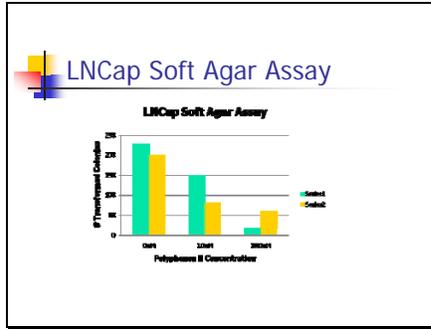
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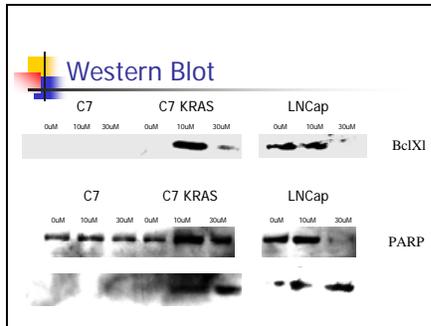
Slide 7



Slide 8



Slide 9



Slide 10



OBSERVATIONS

- Polyphenon E induces apoptosis
- Higher concentrations decrease viability
- More selective for cancer cells over normal

Slide 11



FUTURE STUDIES

- More protein expression analysis
- Drug combination/interaction studies
- Cellular Pathway inhibition studies

Slide 12



Thanks Goes out to

- Florida A & M University
- Dr. Nagi Kumar
- Dr. Rivers and Dr. Kazi
- Dr. Sebti and the other members of the lab
- Ms. Claire Jordan
- All other INSPIRE Interns

Slide 13



Special Thanks Goes To:

- Moffitt Cancer Research Center
- American Cancer Society
- National Institute of Health
- Department of Defense

Slide 14



Any Questions???

Slide 1

Polyphenon E potently inhibits proteasome activity in human multiple myeloma cells, increases p27 and induces cell cycle arrest.

Andrew Dixon
Project Inspire Intern
August 3, 2007
Mentors: Drs. A. Kazi & N. Kumar
Cancer Control & Drug Discovery Dr. Sebt's Labs

Thanks to
Department of Defense
Moffitt Cancer Research Center
American Cancer Society
National Institute of Health
Duckwall Foundation

Slide 2

Background: Proteasome Inhibitors in the treatment of Multiple Myeloma

- MM is a systemic malignancy of plasma cells that is highly treatable but rarely curable.
- It is estimated that 19,900 new cases and 10,790 deaths will occur from MM in the US in 2007
- Most Common hematologic malignancy
- The ubiquitin-proteasome pathway plays a central role in the degradation of proteins involved in several pathways including the cell cycle, cellular proliferation and apoptosis.
- Velcade(Bortezomib or PS-341) was the first proteasome inhibitor identified for the treatment of MM.

Slide 3

Green Tea Polyphenols – a novel, safe proteasome inhibitor in the treatment of Multiple Myeloma

- Although generally well-tolerated, Velcade (bortezomib) still generates toxicity
- There is thus a need to identify natural proteasome inhibitors that are potent and less toxic that could be used for hematological malignancies such as multiple myeloma.
- It has been shown that tea polyphenols, such as (-)-EGCG, potently and specifically inhibit chymotrypsin-like activity of the proteasome.

Slide 4

Specific Aim

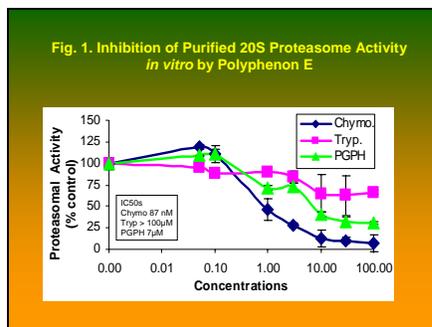
- The aim of this study was to explore the effects of Polyphenon E, a natural green tea extract, on human multiple myeloma cell lines.

Slide 5

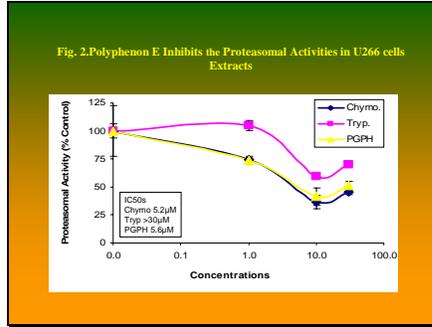
Methods

- Human multiple myeloma U266 and RPMI-8226
- Purified 20S Proteasome (in vitro), and Multiple myeloma cells (U266) extract (in vivo)
- 0, 0.01, 0.1, 1, 10, and 100 μ M (in vitro), and 0, 1, 10, and 30 μ M
- 1 h (in vitro), and 24 h (in vivo)
- Measured different proteasomal activities, protein expression, cell cycle analysis, and soft agar colony assay.

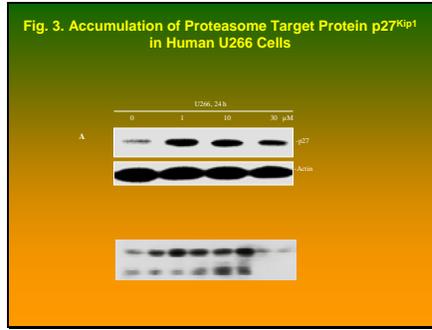
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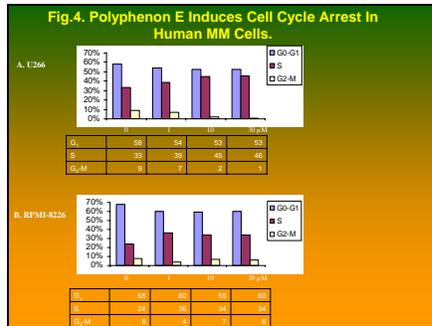
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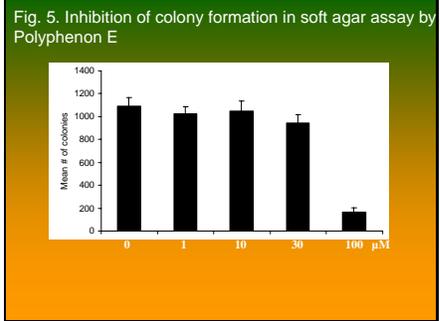
Slide 8



Slide 9



Slide 10



Slide 11

- ### Observations & Future Directions
- Polyphenon E proved to inhibit proteasome activity *in vitro*.
 - Polyphenon E inhibits the proteasomal activity in multiple myeloma cell lines.
 - It increases the accumulation of the proteasome target protein p27^{Kip1} in human MM cell lines.
 - It induces cell cycle arrest in human MM cell lines.
 - Polyphenon E is a potent proteasome inhibitor and must be further tested in animal models and clinical trials for use as an anti-cancer drug for the treatment of MM

Appendix II
Research Papers of Project INSPIRE
Summer 2007

Title: It Takes Two: Beauty and the beHOLDen

Coordinating Center: H. Lee Moffitt Cancer Center
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Protocol Version Date: July 19, 2007

Title: It Takes Two: Beauty and the beHOLDen

This exploratory study assesses the feasibility of using African American beauty salons to promote prostate cancer education and awareness

Abstract:

The primary goal of this exploratory pilot study is to determine the feasibility of utilizing beauty salons to increase prostate cancer awareness among African American women, and ultimately, in the African American community, as a whole. The primary aims are to: 1) assess the current level of prostate cancer awareness among African American women, and 2) explore the feasibility of utilizing beauty salons as an innovative community educational setting to communicate prostate cancer information. This study employs survey methods, which includes face-to-face interviews to stylists and clients, as well as, observations of the salon atmosphere. Quantitative data will be obtained through an orally-administered survey included in the interview. The exploratory findings from this study will be used as a basis for further studies and possible communication interventions.

A. SPECIFIC AIMS

The goal of this study is to assess the feasibility of using African American beauty salons to promote prostate cancer education and awareness. In the African American community, there continues to be a lack of utilization of the traditional healthcare system due to variety of reasons, including preference for folk treatments, inaccessibility to quality care, and general distrust of the medical community.¹⁻⁷ In discussing prostate cancer, some African American males are hampered by fear of and uncertainty about prostate cancer and male sexuality.¹ Many African American males do not believe that they are risk for developing prostate cancer.⁸

African American women often play an important role in the African American community, serving as a "gatekeeper" of the health of the family.⁹ Thus, when addressing men's health issues it is helpful to educate women, who in turn can exhibit a strong influence in the receipt and implementation of health information for their husbands, fathers, sons, brothers, and other significant others. In one study, more than half of the African American men interviewed indicated that their immediate family strongly influenced their decision regarding prostate cancer screening; furthermore, being married was a significant indicator for screening.⁸ The beauty salon provides an ideal community setting, that is frequented by African American women, and the stylist is presented as a key individual and conduit of information in this setting. Therefore, the beauty

salon may represent an excellent site to empower women with knowledge that they can pass on to their male counterparts, and thus help reduce the prostate cancer disparities in the African American community.

Thus, the current proposed study aims are:

1. To assess the current level of prostate cancer awareness among African American women.

It is expected that the information garnered through this aim will illustrate: 1) familiarity with terminology and symptoms, and 2) awareness of the impact of prostate cancer on the African American male population

2. To explore the feasibility of utilizing beauty salons as an innovative community-based venue to communicate prostate cancer information

It is expected that this aim will provide preliminary information about: 1) communication, 2) interest, 3) intervention methods, 4) transfer, and 5) follow-up

A.2. Significance. This study is novel because, to the researcher's knowledge, no research endeavors have been made to utilize the feminine setting of the beauty salon for prostate cancer messages, or any other men's health topics. Using this feminine setting, will engage women and build on the social role of the woman as the gatekeeper of health information for the African American family. It is an endeavor that utilizes the strengths and characteristic features of African American culture and circumvents many of the obstacles that hinder the African American community in responding to the threat of prostate cancer. By using the beauty salon, the barrier of the traditional health system as a setting is circumvented; by using this new setting, dominated by women, the "door" of the family's health is actively opened for change. The findings from this pilot study will serve as a foundation for further research into the feasibility and interest of this setting and implementation of awareness programs in beauty salons.

B. BACKGROUND AND SIGNIFICANCE

In the following section, there is a brief overview of the internship program for which this project was created, and of the department at Moffitt that the student researcher is working within. Then, the unequal burden of prostate cancer among African American men is presented, followed by discussion of various factors that contribute to this disparity. Finally, the justification for this pilot study is found in the narrative on the role of the beauty salon and stylist, as well as, the role of oral tradition in the African American community. A conceptual framework and evidence of previous successful interventions in hair care centers are also shown.

B.1. H. Lee Moffitt Cancer Center & Research Institute: Project INSPIRE. Project INSPIRE, is a 12-week summer internship at the H. Lee Moffitt Cancer Center & Research Institute. Funded by a grant from the National Department of Defense, this program, now in its second year, is focused on reducing the health disparities that occur in prostate cancer among African American men. It aims to tackle this problem by inspiring undergraduate level African American students [from Florida A & M University] to become culturally-sensitive cancer researchers. The premise is that an African American researcher will command better influence over the African American population, as opposed to a researcher of a different race or ethnicity, thus encouraging positive changes in the field of prostate cancer research.

Each intern is paired with a research mentor to provide training and guidance in their field of research (basic, biomedical, clinical, population). Upon completion of the program, each intern will have developed a research project from which he or she prepares a written scientific report and presents an oral PowerPoint presentation. In addition, he or she will have acquired an enriching summer experience at a premiere NCI-designated comprehensive cancer center that fulfills the acronym INSPIRE (Interest, Need, Stimulate, Persevere, Ideas, Relevance, Excellence).

This exploratory study, led by an African American student researcher, will fulfill the requirements of the grant-funded program; more importantly, its approval and implementation is an innovative approach to reducing the prostate cancer disparities in African American men. This project builds on the work of a previous summer FAMU student (Carrol JA) who explored the feasibility of barbershops for communication of prostate cancer information. The barbershop project is now part of the efforts of the Tampa Bay Community Cancer Network's efforts (community network program funded by NCI, see B.2) to impact health disparities in the local community. It is expected that the current project, that is, "It Takes Two: Beauty and the beHOLDen" will be a synergistic addition to the portfolio of TBCCN projects for reaching underserved and at risk groups with critical cancer information.

B.2. Cancer Education & Outreach and the TB-CCN. The Cancer Education & Outreach Department has three key goals: 1) to strengthen community collaborations through community capacity building activities, 2) to develop culturally-sensitive and linguistically-compatible cancer education, training, and outreach initiatives, and 3) to create links for and between education and research projects. As a part of this department, the Tampa Bay Community Cancer Network (TBCCN), one of 25 Community Networks Programs (CNP) funded by the National Cancer Institute (NCI), seeks to reduce and eliminate cancer disparities among minorities and rural underserved populations in Hillsborough, Pasco, and Pinellas counties. The TBCCN consists of partnerships between academic and community based organizations, all working together to reach this goal. Currently, in Phase II, the TBCCN focuses on conducting community based education and screening programs, and this project is consistent with its mission.

B.3. Prostate cancer disparities in African American males. Prostate cancer is the most common cancer among men and the second leading cause of cancer deaths among men in the United States.^{1, 10, 11} Risk factors include age (being 50 or older), family history (having an immediate relative with prostate cancer), diet (high fat and low fiber), and race/ethnicity (of African American descent).^{1, 12} While many minority groups are burdened with cancer disparities, African Americans are disproportionately impacted.^{6, 8, 13, 14} African Americans are the only minority group in which the mortality rate for cancer is higher than that of whites.^{6, 10, 11} African American men have the world's highest incidence of prostate cancer (projected 37% in 2007), nearly twice that of white men, and more than twice the mortality rate of Caucasian men, in part because they tend to be diagnosed at later, more advanced stages of the disease.^{4, 5, 8, 13, 15, 16} The prostate cancer death rate among African American men in Florida is higher than that of the national rate for this same group and about three times the prostate cancer death rate for all Floridian males.^{12, 13} Furthermore, African Americans are typically younger when diagnosed.¹ Given these disparities, it is clear that interventions, specifically aimed at, and conducive with, the African American community, are necessary.

B.4. The African American culture: causes of these disparities. Factors that contribute to these health disparities are multiple and not easily isolated. Even though there are potential biological indicators emerging, there are many other societal factors that aggravate.^{11, 13, 14, 17, 18} While both the Hispanic and Asian population continue to grow at exponential rates, the African American population is stagnant in comparison, even in Florida where African Americans still remain as the largest minority group.^{6, 19} As these minority groups continue to grow, their influence, politically, economically, and socially, becomes closer to that of the majority.

Furthermore, this population is highly marginalized. Large numbers of blacks in the United States have, for generations, been up to three times poorer than the majority, without substantial mobility up the socioeconomic ladder.^{6, 11} Socioeconomic status (SES) is measured by occupation, income level, or educational attainment; almost a quarter of African Americans live below the poverty line. Low SES has been associated with higher rates of mortality, less access to and availability of healthcare, and a low awareness of the threat of cancer and its prevention.^{4-6, 11, 19, 23} Blacks, especially poorer blacks, tend to report feeling that medical procedures are not properly explained to them.² Health information that is commonly disseminated often fails to fully consider the culture and literacy level of the patient.^{1, 11}

Additionally, African Americans, in general, exhibit a lower level of participation in health promotion activities.^{3, 13} With more than 50% of cancers being associated with modifiable lifestyle factors, this presents a curable problem.^{8, 11, 13, 20} Moreover, in the Black culture, whether an American identifies most strongly with being African, Caribbean, or American, folk treatments hold a high significance and often are the preferred choice before seeking formalized health care.¹ Efforts to conduct further research on prostate cancer and how it affects African Americans are further hindered by a lack of trust of the medical community.^{1, 3, 7, 11, 21} Some studies show that blacks consider health care professionals as the best source for cancer information.⁷ Nonetheless, while blacks trust that the medical community has the information that they need, they may not trust them to deliver said information.

Information about prostate cancer needs to be placed in a setting that is trusted and frequented by the African American community. African American women may be unfamiliar with terminology and symptoms associated with prostate cancer, as well as, pertinent statistics related to the African American man's risk for prostate cancer. The beauty salon may thus serve to educate African American women about how prostate cancer affects their community, and to create an increased awareness and participation in prevention. African American women who obtain health information from trusted individuals, their stylist, may then serve as a trusted channel to pass along this knowledge to African American males, increasing men's awareness and knowledge.

B.5. The African American beauty salon: an innovative education setting. The beauty salon offers a potential solution to the problems that entrench the African American community with this prostate cancer burden. Embedded in African American culture is the importance of family and community support.¹ Women tend to be the "gatekeepers" of family health, typically seeking and transmitting health information; African American women especially are a source for information and support in their family, and among friends.^{3, 15, 22} It is these simple facts that suggest that it is worthwhile and imperative to educate African American women about prostate cancer. In this way, indirectly, men will be educated about prostate cancer. The title of the study focuses on the importance of women's involvement in men's health; the first should become an active participant, and in essence, hold the latter's health in their hands, minds, and hearts.

The beauty salon is the historical monument of African American women's independence.⁹ Historically, even against a backdrop characterized by gender and racial segregation, not only did it exemplify economic sovereignty, it was also a location that was progressive in sorority, society, and politics.^{3, 20} In fact, the purpose of these salons went beyond attending to a woman's beauty needs; the goal was to improve the economic, social, and political status of African Americans.³ It is only natural that they be exercised to improve the health status of African Americans. As a key institution in this community, it is a comfortable, culturally-friendly location where African Americans are able to maintain their influence, allowing for prostate cancer intervention to occur. This makes it the perfect site for health interventions.

Clients may come to the beauty shop as often as weekly [excluding Sundays and Mondays, when most shops are closed], but typically regularly come every 4 to 8 weeks; in one visit, a woman may spend 1 to 5 hours.³ What takes place during these 7 to 260+ hours, each year? A very intimate relationship is formed between stylist and client.³ This relationship that is established at the first appointment often continues for many years.²⁰ The stylist is a special confidant; someone who is "competent, trustworthy, and likeable".^{3, 9} "Appraisal from cosmetologists... [is not] perceived as judgmental or undesirable." Her credibility is reinforced through active involvement in the community.³ Between conversations about personal life, for example, family and relationships, and society (jobs, local news, and elections) health is often discussed.^{3, 23} Already, beauty and health are naturally linked.²⁴ Furthermore, customers, in discussing their personal life, inevitably may discuss family members' illness, to which the stylist may offer empathy, a suggestion, some piece of sound advice, or even some needed humor.²⁰

Additionally, group conversations also occur in the setting, as all the clients and stylists join in to share their opinion on a topic.³ Some clients may choose not to add their opinion, but everyone in the shop is welcome to, and does, listen in.²⁵ Aside from clients, strangers and family members, both men and women, can be found in the shop, as well.²⁰ This setting, though focused on women, still has the potential to reach African American men directly.

This setting has the necessary components for a successful intervention. It is a comfortable, frequently visited, and respected setting in the community. More specifically, it is a setting that primarily focuses on women, the influential health decision makers of the African American family. Finally, the relationship between the stylist and client and the environment of the salon encourages oral dialogue, the preferred method of communication among African Americans (see B.6), and supports novel possible interventions. This intervention setting will further allow for lifetime reinforcement as the African American woman returns to her stylist, now a trusted educated prostate cancer expert, year after year. To date, we find no prostate cancer interventions that have been situated within beauty shops.

B.6. The importance of oral tradition in the African American community. Traditional African American culture relies heavily on word of mouth, or oral tradition.²⁴ In current data, African Americans continue to illustrate this dependence, acknowledging that they tend to obtain information about cancer from television and radio.^{2, 23} An early intervention in beauty salons utilized a 30 minute film, "Once a Year for a Lifetime" in which five well-known African American female celebrities talked about her or other's personal experience with breast cancer as a means to educate women about detection and diagnosis. The video intervention, itself set in a beauty salon, was well received.²³

In a more recent intervention, live theatre has been utilized to encourage awareness, communication, and activism in African American community about substance abuse. The combination of an emotional response, as encouraged by a play, coupled with information, seems to be a potent intervention tool. The play, TUNNELS, performed six times over a two-week period at a historically black university in North Carolina, elicited a significant change in attitudes about substance abuse and interest in seeking further information about the topic; these behavioral changes were still present at follow-up, three months after viewing the play. Furthermore, the messages of the play remained in the minds of the viewers and easily encouraged dialogue with those who did not even witness the intervention.²⁶

An intervention in the beauty salon, which could last longer than a two week period, could have an even greater impact. Though no studies have utilized live theatre to facilitate increased awareness about cancer, previous studies would suggest that theatre can be used successfully in the African American community for long-term impacts. Thus, reaching African American community may be best met by building upon this oral tradition. This preference for communication through the spoken word instead of the written word, easily incorporates the goals of Community-Based Participatory Research and the development of social supports and networks through the use of community involvement and health advisors (see B.7)

B.7. Conceptual framework. The proposed exploratory pilot study is guided by the Empowerment Theory and the underlying principles of Community-Based Participatory Research (CBPR), which emphasizes the importance of creating and developing "research partnerships", in which the communities actively participate in determining the direction of proposed research.^{4, 22} For CBPR to occur it must actually be "community based, rather than merely community placed".⁵ In this manner, research becomes empowering.⁵

Furthermore, this study builds upon the Community Health Advisor (CHA) model where members of the community recognize ownership of the problems and solutions that evolve.⁴ The "natural helper" is one such example. Also known as "weak ties" or "old heads", these contacts are infrequent, but regular, acquaintances who people "naturally turn [to] for advice, emotional support, and tangible aid...providing information, [and] spontaneous assistance."^{20, 25} Stylists

themselves are actually natural helpers, and can present and reinforce various health messages.²⁴ Beauty stylists, as natural helpers, may provide a solution that specifically counteracts each barrier that exists to prevent increased awareness among African Americans about prostate cancer. They can create a personalized message to each client, utilizing the most appropriate intervention method and educational approach based on their intimate relationship with each individual client.

B.8. Rationale and feasibility for selecting African American beauty salons and the appropriate theoretical framework. Similar studies and projects have utilized beauty salons and barbershops to promote health. For example, Linnan, et.al. Through the North Carolina BEAUTY and CUTS projects (2001 to present) have made an impressive impact in the African American community by using beauty salons and barbershops as valuable venues for relaying health information. Further, they report that such community-based programs have continued to create behavior change after the study was completed which illustrates the sustainability of programs. This may be related to the high “loyalty factor” associated with these businesses, with African Americans faithfully returning throughout the year.^{3, 24, 27} Additionally, these studies also suggest that the discussion of cancer already occurs naturally in the salon setting, and at least in the barber setting, cancer messages can be purposefully crafted and presented as well.^{3, 24}

Other researchers have reported similar success in using barbershops in an attempt to reduce the prostate cancer disparities among African American men.^{1, 15, 22} However, to date, no research endeavors have been made to utilize the feminine setting of the beauty salon for men’s health education. Therefore, the overall goal of this pilot study is to assess the feasibility of using African American beauty salons to promote prostate cancer education and awareness.

B.9. Summary. Prostate cancer continues to present disproportionately in the African American male population. This disparity is due to both societal factors that plague this community and steadfast cultural beliefs held relating to health and healthcare. The beauty salon, with stylists serving as community health advisors, is an excellent proposition as a prostate cancer educational site. Women, who serve as the gatekeeper of their family’s health, are directly reached in this comfortable environment, and can perhaps, most effectively translate this specific health information to African American men. This setting also lends itself very neatly to oral communication, a key component of African American culture. Though utilized in the past to communicate information concerning women’s health, to the researcher’s knowledge, this will be the first research effort to use this key setting to provide education and promote awareness about a men’s health topic.

C. RESEARCH DESIGN AND METHODS

C.1. Overview. The proposed exploratory study will garner information concerning the awareness level about prostate cancer among African American women in the Tampa area, and also, about the feasibility of utilizing the beauty salon as a setting for increasing awareness and education. Assessment tools, protocols for the stylists and the clients, as well as, observation field notes, were created to obtain the information of interest. These instruments examine all components necessary in this intervention: the salon, the stylist, the clients, and the significant others.

C.2. Description of research settings. The researcher obtained a list of Tampa area African American beauty salons from a fellow researcher. This list will be compared with a comprehensive listing of all state licensed cosmetology salons in Hillsborough County from the DPBR website. For the purposes of this preliminary exploratory study, a convenience sample of beauty salons will be selected that are located in areas where a large number of African Americans reside (in accordance with the 2000 Census, see Appendix A). The researcher will contact salons in the areas of interest to assess their conduciveness for pilot study. Major concerns are the number and nature of stylists, as well as, the number and nature of clients, as well as proximity to the University of South Florida & Moffitt Cancer Center. From these contacted salons, the researcher will select five salons as research sites. Selected salon managers/owners

will be contacted for permission to conduct research in their business and arrangements will be made to briefly discuss the intent of the pilot study.

C.3. General recruitment and eligibility

Eligibility criteria

Stylists. Participants will be 1) self-identified Black/African American, 2) Florida state licensed cosmetologist who concentrates on hair, and 3) aged 18 years or older. The expected sample size for stylists is 15 (3 from each salon).

Clients. Participants will be: 1) self-identified Black/African American, 2) aged 18 years or older, and 3) having at least one Black/African American “significant other reach” (defined as husband, father, brother, or son with whom she speaks with at least twice per month). The expected sample size for clients is 30 (6 from each salon, 2 from each sampled stylist).

C.4. Methods

C.4.1. Formative Research

Aim 1. To assess the current level of prostate cancer awareness among African American women
Procedure. At the selected salons, the researcher will orally administer an awareness survey consisting of 8 questions about prostate cancer to selected beauty salon stylists and selected patrons.

Awareness Instrument. The awareness instruments for both the stylists and the clients begin with some basic demographic questions, such as age, ethnicity, socioeconomic status, and family history (See Appendices B & C: Part 1). Most importantly, it identifies the “significant other reach” of each participant; this project is inadequate unless the information that these women may receive is transferred to African American males.

The awareness questions examine familiarity with terminology associated with the prostate and cancer, as well as, African American specific statistics. (See Appendices B & C: Part 2) Such information will serve as an overall gauge of prostate cancer awareness. The questions are framed in a true-or-false or scaled format, and are based upon key facts that the researcher withdrew from literature reviewed and the American Cancer Society and National Cancer Institute websites.

Data Analysis. The questionnaires will be numbered, and be identified with a code identifying the beauty salon site, the interviewer, and the date. No names or personal identifying information will be collected. Data will be entered into a database and exported for analysis to generate descriptive statistics on the demographic variables and other quantifiable questions. Each administered quiz will be graded according to percentage of questions answered correctly. These results will be placed in a pie graph for analysis. The data will determine how knowledgeable and familiar African American women in the Tampa area are about prostate cancer. A majority of quizzes with a percentage of 70%, or below, will indicate a low awareness.

Aim 2. To explore the feasibility of utilizing beauty salons as an innovative community educational setting to communicate prostate cancer information

Procedure. In conjunction with the awareness questions, the researcher will administer a brief survey to selected beauty salon stylists and selected patrons concerning the feasibility of communicating prostate cancer information within the beauty salon setting. The researcher will take field notes at the end of the surveys about general atmosphere of the salon, observing various features of the setting that could lend it to such an educational endeavor, including but not limited to, general naturally occurring conversation, physical environment and setup, print and media materials naturally available and existing, and visitors to the salon (see Appendix D). The

observation of said significant others who may visit the salon with also be especially noted during this time period. However, the survey will serve as the major tool for data collection.

Feasibility Instrument. The survey questions will assess the following elements. (See Appendices B & C: Part 3) First, it will look at the communication both between stylists and clients and illuminate what is the common subject matter discussed in the salon and how it can be tailored appropriately to deliver prostate cancer messages. It also will determine interest of stylists and clients in sharing and receiving prostate cancer messages, respectively. Additionally, it will also seek to determine the preferred method for dissemination of such information (i.e. 1-1, video, kiosk, skits, poster, etc). Finally, it will also explore the potential for transfer of prostate cancer information to African American men and continued follow-up by the stylist with the client. The instrument focuses on the African American woman's influence in his life, especially concerning his health and the likelihood that prostate cancer information will be received, accepted, and implemented by him.

These four components, communication, interest, intervention methods, and transfer/follow-up, are all necessary in determining the success of the beauty salon as an effective educational setting. The questions are framed in a true-or-false or scaled format. These questions were reviewed by multiple Moffitt researchers who interact frequently with the African American community, as well as by young adult African American women.

Data Analysis. The surveys will be numbered, and identified with a code identifying the beauty salon site, the interviewer, and the date. No names or personal identifying information will be collected. Data will be entered into a database and exported for analysis to generate descriptive statistics on the demographic variables and other quantifiable questions. Questionnaire answers will be tabulated in an Excel spreadsheet, categorized, and graphed in various forms for significance. These qualitative and quantitative data will determine feasibility in the use of the beauty shop as a potential venue to communicate prostate cancer information.

D. HUMAN SUBJECTS

D.1. Source of materials. The data that will be obtained from participants, specifically for research purposes, consists of orally administered surveys and observational field notes.

D.2. Potential risk. There are no physical risks to the participants posed by participating in this study. This is a minimal risk study.

D.3. Protection against risks. All key personnel have received training in research ethics. Confidentiality will be maintained by using anonymous surveys, using subject numbers on data, rather than subject's names. Subject data will only be available to research staff involved with the study. Identifying information will not be reported. All participants will receive literature related to prostate cancer and contact information to reach Moffitt's Cancer Education and Outreach department, if they have additional questions not related to the study.

D.4. Recruitment and informed consent process. The informed consent process will include an explanation of the project by researcher followed by a verbal, rather than signed, consent by participant.

D.5. Potential benefits to participants and importance of knowledge to be gained. There is no direct benefit to study subjects, but the information that is produced in the study has the potential to help community members in the future. Participants will receive information about prostate cancer (from the American Cancer Society) and links to other resources where they may seek further information, if they choose.

D.6. Data and safety monitoring plan. As part of the regular ethical research review protocol, the proposed study will first be submitted to Moffitt Cancer Center's Protocol Review and Monitoring Committee. After the study has been approved in this step, the study will be submitted to the

University of South Florida Institutional Review Board. The research protocol and all other study materials will be approved by the scientific review committees.

D.7. Confidentiality safeguards. All information provided by research participants will be for research purposes only and will be kept in strict confidence. There will be no identifying data. Only personnel working with the study will have access to data.

D.8. Inclusion of woman and minorities.

Inclusion of women. This study will include only women. The primary aim of this study is to assess the current level of prostate cancer awareness among African American women. The ultimate goal is to explore the feasibility of utilizing the beauty salon to communicate prostate cancer information to the African American woman, with the expectation that said information will be transferred to, and received by, the African American man.

Inclusion of minorities. This study will include only African Americans. The primary aim of this study is to assess the current level of prostate cancer awareness among African American women. The ultimate goal is to explore the feasibility of utilizing the beauty salon to communicate prostate cancer information to the African American woman, with the expectation that said information will be transferred to, and received by, the African American man.

D.9. Inclusion of children. (not applicable)

D.10. Vertebrate animals. (not applicable)

E. SUMMARY OF STRENGTHS AND LIMITATIONS

This project showcases a variety of strengths. It is a novel approach to addressing the problem of prostate cancer disparities in African American men. No previous research has been done to explore the feasibility of utilizing the beauty salon, a setting predominated by women, to encourage increased prostate cancer awareness, a disease affecting only men. It is an endeavor that utilizes the strengths and characteristic features of African American culture and circumvents many of the obstacles that hinder the African American community in responding to the threat of prostate cancer. It builds upon a solid foundation of previous studies and projects that utilize hair care settings, while offering a new perspective that needs to be explored.

As with any research endeavor, there are certain limitations in conducting this research. Given the time constraints of the internship, a small sample size and fairly straightforward research design must be employed in order for the study to be manageable. It is expected that the methods employed will provide beginning evidence of the potential feasibility of the beauty shop as a communication venue and fuel our future research efforts. Another limitation is that though many African American women patronize the salon, access to the salon may be limited in some aspects, on account that some women choose not to frequent a salon.

In the future, it might be interesting to see how clients' responses might differ depending upon which significant other they are attempting to educate. Also, it would be interesting to explore how African Americans of different socioeconomic levels respond to different intervention approaches in the beauty salon. Another important factor to assess in future endeavors is the subtle influences that African American women have upon family health, specifically as it relates to prostate cancer. For example, many African American women cook most family meals, which could be key in prostate cancer prevention in the African American community. This study should serve as a foundation for future endeavors utilizing the beauty salon for prostate cancer education.

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APPENDIX A- Potential Selected African American Beauty Salons in Tampa, FL
Census Tracking Map 2000
Number of African Americans living in areas of Tampa, FL

Potential Beauty Salons (and ZipCodes)

1. Cole Beauty & Barber Shop (33610)
2. Donna's Beauty Salon (33610)
3. Faithful Creations Hair & Nail Salon (33610)
4. Ms. Dee's World of Beauty (33610)
5. Perfect 10 Nail Salon (33610)
6. Total Image Hair Salon (33610)
7. The Wig Boutique & Beauty Salon (33610)
8. Panache Salon (33612)
9. Hair Vision Salon (33617)
10. Harriet Hair & Nail Salon (33617)
11. New Beginnings Hair & Nail Salon (33619)

Appendix B- Protocol for Beauty Stylists

Hi, my name is Lori Gordon. I am a 4th year pharmacy student at Florida A & M University (FAMU) and I am a summer research intern at the Moffitt Cancer Center, near the University of South Florida (USF). I am working on a study to examine the possibilities of using beauty salons to educate African American women about prostate cancer. With this information, African American women could have a positive impact on the health of our significant others, whether they are husbands, fathers, sons, brothers, or any other male in our life that we care about. Would you be willing to answer some questions about this topic?

NO: That's fine. Thank you for your time.

YES: Thanks. Before we begin, I'd like to make sure that you understand what we are going to do. I'd like to talk with you for about 5-10 minutes about prostate cancer, as well as, your natural relationships in the salon with your clients and your interest in educating your clients about prostate cancer. Everything you say will be kept confidential and you don't need to answer any questions you don't want to. Do you have any questions for me before we begin? [Address any questions or concerns.] Are you still interested in taking part?

NO: That's fine. Thank you for your time.

YES: Excellent. Let's begin...[Upon completion] If you are interested, here is some information about prostate cancer. Again, thank you for your time.

Part 1- Demographic Info

First I would just like to collect some background information about you. The information you provide will not be identified with you and it will not be shared with others for any reason.

1. Age

2. Gender

3. What is your ethnicity/cultural background? (circle one)

African-American

Caribbean-American

Haitian-American

African

Hispanic/Latino

BiRacial/Mixed (please specify)

Refused

4. Yes/No: Do you consider yourself Black/African American?

5. Who are any Black/African American males with whom you speak with at least twice per month (i.e. father, husband, son, brother, etc.)?

_____	_____
_____	_____
_____	_____

6. Has anyone in your family had any type of cancer?

Probe: If yes, what types? Has anyone in your family had prostate cancer?

Part 2- Prostate Cancer Awareness

The following section will quiz you on your current knowledge about prostate cancer and how it affects our community. This is not to be an intimidating exercise; it is OK if you do not know an answer. If you do not know an answer, you may take your best guess or simply reply, "I don't know".

Prostate Cancer & Your Community

1. On a scale of 1 to 5 (5 being the highest), how much do you know about prostate cancer?

1 2 3 4 5

2. True/False: More new cases of prostate cancer occur in African American males than in any other racial or ethnic group each year.

3. True/False: When compared to white males, prostate cancer is more common in African American males and they are more likely to die from it. This is not a serious problem.

4. Where do you usually receive information from about prostate cancer?

5. On a scale of 1 to 5 (5 being very important), how important is prostate cancer awareness to you?

1 2 3 4 5

Prostate Cancer: Terminology & Symptoms

1. What is the prostate?

Probe: Can you identify it in this picture? [shows stylist unlabeled colored picture]

2. Yes/No: If your doctor tells your father (or other significant other) that he has a benign tumor, do you think he has prostate cancer?

3. True/False: The symptoms of prostate cancer are always apparent and obvious, so an African American male does not need to visit his doctor unless he is noticing certain symptoms.

Part 3- You as the Stylist Educator

The following section will give me an idea on how you function in your normal role as a stylist and how this role may be expanded to create more awareness about prostate cancer in your community through the beauty salon setting.

Communication

1. How long have you been a hair stylist?

2. How many clients do you see in a week?

3. On average, how much time do you spend with each client?

4. You would describe your relationship with most of your clients as:

Excellent

Good

Average

Poor

Indifferent

Probe: When you say _____, can you explain why you feel this way?

5. What are the three most common things you speak with your clients about?

6. Do you and a client ever talk about a health subject?

Probe: If yes, what subjects?

Interest

1. With proper training, how interested would you be in sharing information with your clients about prostate cancer?

Very interested

Somewhat interested

Not interested

2. In thinking about how the beauty salon could be used to get prostate cancer information into the African American community, what comes to mind?

Probe: Do you like the idea? Is there a better venue that African American women may visit? What are some key points we should think about?

Intervention Methods

1. Which would be your three preferred methods for educating clients about prostate cancer?

Person-to-person

Brochure

Poster

Computer kiosk

Radio

TV/video/DVD

Outside person presents message in the salon (such as a nurse/doctor)

Other (please specify)

Probe: You chose ____, ____, and _____. How often would you like such intervention to take place? What is one benefit of using this method? What is one drawback of using this method? [ask for each of 3 methods]

2. At what point during the hair appointment would be the best time to provide information to the client about prostate cancer?

Probe: While styling? While under the dryer? While waiting for your appointment? During your washing? Other time?

A creative way of providing prostate cancer information may be by using a theatrical presentation. The following questions will give me an idea of what you think about such an endeavor.

3. With proper training, how willing are you to perform a live theatrical presentation in your salon that deals with the topic of prostate cancer?

Very willing
Somewhat willing
Not willing

4. Given the ability to review and approve materials being presented, how willing are you to allow a drama group to perform a live theatrical presentation in your salon that deals with the topic of prostate cancer?

Very willing
Somewhat willing
Not willing

5. Would you be willing to have a live theatrical performance that deals with the topic of prostate cancer performed in your salon on a once-a-month basis?

Probe: Once-a-week? Daily?

6. What are some benefits to having a live theatrical performance in your salon?

7. What are some drawbacks to having a live theatrical performance in your salon?

Transfer & Follow-up

8. True/False: Most of your clients set up their next hair appointment before leaving the salon.

Appendix C- Protocol for Clients

Hi, my name is Lori Gordon. I am a 4th year pharmacy student at Florida A & M University (FAMU) and I am a summer research intern at the Moffitt Cancer Center, near the University of South Florida (USF). I am working on a study to examine the possibilities in using beauty salons to educate African American women about prostate cancer. With this information, African American women could have a positive impact on the health of our significant others, whether they are husbands, fathers, sons, brothers, or any other male in our life that we care about. Would you be willing to answer some questions about this topic?

NO: That's fine. Thank you for your time.

YES: Thanks. Before we begin, I'd like to make sure that you understand what we are going to do. I'd like to talk with you for about 5-10 minutes about prostate cancer, as well as, your natural relationship in the salon with your stylist. In addition, I am also interested in your interest on receiving education about prostate cancer and willingness to share this information with loved ones close to you. Everything you say will be kept confidential and you don't need to answer any questions you don't want to. Do you have any questions for me before we begin? [Address any questions or concerns.] Are you still interested in taking part?

NO: That's fine. Thank you for your time.

YES: Excellent. Let's begin...[Upon completion] If you are interested, here is some information about prostate cancer. Again, thank you for your time.

Part 1- Demographic Info

First I would just like to collect some background information about you. The information you provide will not be identified with you and it will not be shared with others for any reason.

1. Age

2. What is your ethnicity/cultural background?

- African-American
- Caribbean-American
- Haitian-American
- African
- Hispanic/Latino
- BiRacial/Mixed (please specify)
- Refused

3. Yes/No: Do you consider yourself Black/African American?

4. What is your martial status?

- Single
- Married
- Separated
- Divorced
- Widowed

5. Could you indicate, by pointing, your education level?

- Some high school
- High school diploma/GED
- Some college
- Bachelor's degree
- Graduate level degree (Master's/PhD)

6. Could you indicate, by pointing, your household income level?

- Less than 25,000
- 25,000-49,999
- 50,000-74,999
- 75,000-99,999
- 100,000+
- Refused

7. Who are any Black/African American males whom you speak with at least twice per month (i.e. father, husband, son, brother, etc.)?

_____	_____
_____	_____
_____	_____

8. Has anyone in your family had any type of cancer?

Probe: If yes, what types? Has anyone in your family had prostate cancer?

Part 2- Prostate Cancer Awareness

The following section will quiz you on your current knowledge about prostate cancer and how it affects our community. This is not to be an intimidating exercise; it is OK if you do not know an answer. If you do not know an answer, you may take your best guess or simply reply, "I don't know".

Prostate Cancer & Your Community

1. On a scale of 1 to 5 (5 being the highest), how much do you know about prostate cancer?

1 2 3 4 5

2. True/False: More new cases of prostate cancer occur in African American males than in any other racial or ethnic group each year.

3. True/False: When compared to white males, prostate cancer is more common in African American males and they are more likely to die from it. This is not a serious problem.

4. Where do you usually receive information from about prostate cancer?

5. On a scale of 1 to 5 (5 being very important), how important is prostate cancer awareness to you?

1 2 3 4 5

Prostate Cancer: Terminology & Symptoms

1. What is the prostate?

Probe: Can you identify it in this picture? [shows client unlabeled colored picture]

2. Yes/No: If your doctor tells your father (or other significant other) that he has a benign tumor, do you think he has prostate cancer?

3. True/False: The symptoms of prostate cancer are always apparent and obvious, so an African American male does not need to visit his doctor unless he is noticing certain symptoms.

Part 3- You as the Client Student

The following section will give me an idea about your relationship with your stylist at this salon, and also, about your relationship with important African American males in your life. I will also see how you feel about using these relationships and the salon to create more awareness about prostate cancer in your community.

Communication

1. Complete the sentence: I visit the salon once every ____ weeks.

2. True/False: I visit the salon only when I need my hair done for a special occasion.

3. True/False: I see the same stylist every time I have a hair appointment.

4. You would describe your relationship with your stylist as:

Excellent

Good

Average

Poor

Indifferent

Probe: When you say _____, can you explain why you feel this way?

Interest

1. If they both had the same information, in comparing your stylist and your primary care doctor, who do you feel more comfortable obtaining health information from and why?

2. How interested would you be in learning about prostate cancer from your hair stylist?

Very interested

Somewhat interested

Not interested

3. In thinking about how the beauty salon could be used to get prostate cancer information into the African American community, what comes to mind?

Probe: Do you like the idea? Is there a better venue that African American women may visit? What are some key points we should think about?

Intervention Methods

1. Which would be your three preferred methods for learning about prostate cancer?

Person-to-person

Brochure

Poster

Computer kiosk

Radio

TV/video

Outside person presents message in the salon (such as a nurse/doctor)

Other (please specify)

2. At what point during the hair appointment would you be most receptive to learning about prostate cancer?

Probe: While styling? While under the dryer? While waiting for your appointment? During your washing? Other time?

A creative way of providing prostate cancer information may be by using a theatrical presentation. The following questions will give me an idea of what you think about such an endeavor.

3. Yes/No: I would enjoy a live theatrical presentation performed by my stylist.

Probe: Why or why not?

4. Yes/No: I would enjoy a live theatrical presentation performed by a drama group.

Probe: Why or why not?

5. True/False: If I were to view a live theatrical presentation about prostate cancer in the salon, I would enjoy a humorous, Medea-style more than I would enjoy a serious, Lifetime movie-style presentation.

Transfer & Follow-up- For the following questions, I would like for you to imagine one significant other in your life; it may be your husband, your father, your brother, your son, or any other male whom you are very close to. [wait for client to visualize significant other in mind] Now I am going to ask you some questions about this significant other.

1. In thinking about your family, who has the most influence over his health?

Probe: Is it him? Is it you? Is it his parents? Is it his children? Is it his friends? Is it his doctor?

2. If given the necessary information, how comfortable would you be in sharing information about prostate cancer with him? Rate on a scale of 1 to 5 (with 5 being the highest).

1 2 3 4 5

3. How open do you think he would be in learning about prostate cancer from you? Rate on a scale of 1 to 5.

1 2 3 4 5

4. Currently, how involved are you in his personal health care? Rate on a scale of 1 to 5.

1 2 3 4 5

5. In answering those last three questions, who were you thinking of (husband, father, son, brother)?

Probe: Would your answers be different if you were discussing prostate cancer with someone else (husband, father, son, brother)? Why did you choose this significant other over someone else?

Appendix D- Observations of the Salon
Diagram of Salon Setup

Interactions Occurring?

Conversation Topics Discussed?

Available Print/Media Materials

Visitors to Salon (Male/Female? Purpose? Length of Visit)

Other General Observations

Title: It Takes Two: Beauty and the beHOLDen

This exploratory study assesses the feasibility of using African American beauty salons to promote prostate cancer education and awareness

Abstract:

The primary goal of this exploratory pilot study is to determine the feasibility of utilizing African American beauty salons to increase prostate cancer awareness among African American women, and ultimately, in the African American community, as a whole. The primary aims are to: 1) assess the current level of prostate cancer awareness among African American women, and 2) explore the feasibility of utilizing beauty salons as an innovative community educational setting to communicate prostate cancer information. This study employs survey methods, which includes face-to-face interviews to stylists and clients, as well as, observations of the salon atmosphere. Quantitative data will be obtained through an orally-administered survey included in the interview. The exploratory findings from this study will be used as a basis for further studies and possible communication interventions.

I. Background/Significance

H. Lee Moffitt Cancer Center & Research Institute: Project INSPIRE. Project INSPIRE, is a 12-week summer internship at the H. Lee Moffitt Cancer Center & Research Institute. Funded by a grant from the National Department of Defense, it is focused on reducing the health disparities that occur in prostate cancer among African American men. It aims to tackle this problem by inspiring undergraduate level African American students [from Florida A & M University] to become culturally-sensitive cancer researchers. The premise is that an African American researcher will command better influence over the African American population, as opposed to a researcher of a different race or ethnicity, thus encouraging positive changes in the field of prostate cancer research. This exploratory study, led by an African American student researcher, will fulfill the requirements of the grant-funded program; more importantly, its approval and implementation is an innovative approach to reducing the prostate cancer disparities in African American men. This project builds on the work of a previous summer FAMU student (Carrol JA) who explored the feasibility of barbershops for communication of prostate cancer information. The barbershop project is now part of the efforts of the Tampa Bay Community Cancer Network's efforts (community network program funded by NCI) to impact health disparities in the local community. It is expected that the current project, that is, "It Takes Two: Beauty and the beHOLDen" will be a synergistic addition to the portfolio of TBCCN projects for reaching underserved and at risk groups with critical cancer information.

Prostate cancer disparities in African American males. Prostate cancer is the most common cancer among men and the second leading cause of cancer deaths among men in the United States. Risk factors include age (being 50 or older), family history (having an immediate relative with prostate cancer), diet (high fat and low fiber), and race/ethnicity (of African American descent). While many minority groups are burdened with cancer disparities, African Americans are disproportionately impacted. African Americans are the only minority group in which the mortality rate for cancer is higher than that of whites. African American men have the world's highest incidence of prostate cancer (projected 37% in 2007), nearly twice that of white men, and more than twice the mortality rate of Caucasian men, in part because they tend to be diagnosed at later, more advanced stages of the disease. The prostate cancer death rate among African American men in Florida is higher than that of the national rate for this same group and about three times the prostate cancer death rate for all Floridian males. Furthermore, African Americans are typically younger when diagnosed. Given these disparities, it is clear that interventions, specifically aimed at, and conducive with, the African American community, are necessary. [1, 3-8]

The African American culture: causes of these disparities. Even though there are potential biological indicators emerging, there are many other societal factors that aggravate. While both the Hispanic and Asian population continue to grow at exponential rates, the African American population is stagnant in comparison, even in Florida where African Americans still remain as the largest minority group. Furthermore, this population is highly marginalized. Large numbers of blacks in the United States have, for generations, been up to three times poorer than the majority, without substantial mobility up the socioeconomic ladder. Low socioeconomic status has been associated with higher rates of mortality, less access to and availability of healthcare, and a low awareness of the threat of cancer and its prevention. Health information that is commonly disseminated often fails to fully consider the culture and literacy level of the patient. Additionally, African Americans, in general, exhibit a lower level of participation in health promotion activities. With more than 50% of cancers being associated with modifiable lifestyle factors, this presents a curable problem. Efforts to conduct further research on prostate cancer and how it affects African Americans are further hindered by a lack of trust of the medical community. [1-2, 6, 8-9] Information about prostate cancer needs to be placed in a setting that is trusted and frequented by the African American community. The beauty salon may serve as such setting to educate African American women about prostate cancer.

The African American beauty salon: an innovative education setting. The beauty salon offers a potential solution to the problems that entrench the African American community with this prostate cancer burden. Embedded in African American culture is the importance of family and community support. Women tend to be the “gatekeepers” of family health, typically seeking and transmitting health information; African American women especially are a source for information and support in their family, and among friends. It is these simple facts that suggest that it is worthwhile and imperative to educate African American women about prostate cancer. In this way, indirectly, men will be educated about prostate cancer. The title of the study focuses on the importance of women’s involvement in men’s health; the first should become an active participant, and in essence, hold the latter’s health in their hands, minds, and hearts.

The beauty salon is the historical monument of African American women’s independence. The purpose of these salons went beyond attending to a woman’s beauty needs; the goal was to improve the economic, social, and political status of African Americans. It is only natural that they be exercised to improve the *health* status of African Americans. As a key institution in this community, it is a comfortable, culturally-friendly location where African Americans are able to maintain their influence, allowing for prostate cancer intervention to occur. This makes it the perfect site for health interventions.

Clients may come to the beauty shop as often as weekly [excluding Sundays and Mondays, when most shops are closed], but typically regularly come every 4 to 8 weeks; in one visit, a woman may spend 1 to 5 hours. During this time, a very intimate relationship is formed between stylist and client. The stylist is a special confidant; someone who is “competent, trustworthy, and likeable”. Her credibility is reinforced through active involvement in the community. Between conversations about personal life, for example, family and relationships, and society (jobs, local news, and elections) health is often discussed. Furthermore, customers, in discussing their personal life, inevitably may discuss family members’ illness, to which the stylist may offer empathy, a suggestion, some piece of sound advice, or even some needed humor. [1-2,4,10]

This setting has the necessary components for a successful intervention. It is a comfortable, frequently visited, and respected setting in the community. More specifically, it is a setting that primarily focuses on women, the influential health decision makers of the African American family. Finally, the relationship between the stylist and client and the environment of the salon encourages oral dialogue, the preferred method of communication among African Americans (see following section), and supports novel possible interventions. This intervention setting will further allow for lifetime reinforcement as the African American woman returns to her stylist, now a

trusted educated prostate cancer expert, year after year. To date, we find no prostate cancer interventions that have been situated within beauty shops.

The importance of oral tradition in the African American community. Traditional African American culture relies heavily on word of mouth, or oral tradition. In current data, African Americans continue to illustrate this dependence, acknowledging that they tend to obtain information about cancer from television and radio. In a recent intervention, live theatre has been utilized to encourage awareness, communication, and activism in African American community about substance abuse. The combination of an emotional response, as encouraged by a play, coupled with information, seems to be a potent intervention tool, eliciting significant changes in attitudes and interest in seeking further information about the topic; these behavioral changes were still present at follow-up. Furthermore, the messages of the play remained in the minds of the viewers and easily encouraged dialogue with those who did not even witness the intervention. [11]

An intervention in the beauty salon, which could last longer than a two week period, could have an even greater impact. Though no studies have utilized live theatre to facilitate increased awareness about cancer, previous studies would suggest that theatre can be used successfully in the African American community for long-term impacts. Thus, reaching African American community may be best met by building upon this oral tradition. This preference for communication through the spoken word, instead of the written word, easily incorporates the goals of Community-Based Participatory Research and the development of social supports and networks through the use of community involvement and health advisors (see following section).

Conceptual framework. The proposed exploratory pilot study is guided by the Empowerment Theory and the underlying principles of Community-Based Participatory Research (CBPR), which emphasizes the importance of creating and developing “research partnerships”, in which the communities actively participate in determining the direction of proposed research. For CBPR to occur it must actually be “community based, rather than merely community placed”. In this manner, research becomes empowering.

Furthermore, this study builds upon the Community Health Advisor (CHA) model where members of the community recognize ownership of the problems and solutions that evolve. The “natural helper” is one such example. Also known as “weak ties” or “old heads”, these contacts are infrequent, but regular, acquaintances who people “naturally turn [to] for advice, emotional support, and tangible aid...providing information, [and] spontaneous assistance.” [3, 10] Stylists themselves are actually natural helpers, and can present and reinforce various health messages. They can create a personalized message to each client, utilizing the most appropriate intervention method and educational approach based on their intimate relationship with each individual client.

Rationale and feasibility for selecting African American beauty salons and the appropriate theoretical framework. Similar studies and projects have utilized beauty salons and barbershops to promote health. For example, Linnan, et.al. through the North Carolina BEAUTY and CUTS projects (2001 to present) have made an impressive impact in the African American community by using beauty salons and barbershops as valuable venues for relaying health information. Further, they report that such community-based programs have continued to create behavior change after the study was completed which illustrates the sustainability of programs. Other researchers have reported similar success in using barbershops in an attempt to reduce the prostate cancer disparities among African American men. However, to date, no research endeavors have been made to utilize the feminine setting of the beauty salon for men’s health education. Therefore, the overall goal of this pilot study is to assess the feasibility of using African American beauty salons to promote prostate cancer education and awareness. [1, 10]

Significance. This study is novel because, to the researcher’s knowledge, no research endeavors have been made to utilize the feminine setting of the beauty salon for prostate cancer messages, or any other men’s health topics. Using this feminine

setting, will engage women and build on the social role of the woman as the gatekeeper of health information for the African American family. It is an endeavor that utilizes the strengths and characteristic features of African American culture and circumvents many of the obstacles that hinder the African American community in responding to the threat of prostate cancer. By using the beauty salon, the barrier of the traditional health system as a setting is circumvented; by using this new setting, dominated by women, the “door” of the family’s health is actively opened for change. The findings from this pilot study will serve as a foundation for further research into the feasibility and interest of this setting and implementation of awareness programs in beauty salons.

II. Research Aims

1. To assess the current level of prostate cancer awareness among African American women.

It is expected that the information garnered through this aim will illustrate:

- 1) familiarity with terminology and symptoms, and 2) awareness of the impact of prostate cancer on the African American male population

2. To explore the feasibility of utilizing beauty salons as an innovative community-based venue to communicate prostate cancer information

It is expected that this aim will provide preliminary information about: 1) communication, 2) interest, 3) intervention methods, 4) transfer, and 5) follow-up

III. Methods

For the purposes of this preliminary exploratory study, a convenience sample of beauty salons will be selected that are located in areas where a large number of African Americans reside (in accordance with the 2000 Census). The researcher will contact salons in the areas of interest to assess their conduciveness for pilot study. Major concerns are the number and nature¹ of stylists, as well as, the number and nature of clients, as well as proximity to the University of South Florida & Moffitt Cancer Center. Managers/owners will be contacted for permission to conduct research in their business and arrangements will be made to briefly discuss the intent of the pilot study.

Stylists. Participants will be 1) self-identified Black/African American, 2) Florida state licensed cosmetologist who concentrates on hair, and 3) aged 18 years or older. The expected sample size for stylists is 15 (3 from each salon). Clients. Participants will be: 1) self-identified Black/African American, 2) aged 18 years or older, and 3) having at least one Black/African American “significant other reach” (defined as husband, father, brother, or son with whom she speaks with at least twice per month). The expected sample size for clients is 30 (6 from each salon, 2 from each sampled stylist).

Procedure. At the selected salons, the researcher will orally administer an awareness survey consisting of 8 questions about prostate cancer to selected beauty salon stylists and selected patrons. In conjunction with the awareness questions, the researcher will administer a brief survey concerning the feasibility of communicating prostate cancer information within the beauty salon setting. The researcher will take field notes at the end of the surveys about general atmosphere of the salon, observing various features of the setting that could lend it to such an educational endeavor, including but not limited to, general naturally occurring conversation, physical environment and setup, print and media materials naturally available and existing, and visitors to the salon. The observation of said significant others who may visit the salon with also

¹ By nature, the researcher is referring to: the typical age range of clients (whether the patrons are generally adults, students, or children, race and ethnicity of majority of clients, general socioeconomic status of most clients, times when the salon is most/least busy, what media outlets are already present in the salon (magazines, TV, radio?), etc.

be especially noted during this time period. However, the survey will serve as the major tool for data collection.

Awareness & Feasibility Instruments. The instruments for both the stylists and the clients begin with some basic demographic questions, such as age, ethnicity, socioeconomic status, and family history. Most importantly, it identifies the "significant other reach" of each participant; this project is inadequate unless the information that these women may receive is transferred to African American males.

The awareness questions examine familiarity with terminology associated with the prostate and cancer, as well as, African American specific statistics. Such information will serve as an overall gauge of prostate cancer awareness. The questions are framed in a true-or-false or scaled format, and are based upon key facts that the researcher withdrew from literature reviewed and the American Cancer Society and National Cancer Institute websites.

The feasibility questions will assess the following elements. First, it will look at the communication both between stylists and clients and illuminate what is the common subject matter discussed in the salon and how it can be tailored appropriately to deliver prostate cancer messages. It also will determine interest of stylists and clients in sharing and receiving prostate cancer messages, respectively. Additionally, it will also seek to determine the preferred method for dissemination of such information (i.e. 1-1, video, kiosk, skits, poster, etc). Finally, it will also explore the potential for transfer of prostate cancer information to African American men and continued follow-up by the stylist with the client. The instrument focuses on the African American woman's influence in his life, especially concerning his health and the likelihood that prostate cancer information will be received, accepted, and implemented by him.

These four components, communication, interest, intervention methods, and transfer/follow-up, are all necessary in determining the success of the beauty salon as an effective educational setting. The questions are framed in a true-or-false or scaled format. These questions were reviewed by multiple Moffitt researchers who interact frequently with the African American community, as well as by young adult African American women.

Data Analysis. The questionnaires will be numbered, and be identified with a code identifying the beauty salon site, the interviewer, and the date. No names or personal identifying information will be collected. Data will be entered into a database and exported for analysis to generate descriptive statistics on the demographic variables and other quantifiable questions. Each administered quiz will be graded according to percentage of questions answered correctly. These results will be placed in a pie graph for analysis. The data will determine how knowledgeable and familiar African American women in the Tampa area are about prostate cancer. A majority of quizzes with a percentage of 70%, or below, will indicate a low awareness. Survey answers will be tabulated in an Excel spreadsheet, categorized, and graphed in various forms for significance. These qualitative and quantitative data will determine feasibility in the use of the beauty shop as a potential venue to communicate prostate cancer information.

Limitations

Given the time constraints of the internship, a small sample size and fairly straightforward research design must be employed in order for the study to be manageable. It is expected that the methods employed will provide beginning evidence of the potential feasibility of the beauty shop as a communication venue and fuel our future research efforts. Another limitation is that though many African American women patronize the salon, access to the salon may be limited in some aspects, on account that some women choose not to frequent a salon.

IV. Conclusions & Future Directions

In the future, if the results support potential utilization of the beauty salon to effectively raise awareness about prostate cancer in the African American community, the researcher would like

to see the expansion and implementation of the beauty salon project. Another important factor to assess in future endeavors is the subtle influences that African American women have upon family health, specifically as it relates to prostate cancer. For example, many African American women cook most family meals, which could be key in prostate cancer prevention in the African American community. This study should serve as a foundation for future endeavors utilizing the beauty salon for prostate cancer education.

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Racial and Geographical Differences in the Quality of Life (QOL) in Men Treated for Localized Prostate Cancer

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INTRODUCTION

Background

The American Cancer Society estimates that there will be about 218,890 new cases of prostate cancer in the United States in 2007 (American Cancer Society 2007). In 2006, the American Cancer Society estimated that 1 in 6 men will get prostate cancer during his lifetime, and 1 in 36 will die of this disease (American Cancer Society 2006). Men who are 50 and older are more likely to be diagnosed with prostate cancer. Epidemiological studies have shown that having a father or brother with prostate cancer increases the risk of an individual by approximately two-to-three fold, on average (Gann 2002).

Studies have also shown that African-American men have had a significantly higher incidence of and mortality from prostate cancer than Caucasian men (Morton 1994, Smith et. al 1998, Catalona 2002), with an incidence of nearly 1.6 times that of Caucasian men (ACS 2007). Mortality is 2.4 times greater for African American men than Caucasian men (ACS 2007). There is no definitive data as to whether these differences are explained solely by differences in socioeconomic status, stage of disease at diagnosis or biological make up.

As a result of new screening methods, such as prostate-specific antigen (PSA) testing, and an increased awareness of prostate cancer, more men are being diagnosed with early stage prostate cancer. Healthcare providers are faced with choosing the best treatment option for their patients in order for patients to have a better health related quality of life (HRQOL). There are several treatment options for prostate cancer. The most common options are watchful waiting, surgery, radiation therapy, and hormone therapy (NCI 2006). The three main treatment options for early stage prostate cancer are radical prostatectomy, external beam radiation therapy and brachytherapy (American Cancer Society 2007, Potosky et. al. 2002).

Health related quality of life is a critical end point after treatment for any condition, localized prostate cancer is no exception. Treatment for localized prostate cancer can be both helpful and hurtful to patients. As a result in advance treatment options, patients are living longer lives after treatment, however, they experience some decline in quality of life after treatment. Therefore the choice between life with discomfort or a shorter life expectancy becomes an issue.

Problem Statement

Quality of life is a major component to treating any cancer. However, often quality of life is not a concern that the providers take into consideration, and healthcare professionals underestimate the effects cancer treatments have on the individual. Quality of life outcomes such as sexual function, bowel function, and urinary function are important to patients, therefore this study will evaluate these aspects for patients who undergo treatment for localized prostate cancer.

Fortunately, quality of life has become a major end point in the treatment of patients with prostate cancer. Studies have shown that after treatment for prostate cancer, patients experience some decrease in HRQOL ([Lubeck et al. 1999](#)). Furthermore, depending on the treatment, some patients experience a greater decrease in HRQOL ([Davis et al. 2001](#)). Although there are numerous studies that looked at how treatment for prostate cancer effect the quality of life of patients ([Litwin et al. 2000](#), [Merrick GS et al. 2001](#), [Dahn JR et al 2004](#), [Cooperberg MR et al. 2003](#), [Lubeck DP et al. 1999](#), [Brandeis JM et al 2000](#), [Hanlon AL et al. 2001](#)), fewer studies have looked at the differences in quality of life after treatment between African Americans and Caucasians ([Lubeck et al 2001](#), [Bacon CK et al. 2002](#), [Hoffman RM et al. 2001](#)). What is more interesting is the fact that no study has compared patients in the South to patients in the North.

Thus, the first objective of this study is to examine racial differences in quality of life between African Americans and Caucasians after treatment for localized prostate cancer. It is hypothesized that African Americans have poorer quality of life after treatment given that at diagnosis they present with a higher stage of cancer as a result of delayed treatment or they may choose a less aggressive treatment. Furthermore, a study showed that African American men had worse clinical characteristics at presentation and lower QOL health status scores at baseline when compared to other racial groups ([Lubeck et al. 2001](#)). African American men are also known to receive treatment at a later disease stage than Caucasians due to the fact that they do not get screened until the disease has reached a later stage ([Thompson I et al. 2001](#), [Jemal A et al. 2002](#)). Studies have also showed that African Americans receive different treatments than Caucasians when presented with the same stage of the disease ([Harlan L et al. 1995](#)). These findings further support the above hypothesis. Examining the differences in quality of life between these two groups will help healthcare professionals educate patients better on post treatment effects and what to expect. The second objective of this study is to assess whether there are geographical differences in quality of life after treatment for localized prostate cancer. Differences in socioeconomic status can lead to differences in treatment outcomes. One study found that lower annual income was significantly associated with lower pretreatment quality of life ([Penson et al 2001](#)). These disparities are partly explained by socioeconomic status, which suggests that lower socioeconomic status has a negative impact on closing the gap between treatment outcomes. As a result of the Civil War, the South has suffered economically. The south is known to be at a disadvantage financially when compared to other parts of the United States (www.wikipedia.com). These differences can have a major effect on education and income. Therefore, patients in the south may be less educated compared to patients in the north, which can lead to poor treatment choices or access to state of the art care. If patients in the north are more educated and higher levels of socioeconomic status than patients in the south this may have an effect on quality of life.

Study Significance

The incidence of prostate cancer has risen in the last decade. For the year 2003, the Centers for Disease Control and Prevention reported geographical differences in incidence and mortality rates per 100,000 in the United States. The total incidence rate for the U.S. in 2003 was 150.0, however, the northeast lead by 159.2. The total death rate was 26.6 but more interestingly, the south led in death rates with 27.5 (http://www.cdc.gov/cancer/npcr/uscs/2003/facts_major_findings.htm). These findings may be due to patients in the north having more access to care therefore receiving treatment before the disease progress to later stages resulting in death. Yet knowledge about the difference in HRQOL between African American and Caucasian men is still limited. Therefore this study will examine these differences. One of the mysteries in prostate cancer research is the difference between the incidence and survival rates of Caucasian and African American men in the United States. Not only are there disparities in incidence and survival rates, there is also disparities in QOL post treatment for localized prostate cancer ([Lubeck et al 2001](#)). There have been few studies that compared racial differences in quality of life after treatment for localized prostate cancer using large numbers of African Americans. This study will provide information about treatment outcomes by race and region. Furthermore, this study is necessary because it may

answer some of the questions concerning quality of life outcomes after treatment for localized prostate cancer. Since no studies have compared patients in the South to patients in other regions of the U.S., these findings can better inform providers on whether there are geographic differences in outcomes. Additionally, policies can be put in place that require equal treatment to patients who present with the same stage of the disease, which may lead to equal outcomes between the two races and by regions of the country.

Literature Review

Early detection and screening has played a major role in patient's longevity after diagnosis and treatment. Localized prostate cancer and treatments for it are known to cause declines in the HRQOL of patients. The major disease-specific QOL domains that are affected by treatments are bowel, sexual, and urinary functioning. Studies have shown that different treatments have different outcomes in quality of life.

There have been studies that looked at racial differences in the clinical progression of patients after treatment (Cohen et. al. 2006), racial differences in mortality (Godley et. al. 2003), and racial and ethnic differences in advanced-stage prostate cancer (Hoffman et. al. 2001). To date there has been little research that had a primary goal of comparing the quality of life of African Americans to Caucasians after treatment for localized prostate cancer. Furthermore, there have been no studies that compared patients in the southern region to patients in other regions of the United States. Geographical differences in quality of life after treatment for localized prostate cancer have not been researched. For that reason, the present study will address this gap in the literature and assess if there are differences in outcomes based on where patients live in the United States.

After conducting a literature review on prostate cancer and treatment effects on quality of life, the majority of the studies are cross-sectional (Bacon et al 2002, Brandeis et al 2000, Davis et al 2001, Wei et al 2002) and did not have a primary goal of comparing the quality of life between African Americans to Caucasians after treatment. When trying to determine treatment effect on quality of life study design is important. A longitudinal study design paints a much clearer picture of treatment effect compared to a cross-sectional design. Longitudinal studies can also accurately measure changes in quality of life. Therefore this study will assess racial and geographical differences in quality of life outcomes using data from longitudinal database. The results from this study may increase our understanding of quality of life outcomes by race and geography. This study may also serve as a guide to other researchers when looking at regional differences in a particular disease state.

Methods

Prostate cancer burden

The burden of prostate cancer is starkly self-evident in the United States. It is important to know that socioeconomic factors can also play a major role in the differential burden of prostate cancer. African American men with prostate cancer are more likely to be less educated, poor, uninsured, and diagnosed at a later stage when compared to Caucasians (ACS 2007). African American men also have poorer treatment outcomes and reduced QOL after treatment when compared to Caucasian men. This study is designed to assess these disparities and look more closely at differences geographically. Therefore the first objective of this study is to examine racial differences in quality of life between African Americans and Caucasians after treatment for localized prostate cancer. It is hypothesized that African Americans have poorer quality of life after treatment given that at diagnosis they present with a higher stage of cancer as a result of delayed treatment or they may choose a less aggressive treatment. The second objective of this study is to assess whether there are geographical differences in quality of life after treatment for localized prostate cancer.

Data Source

The study population for this study will be obtained from the CaPSURE database. CaPSURE was started in 1995 and includes 65 clinical practices, including three university-affiliated sites and 31 community practices within the United States (refer to appendix II). This database was created to provide clinicians and other healthcare providers a better understanding of prostate cancer and the effects its treatments have on quality of life. There is also information on clinical and economic effects of prostate cancer on individual patients. The CaPSURE database is a longitudinal observational database that is overseen by a panel of urologists, internists, and outcomes researchers ([Lubeck et al 1996](#)). Additional information on this database is reported elsewhere ([Lubeck et al 1996](#)).

Sample

For the purpose of this study, patients that reside in the southern and northern regions of the United States with localized prostate cancer will be evaluated. Patients who were treated from 1995 to 2007, 30 years and older, and regardless of treatment type, will be included in the study. The chart in Appendix I is a breakdown of prostate cancer stages. Patients who are in stage II or B based on the chart will be included. Patients who have locally advanced or metastatic prostate cancer will be excluded. African Americans and Caucasians are the top two groups with the highest incidence and mortality rates in the United States; therefore, patients who are not African American or Caucasian will be excluded from this study. Patients will have to have had completed a pretreatment HRQOL questionnaire and at least 1 post treatment HRQOL questionnaires. The time periods will be post treatment, 6 months, and 12 months after treatment. The same patients will be examined at each time period to allow assessment of treatment effects on quality of life.

QOL Outcomes and Measures

General QOL

General quality of life will be measured by the RAND36-item health survey. This self-administered survey has also been tested for reliability and validity (test-retest reliability 0.78 or greater and internal consistency 0.78 to 0.93) ([Ware et al 1992](#)) and has been widely used in various research endeavors examining quality of life. Differences between 6.5 and 8.3 are considered to be clinically significant ([Juniper et al 1994](#)). This instrument consists of 8 multi-item scales (4 emotional domains / 4 physical domains). The outcomes that will be assessed are physical function, role function, bodily pain, general health, mental health, role function emotional, social function, and energy and/or fatigue.

Disease-specific QOL

Disease-specific health related quality of life will be measured by the UCLA Prostate Cancer Index. The UCLA-PCI has been used widely in prostate cancer research and has been tested for reliability and validity ([Litwin et al 1998](#)). Litwin and others reported that the UCLA-PCI test-retest reliability ranged from 0.66 to 0.93, and internal consistency ranged from 0.65 to 0.93 ([Litwin et al 1998](#)). Each scale is scored from 0 to 100. A score of 0 would indicate a poor outcome, which indicates higher scores, reflects a more satisfactory outcome. A difference of 10 points on a scale would be considered clinically significant ([Brandeis et al 2000](#)). This instrument consists of 20 questions and has 6 separate domains such as urinary function, urinary bother, bowel function, bowel bother, sexual function, and sexual bother that will be assessed in this study.

Regional breakdown

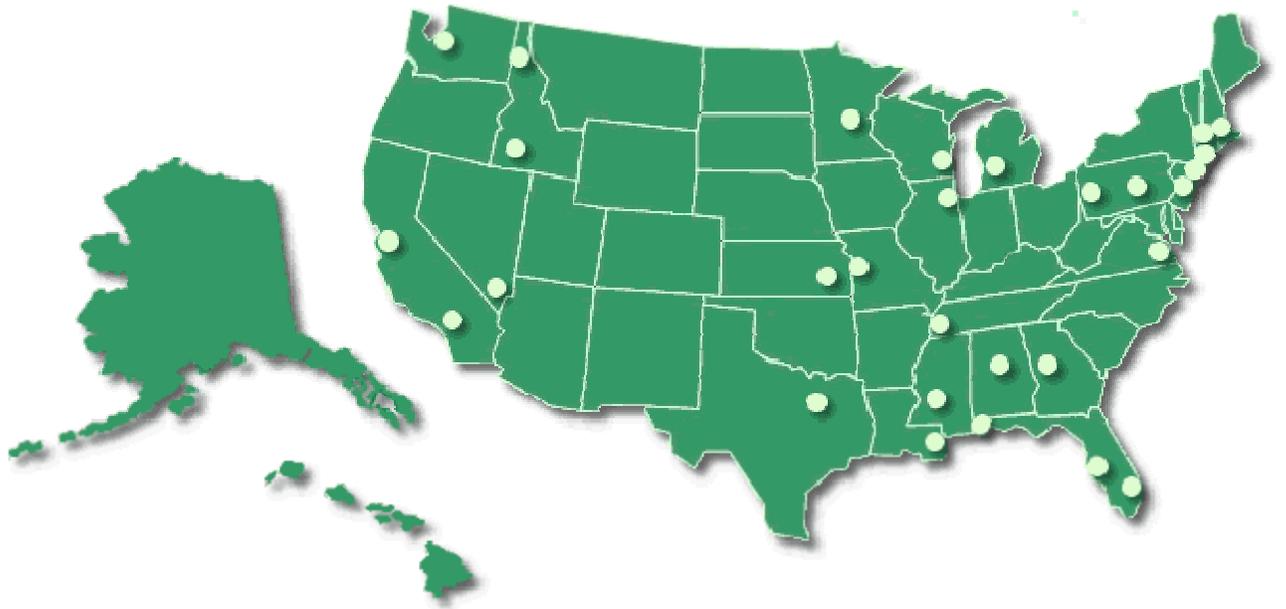
In order to address the second objective of this study, patients in the south will be compared to patients in the other three regions of the U.S. Patients will be divided up based on the U.S. census regional breakdown. The four regions of the U.S. are South, Northeast, Midwest, and

West (refer to appendix III). Patients living in the south will be compared to those living in the Northeast, Midwest, and West. Patients' location will be identified based on their address. This method will be used in order to not confuse treatment location with actual physical address.

Statistical Analyses

Descriptive statistics such as frequencies, means, and standard deviations will be used to summarize demographic, disease and treatment information of the study population. In addition, inferential statistical analyses (including correlational and multiple regression) will be conducted as appropriate to address the objectives of this study. Specifically, these analyses will assess racial differences, explore geographic differences, and document magnitude of changes in QOL over time (pre/post-treatment).

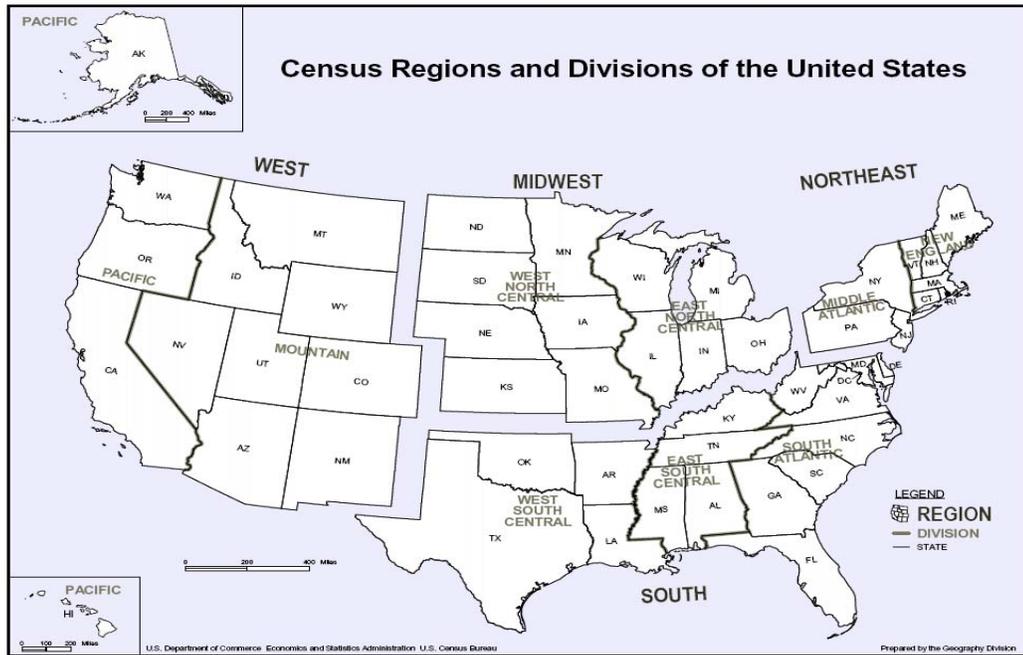
Appendix II
CaPSURE Study Sites



www.capsure.net

○ One dot may represent more than one location

Appendix III
Map of Census Regions in the United States



http://www.census.gov/geo/www/us_regdiv.pdf

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Polyphenon E potently inhibits proteasome activity in human Multiple myeloma cells, increases p27 and induces cell cycle arrest.

By
Andrew Dixon

Mentors: Dr. A. Kazi & Dr. N. Kumar

August 13, 2007

Abstract

In this study, I wanted to explore the effects of Polyphenon E, a green tea extract, on human Multiple myeloma (MM) cells. I found out that Polyphenon E inhibits proteasome activity, in vitro. It inhibits proteasomal activity in MM cells. Polyphenon E increases the accumulation of the proteasome target protein p27^{Kip1} in human MM cells. It also induces cell cycle arrest in human MM patients and is a possible anti-cancer drug for MM patients.

Introduction

Multiple myeloma (also known as myeloma or plasma cell Myeloma) is the most common hematologic malignancy. MM is a cancer of the plasma cells, which is an important part of the immune system that produces antibodies to help fight off infection and disease. The disease causes excessive numbers of abnormal plasma cells in the bone marrow and overproduction of intact monoclonal immunoglobulin protein. MM is a highly treatable, but rarely curable disease. MM represents approximately 1 % of all cancers and 2% of all cancer deaths; it occurs more frequently in men than women. Today, there are more than 50,000 people in the U.S. living with MM. African Americans and Native Pacific Islanders have the highest reported incidence of the disease and Asians are the lowest. Among African Americans, it is one of the leading causes of cancer death. It is estimated that 19,900 new cases will come and of the cases 10,790 deaths will occur from MM in the US in the year 2007. However, new therapies are being developed to help patients live longer and healthier lives.

Almost all of the cases of people diagnosed with MM are ranging in the age limit of people over 40, and more than half are occurring in people over the age of 71. It is believed that Myeloma may be resulting from a lifelong accumulation of toxins or antigenic challenges. For example, people in agricultural occupations, petroleum workers, workers in leather industries, and cosmetologists seem to have a higher than average chance of developing MM, due to the exposure of herbicides, insecticides, petroleum products, heavy metals, plastics, various dusts (asbestos), and even those who are exposed to large amounts of radiation, which can all be risk factors for MM. However, there is no way to prove that it is being caused by any one factor it may be the result of several factors acting together.

Normally plasma cells develop from B cells (class of lymphocytes) when foreign substances, such as bacteria, enter the body. In response, groups of plasma cells produce proteins (antibodies) that help fight disease and infection off. Each plasma cell develops in response to a particular foreign substance within the body, and it produces antibodies specific to that substance. So, there are many different antibodies produced in the body. However, transformation of a normal B cell into a malignant plasma cell involves a multi-step process that includes multiple genetic abnormalities. In the end, the resulting plasma cells continue to divide unchecked, generating

more malignant plasma cells. Those Myeloma cells travel through the bloodstream and collect in the bone marrow, where they cause permanent damage to healthy tissue.

Plasma cells usually make up a very small portion, less than 5 percent, of cells in the bone marrow. However, Myeloma plasma cells have specific adhesion molecules on their surface allowing them to target bone marrow where they attach to structural cells (stroma cells). Once the Myeloma cells attach to bone marrow stromal cells, several interactions cause the Myeloma cells to grow. Cytokines, (chemical messengers), are produced by both Myeloma and stromal cells. The cytokines stimulate growth of Myeloma cells and inhibit apoptosis leading to proliferation of Myeloma cells and ultimately resulting in bone destruction. Myeloma cells also produce growth factors that promote angiogenesis. These new blood vessels provide the oxygen and nutrients that promote tumor growth. Angiogenesis encourages reproduction of Myeloma cells, which increase in number and begin to enter and take over for most of the cells in the bone marrow. Because the mature Myeloma cells may fail to activate the immune system, this may produce substances that decrease the body's normal immune response to a foreign body causing the cells to be able to grow unnoticed. Tumors grow by invading the hard outer part of the bone, the solid tissue. In this case of Myeloma cells, they spread into the cavities of all the large bones of the body forming multiple small lesions; this describes why the disease is entitled "Multiple Myelomas".

The first treatment approved for patients with MM was Velcade (bortezomib); it is classified as a proteasome inhibitor. It was approved in 2003 and received full approval for use in patients who have received one prior therapy in 2005. Velcade is a potent, specific, and reversible proteasome inhibitor and the first drug of this type to enter clinical trials. The proteasome is an enzyme complex that exists in all cells and plays an important role in degrading proteins involved in the angiogenesis, the cell cycle, cytokine production, cell adhesion, apoptosis, and other important cellular processes. Many of the processes that rely on proteasome function can contribute to the growth and survival of cancer cells. Velcade works by disrupting normal cellular processes, proteasome inhibition promotes apoptosis. Research shows that cancer cells are more susceptible to the effects of proteasome inhibition than normal cells. Because of the reversibility of the proteasome inhibition with Velcade, normal cells can recover from its effects while the cancer cells are more likely to undergo apoptosis. It seems that Velcade appears to act directly on the Myeloma cells to cause apoptosis as well as indirectly inhibiting cell growth and survival by acting on the bone microenvironment. Many of the Decade's anti-Myeloma effects are believed to be due to its ability to block a key survival protein, called nuclear factor κ B (NF- κ B). NF- κ B is found within the cell and acts by turning on genes that cause production of proteins that stimulate cell growth. When a cell receives an external signal proteins such as NF- κ B transfer the message to the nucleus of the cell, causing some type of response (cell growth). NF- κ B also sends a message for cells to increase the expression of various molecules on their cell surface. In reference to Myeloma, the surface molecules allow Myeloma cells to stick to cells in the bone marrow. This interaction stimulates the bone marrow cells to produce factors that promote the growth and survival of Myeloma cells, which pushes angiogenesis to feed the tumors. So, by blocking NF- κ B, Velcade inhibits Myeloma cell growth and induces Myeloma cell death. It also inhibits the production of growth and survival factors by blocking the production of surface molecules on the Myeloma cell surface and the interaction between Myeloma and bone marrow cells, resulting in the inhibition of angiogenesis.

Even though Velcade makes to be an approved treatment, it is still toxic. The purpose of this research is to possibly find another drug that is not toxic and still have the same effect. Evidence from several studies suggests that green tea or its components may have cancer chemopreventive effects. Polyphenon E is the drug of interest in this case due to the characteristics of the substance. Polyphenon E is a standardized botanical drug substance containing a mixture of catechins originating from green tea. Polyphenon E is manufactured as a hot water extract of green tea leaves that is further extracted with ethyl acetate. The resulting crude extract is dissolved in methanol and purified by affinity column fractionation. Once dry, the final product will contain about 85 to 95 percent total catechins. The main component that makes

up 56 to 72 percent of the material is epigallocatechin gallate (EGCG). It has been shown that tea polyphenols such as EGCG potently and specifically inhibit chymotrypsin-like activity of the proteasome. Polyphenon E may also contain small amounts of caffeine, theobromine, and gallic acid.

Materials and Methods

Human Multiple Myeloma U266 and RPMI-8226

The two cell lines used in this research.

Purified 20S Proteasome

This proteasome is a multicatalytic complex that constitutes the catalytic component of the ubiquitous proteolytic machinery of the 26S proteasome. The 20S proteasome system plays a critical role in the specific degradation of cellular proteins. The proteasome's two important functions are to: (1) promote tumor cell proliferation and (2) to protect tumor cells against apoptosis.

Polyphenon E

Polyphenon E is a botanical drug substance containing a mixture of catechins originating from the leaves of green tea. The drug appears in a light red to a dull reddish-yellow powder. It is freely soluble in water, methanol, tetrahydrofuran, *N,N*-dimethylformamide, ethanol, and 1,4-dioxane; and is insoluble in hexane and petroleum ether.

The drug is manufactured by using a hot water extract of green tea, which is then extracted further with ethyl acetate. The resulting crude extract is dissolved in methanol and purified by affinity column fractionation. Once it is dry, the final product contains 85 to 95 percent of total catechins. The main component in the drug is EGCG, which comprises 56 to 72 percent of the material. Other catechins present are EC, ECG, EGC, GCG, CG, GC, and catechin. Polyphenon E contains minimal amounts of caffeine and small amounts of gallic acid and theobromine.

p27^{Kip1}

p27^{Kip1}, was the protein used in this experiment because Polyphenon E is supposed to inhibit proteasome activity and this protein can survive in this environment to give off its presence.

Actin

The loading control (actin) of all the protein was equal, so the increase in protein is due to the drug.

In vitro

Cells were plated in separate Petri dishes with the same amount (10 mL). Plates were labeled for both cell lines in preparation for concentrations of drug to be added.

In vivo

Drug was added to plates based on concentrations wanted. After concentrations were added, plates were placed in incubator for. This process was repeated on the desired time period (12, 24, 48, and 72 hours).

Western blot analysis

The U266 and RPMI-8226 cells were treated with various concentrations of the drug (Polyphenon E) for the hours indicated. Then antibodies were put to the protein and the Western blot procedure was performed.

Flow Cytometry analysis

Cells were harvested in process using trypsinization, they were pelleted and washed in PBS thoroughly before sitting overnight in an ethanol tube. After sitting, the samples were washed

with PBS and pelleted in PI staining solution. Samples were left in tubes at room temperature for 30 minutes before analysis took place by the flow cytometer.

Soft agar assay

Six-well plates were used in preparing the cells for imaging. After the preparations of the cells were put in the plates, the plates were placed in incubation overnight. The plates were then imaged and the cell colonies were counted.

Results

See Figures page

The *in vitro* method proved to show that the drug inhibits proteasome activity. (Fig. 1)

By examining the extracts, the drug proved to inhibit the U266 cell's proteasomal activity also. (Fig. 2)

In comparing the time intervals, it's shown that the target protein (p27^{Kip1}) was accumulated in the U266 cell line. (Fig. 3)

The drug induced cell cycle arrest in both cell lines, in the S-phase of the cycle. (Fig. 4)

There was a decrease in cell colonies as the concentration went up in both cell lines. (Fig. 5)

Discussion

This research was done to see if this drug could be another possible treatment for MM and replace Velcade, because it is less toxic. By exploring the effects of Polyphenon E, I conclude that Polyphenon E proved to inhibit proteasome activity in vitro. Polyphenon E inhibits the proteasomal activity in MM cell lines. It increases the accumulation of the proteasome target protein p27 in human MM cell lines. Polyphenon E also induces the arrest of human MM cells in the S-phase of the cell cycle. Polyphenon E is a potent proteasome inhibitor and can be possibly used as an anti-cancer drug for the treatment of MM, however it must be further tested in animal models and clinical trials.

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Figure 1

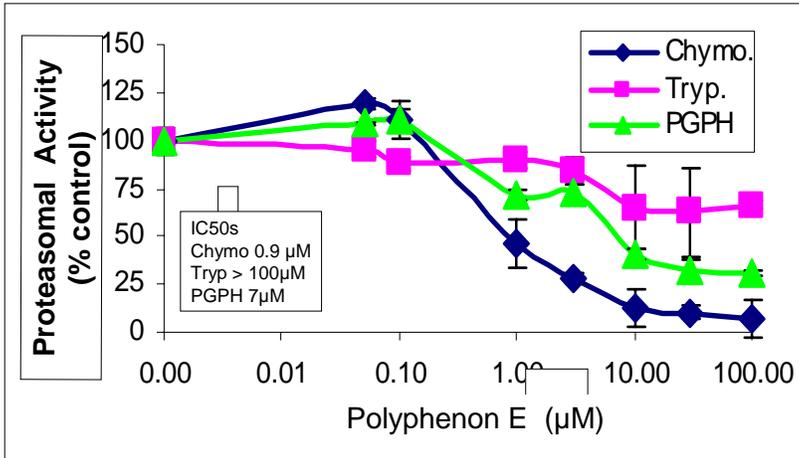


Figure 2

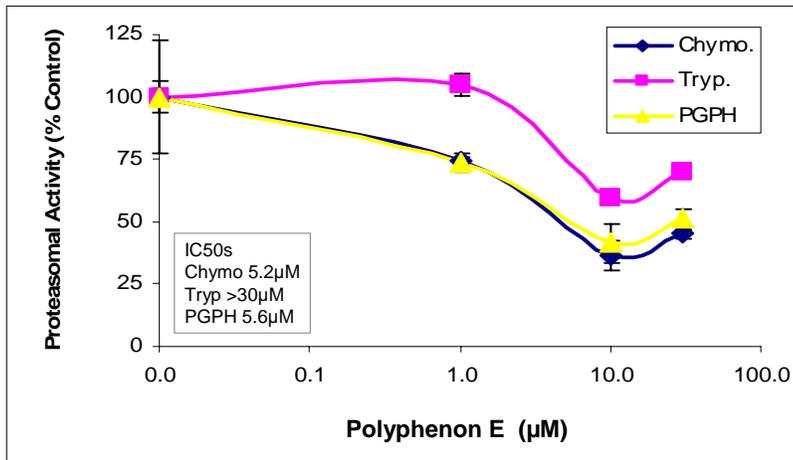


Figure 3

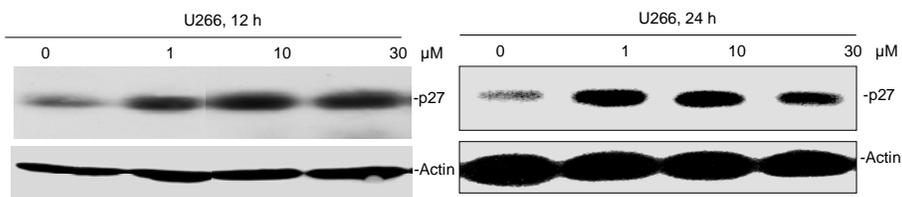


Figure 4

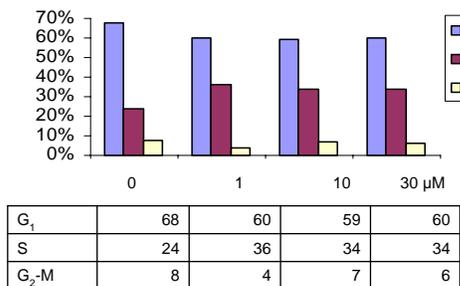
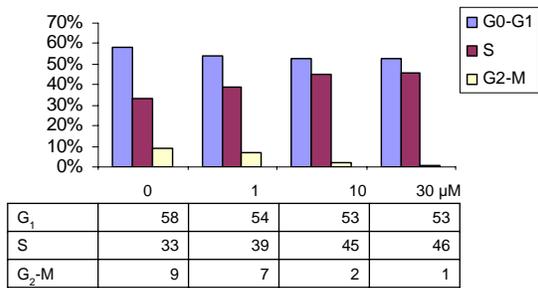
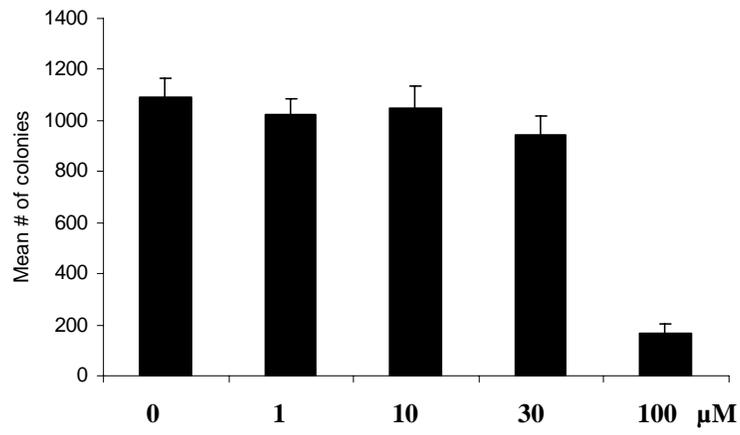


Figure 5



Mechanisms of Cellular Apoptotic Induction Caused by Polyphenon E in Prostate Cancer Cell Lines.

Maclin Williams
Project INSPIRE intern

Mentor: Dr. A. Kazi

Research done in Dr. Said Sebti's Lab

INTRODUCTION

According to the American Cancer Society, prostate cancer (PCA) is the most common form of cancer in American after skin cancer. It is estimated that 27,000 people will die of the disease in 2007 making it the second leading cause of death in men from cancer. At the current time, there are three major treatment options offered after a positive diagnosis. These options are surgery to remove the tumor or the entire prostate itself, radiation treatments that are localized to the mutated regions of the prostate and estrogen hormone treatments used to counteract the tumor promoting effects of testosterone. However, there is a lack of evidence to confirm the effectiveness of these treatment options mainly due to high accounts of tumor reoccurrence and poor quality of life issues that disease survivors must endure. For these reasons it is imperative to find more treatment options to further the fight of PCA and hopefully to guarantee better living conditions for men once the disease goes into remission.

Asian countries constitute 20% of the tea consumed world wide and there is a noticeable decrease in the presence of many cancers compared to the Western World, men in American are four times more likely to die from prostate cancer than in Japan (14). Studies have shown that tea consumption (mainly green and black teas) lowers the risk of developing prostate and breast cancer. Such credible findings warrant future study of these teas, and their main chemoprevention components to further the field of cancer research.

The polyphenol extracts of the green and black teas have proven to show the cancer fighting properties that have been a part of various studies in a last few years. These polyphenol extracts, taken from the dried leaves of the *Camellia sinensis* plant, were tested and proven to cause apoptosis in cancer cells of the stomach, lungs, prostate, colon, leukemia, oral tumors, liver, breasts, cervix and HPV-immortalized cervical epithelial cells. The apoptosis of these cells were assessed by 1) formation of internucleosomal DNA fragments by agarose gel electrophoresis 2) confocal microscopy and 3) flow cytometry after tagging DNA fragments by fluorescence label (2). These polyphenols have very potent antioxidant activity acting as a scavenger of free radicals in the blood, an anti-mutagenic property. The chemopreventative effects of polyphenols include 1) protection against mutagenicity and genotoxicity 2) inhibition of biochemical markers of tumor initiation 3) inhibition of biochemical markers of tumor promotion 4) effects of detoxification enzymes and the 5) trapping of activated metabolites (11). Green Tea Polyphenols (GTP) are also inducers of cell cycle arrest in

cancer cells, causing a halt to occur in the $G_1 - G_0$ phase of the cell cycle (2), indicating proliferation inhibition since mitosis and cell division is not reached.

GTP has been found to significantly inhibit vascular endothelial growth factor (VEGF), a marker protein for angiogenesis, the formation of new blood vessels necessary to continue feeding tumor cells. (12) The increased expression of this protein goes hand-in-hand with more expansive tumor growth (1). It is important to discover the particular step in the expression pathway of this protein that GTP affects so that the impact the drug has on the circulatory system as a whole can be studied. There is also a correlation between levels of VEGF and Insulin-like growth factor-I (IGF-I) where GTP inhibits IGF-I and therefore VEGF in order to stop neovascularization and the tumor cell proliferation (1).

It has been shown that the progression of PCA in transgenic adenocarcinoma of the mouse prostate (TRAMP) model is IGF-I dependent. Also, the protein expression of phosphorylated extracellular-signal regulated kinase (pERK) was greater than phosphorylated Akt (pAkt), so pERK expression is the marker of choice for the diagnosis of PCA in the IGF-I model. Another point is that elevated levels of IGF-I combined with decreased levels of IGF binding protein (IGFBP)-3 shows an increased risk for PCA development and progression. The findings prove that GTP modulates the IGF/IGFBP-3 ratio, which was found to be associated with the inhibition of pAkt and pERK by half (1). Studies must be done in order to find out how the particular mechanisms in these pathways are impacted by GTP, as with finding out whether the lowering of the IGF/IGFBP ratio inhibit the phosphorylation of Akt or ERK.

Androgens are essential for normal prostate physiology and are shown to play a key role in the development of the pathogenesis of PCA, Ornithine decarboxylase (ODC) being an androgen-responsive protein used in PCA diagnosis. Among all the organs in the human body, the highest concentration of ODC is in the prostate; the activity of the protein is significantly higher in PCA tissue than in normal prostate tissues. Therefore, ODC could serve as another target for prevention and therapy of human PCA (6). ODC is used as a marker for increased cellular growth and proliferation and GTP has demonstrated to inhibit the ODC induction that is caused by tumors. ODC is regulated by androgens via the androgen receptor binding consensus sequence within the tumor promoter, so it has been shown that ODC inhibition is an effective platform to examine the effect of GTP on PCA. (6)

GTP results in an upregulation of Bax protein and a decrease in Bcl-2 protein, so the increase in the Bax/Bcl-2 ratio is a favorable sign of apoptosis (12). Bcl-2 is an anti-apoptotic protein that is linked to the immunoglobulin locus by chromosome translocation in follicular lymphoma and such is found to inhibit cell death (12). Since the expression of Bcl-xL is more abundant in prostate carcinomas of higher Gleason grades (4), GTP's ability to induce apoptosis can be correlated with the decreased expression of the Bcl-xL protein. The particular step in the Bcl-xL expression pathway that GTP effects must be found and studied so that its impact on other protein expression pathway sequences will be able to be accounted for.

The specific cell lines that studied in this experiment were LNCaP and DU-145 prostate cancer cell lines and with C7 and C7 Kras pancreatic cell lines, each of which exhibited particular characteristics to serve a specific purpose to this study. LNCaP cells are generally an androgen-sensitive prostate cancer cell line (7) that is used to test GTP's effect on cells that increase their protein expression in the presence of androgen hormones. DU-145 prostate cancer cell lines are reportedly androgen-receptor negative by most studies. Even though a small number of the studies provide evidence that DU-145 expressed androgen receptor (AR) mRNA, the relative levels of AR mRNA and the respective protein in DU-145 are much lower than that in LNCaP (3). In knowing that PCA cells can increase proliferation in the presence of testosterone (hence the estrogen therapy) it must also be noted that they can also proliferate in the absence androgen hormones so it is imperative that both an androgen receptor positive and negative cell line be tested. The pancreatic cells lines of C7 and C7 Kras were used in order to compare GTP's effect on normal (C7) cells versus mutagenic (C7 Kras).

MATERIALS AND METHODS

INITIAL CELL CULTURE STOCK SOLUTION

1. Remove the vial of prospective cell line from liquid nitrogen container
2. Thaw the cells in water bath incubator at 37° C for about 10 to 15 minutes
3. Put the entire vial of cell solution into a cell culture flask with of respective media comparative to amount size of the flask.
 - a. DU-145 cells – DMEM with 10% Fetal Bovine Serum (FBS) + 1% Penicillin Streptomycin (PS)
 - b. LNCaP cells – RPMI with 10% FBS + 1% PS
4. Put the flask in the cell culture incubator at 37°C and 5% CO₂ until the cells multiply to a certain consistency needed for sub-culture and drug treatment.

CELL SUBCULTURE FOR DRUG TREATMENT

1. DU-145, LNCaP, C7 and C7 Kras cells are adherent cells, so aspirate the media from the cell culture flask enduring not to touch the bottom of the flask for risk of losing living cells
2. Add enough Tripson to slightly cover the bottom of the flask
3. Place the flask in the incubator and let sit for enough time for cells to detach from the bottom of the flask. Be sure not to Tripsonize cells for over 15 minutes at a time because it can be harmful to the cells
4. If needed, slightly tap on the side of the flask to loosen up the cells from the bottom of the flask
5. Add the same amount of serum free media to the flask that was used when tripson was added
6. Add the cell suspension to a 15 mL or 50 mL vial depending on how much liquid is there.
7. Centrifuge the vial at 2000 rpm for 5 minutes at 4°C
8. Aspirate supernate ensuring not to touch the cell pellet with the aspirator.
9. Re-suspend the pellet in 2 mL of serum free media and dilute further if needed

10. Take aliquot of cell suspension and count in histocytometer in order to find out cell concentration
11. Plate the cells in subculture container of choice at cell concentration of choice, add remaining cell suspension into a cell culture flask and add serum containing media to the flask so maintain viable colony and place flask back into incubator
 - a. 6 cm Petri dish, cell concentration of 600,000 – 1,000,000 cells per 3 mL of media
 - b. 96 well plate, 10,000 cells per 100uL of media
12. Place the subculture dishes back in the incubator for 48 hrs in preparation for drug treatment. (serum free media causes the cells to produce more Bcl-xL protein)

SOFT AGAR ASSAY SET UP

1. Prepare 3% bacto agar with dH₂O and melt using microwave until completely dissolved
 - a. Use glass bottle and keep the cap loose while heating
 - b. Heat for 2 minutes first and inspect to see if it is dissolved
 - c. If not then heat again for 1 – 2 minutes and repeat if necessary
2. Place agar in 50°C water bath and wait until agar temperature has come down to 50°C
3. Place the media and a blank bottle into the water bath to adjust the temperature
4. Prepare 0.6% agar in blank bottle
 - a. 20uL agar of 3% and 80mL of completely dissolved media
5. Quickly deliver 2 mL into each well of 12-well plate (bottom layer)
6. Let the bottom layer solidify (takes about 30 minutes)
7. Prepare cells with 0.3% agar from 0.6% agar using complete media
8. Add desired concentration of cells to 0.3% agar and then aliquot into 15 mL tubes according to desired drug concentration
9. Add drugs and mix gently by pipetting up and down without making bubbles
10. Deliver 1 mL of this mixture to the top of the solidified bottom layer of each well of the 12-well plate
11. Let the media solidify for 20-30 minutes and incubate at 37°C in 5% CO₂ for 14-18 days
12. One the last day, add 200 uL of a 1 mg/mL MTT solution to each well and let sit overnight
13. Scan the plate and adjust the shading in order to see the colonies to count

DRUG TREATMENT IN 96 WELL PLATE

1. Aspirate the serum free media from each well of the plates that have been incubating for the past 48 hrs
2. Add 100uL of the respective serum containing media to each well
3. Make varying drug concentrations by diluting the stock solution
 - a. 100mM stock, 10mM, 3mM, 1mM, 300uM, 100uM, 10uM
4. Add 100uL of the drug concentrations to 8 wells of a well plate in the following order
 - a. 1) H₂O 2) 10mM 3) 3mM 4) 1mM 5) 300uM 6) 100uM 7) 10uM 8) H₂O

5. With an 8 tip micro pipette, at 1 uL of drug into the respective wells of the 96 well plate and label the column
6. Incubate for designated amount to time, then perform respective assay

DRUG TREATMENT IN 6 cm Petri dishes

1. Aspirate serum free media from dishes that have been incubating for the past 48 hrs
2. Add 3 mL of the respective serum containing media to each dish
3. Make varying drug concentrations by diluting the stock solution
 - a. 100mM stock, 50mM, 45mM, 15mM, 4.5mM, 1.5mM
4. In order to get final drug concentrations in solution, use varying amounts different drug concentrations
 - a. Final 100uM in 3 mL of solution – add 3uL of 100mM drug concentration
 - b. Final 30mM in 3 mL of solution – add 2 uL of 45mM drug concentration
 - c. Final 10mM in 3 mL of solution – add 2 uL of 15 mM drug concentration
 - d. Final 0mM in 3 mL of solution – add 3 uL of dH₂O

HARVESTING OF TREATED CELL SUBCULTURES

1. Remove media from the 6 cm Petri dishes and place each it into particular 15 mL tube
2. Add 1 mL of tripson to each dish and place back into incubator for 10 minutes to detach the cells from the bottom of the dish
3. After cells have detached from bottom (might need to tap the dish to loosen up the cells), place 2 mL of serum containing media to the dish
4. Remove suspension and add to the respective 15 mL tube
5. Centrifuge at 300 g for 5 minutes
6. Aspirate supernate
7. Add 1 mL of chilled 1x PBS and resuspend pellet
8. Remove 30uL aliquot for Typan Blue Analysis
 - a. Add 120 uL of Typan blue to cell
 - b. Place aliquot onto histocytometer and count the cells
 - c. Dead cells will be blue, living cells will be white
9. Place remainder of PBS suspended pellet into a 1.5 mL micropipette
10. Centrifuge at 300g for 5 minutes
11. Aspirate supernate and place pellet into -80°C freezer for Western Blot Analysis

MTT ANALYSIS

1. After cells in 96 well plate have been treated for designated amount of time add 10uL of MTT solution (5mg/mL for LNCap and 1mg/mL for DU-145)
2. Let incubate for 3 hours
3. Aspirate media from each well
4. Add 100uL of DMSO to each well
5. Read at 540nm in photocytometer

CELL LYSES FOR WESTERN BLOTT

1. Take pellets out of -80°C freezer and add to ice bath

2. Add 30uL lyses buffer to each tube and vortex to resuspend pellet
3. Let sit for 30 minutes, vortexing every 10 minutes
4. Suspension to centrifuge, 13,000g for 15 minutes
5. Remove supernate and add to separate vial and put on ice
6. Scan for protein and set up Western Blot per gel instruction

RESULTS

TRYPAN BLUE ANALYSIS

Trypan blue is a chemical dye used to distinguish living cells from dead ones. The dye can only be processed by living cells, so under the microscope the living cells appear to be white and the dead cells blue from the staining. So, the purpose for this test was to get a correlation between the concentration and amount of time that the cancer cells were treated with the Polyphenon E and the drug's effect on the cells. The proliferation rates of the cells were accounted for in percentage with the non-treated cell proliferation rate being the common denominator. So, the increase in drug concentration had a dose dependent retardation of the proliferation rates of the each of the cell lines (DU-145, LNCaP, C7 and C7 Kras).

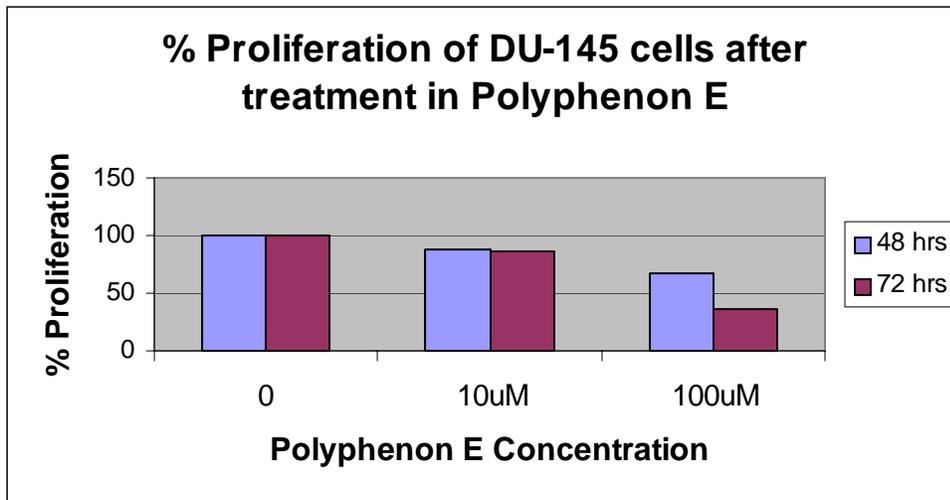


Fig 1, Here in the DU-145 cell line, the proliferation rates decrease to 60% in the 48 hr treatments and to 40% in the 72 hr treatment in the 100uM drug concentrations. This evidence shows that at higher drug concentrations, cancer cell growth is significantly decreased.

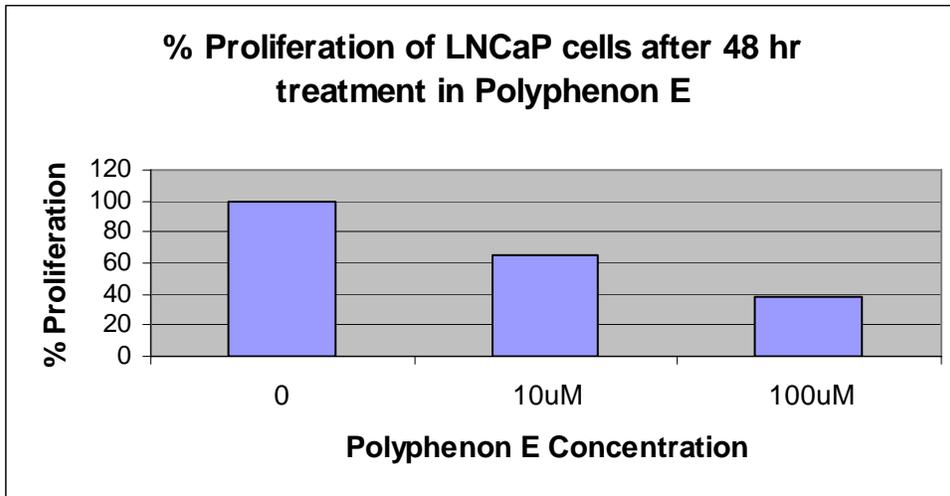


Fig 2, Here the evidence shows that proliferatoin rates in the LNCaP cells decrease at a greater rate starting at lower concentrations then from what is seen in DU-145. Even at 48 hr of treatment the proliferation rates are cut to almost 60% at 10 uM concentration and then to 40% at the 100uM concentration.

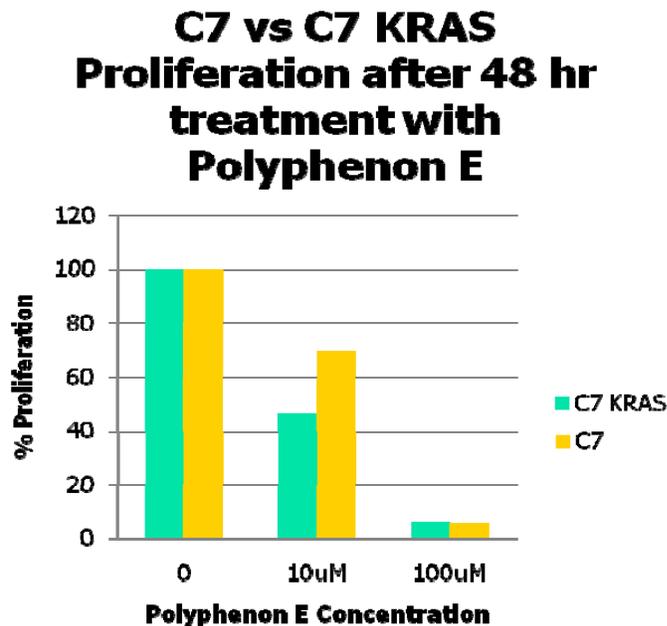
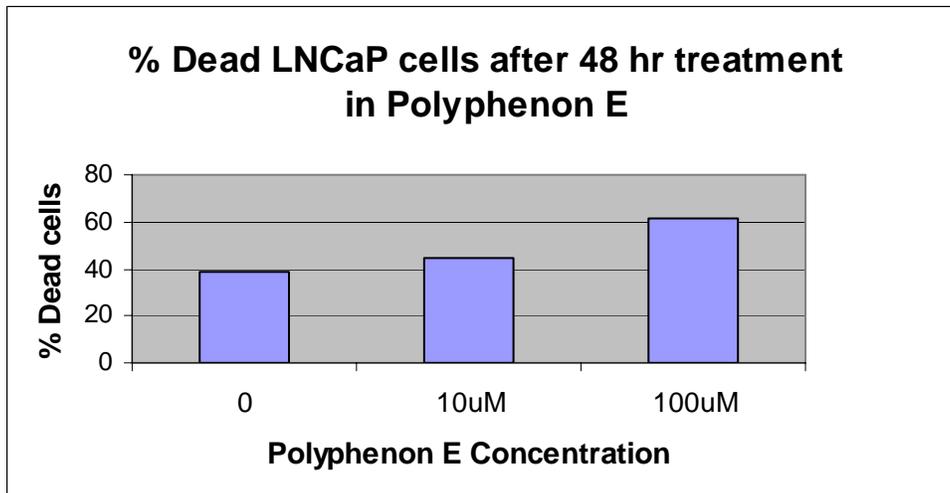
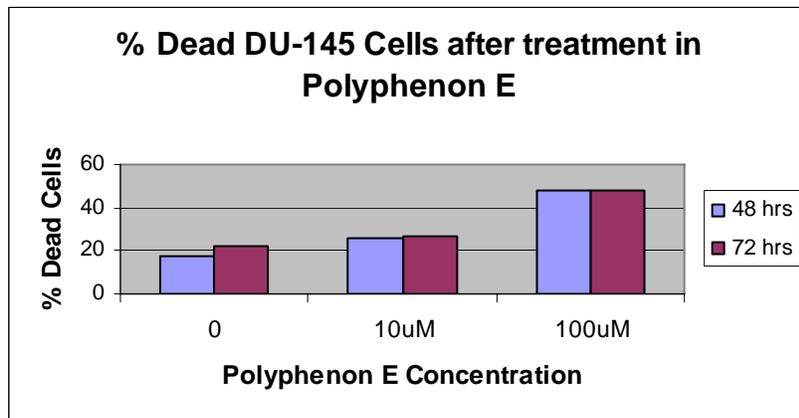
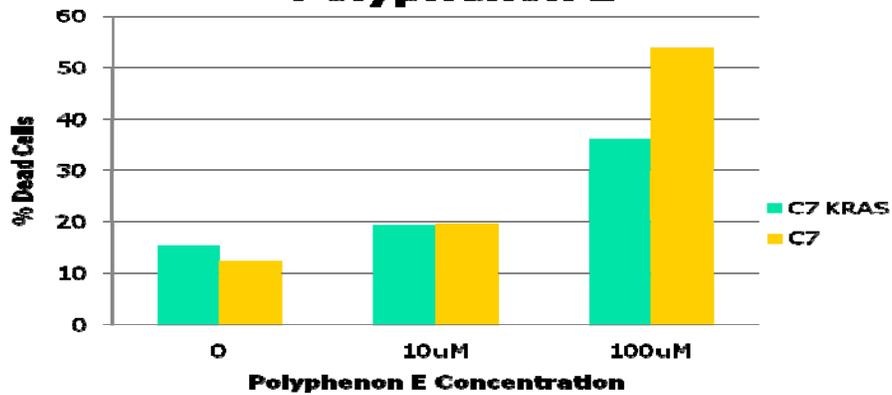


Fig 3, it is shown here that Polyphenon E has a higher tendency to reduce proliferation rates in cancer cells (C7 Kras) than in normal cells (C7) with about a 20% difference in 10uM concentration. Once the concentration got to 100uM, there were hardly any cells to be accounted for.

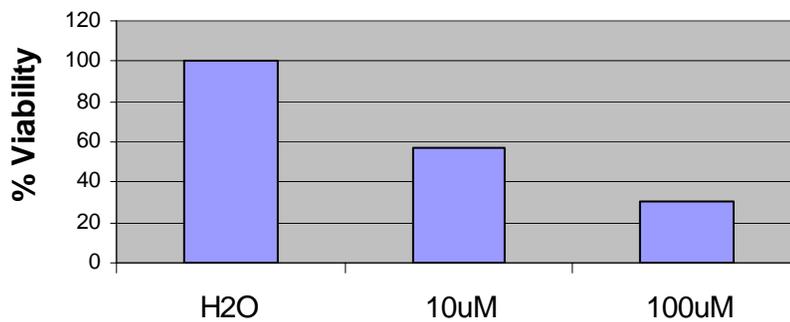
Fig 5, Polyphenon E induces cell death in LNCaP cells to over 60% in the 100uM concentration



% Dead C7 and C7 KRAS cells after 48 hr treatment in Polyphenon E



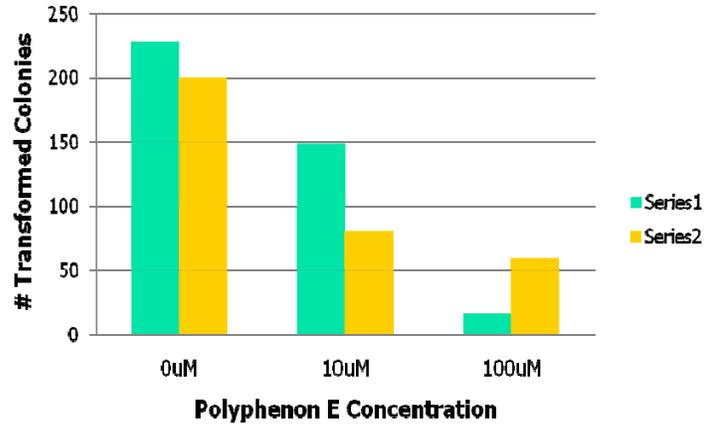
% Viability of LNCaP cells treated with Polyphenon E



SOFT AGAR ASSAY

The soft agar assay is another test to show the effect of the polyphenon E on cancer cell colonies. Only transformed cells can grow in the soft agar so when the cells are put into the agar and allowed to incubate for 16 days there are a number of cancer cell colonies that can be observed. So, with the treatment of the cells with the drug at varying concentrations, it is shown that the increasing concentrations of the drug will significantly decrease the number of formed cancer cell colonies.

LNCap Soft Agar Assay



WESTERN BLOT ANALYSIS

Western blot analysis is used to show protein expression in the cells. The cells were treated with the polyphenon E and then western blot was used to see how the varying concentrations of the drug affected the levels of protein that the cells produced. The antibodies that were used tested for the specific proteins that are a sign for apoptosis, with Bcl-xL and PARP. It was imperative that it was elusive that cell death occurred by apoptosis over any other cause of cell death.

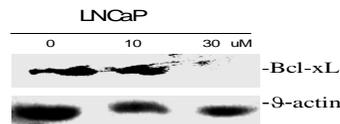


Fig 9, LNCaP cell blot. Bcl-xL is expressed in 0 and 10 uM concentrations and is not expressed in the 30uM concentration. This shows that apoptosis is occurring due to the lack of expression of the Bcl-xL in the higher concentrations of the drug.

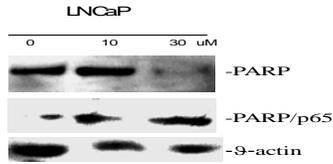


Fig 10, A prominent split in the PARP expression is observed in the higher concentrations of the Polyphenon E. It is obvious that the main band in the 30 uM concentration of the LNCaP has gone down compared to the lower concentrations even though the second band is prominently displayed.

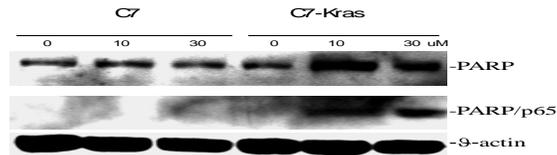


Fig 11, Seeing that there is no split in the PARP in the C7 cells, it is shown that there no apoptosis occurring. In the C7 Kras, there is no apoptosis in the 0 uM concentration, but there is a prominent split in the 10 and the 30uM concentrations to show the start when apoptosis starts occurring.

DISCUSSION

The first experiments (trypan blue, MTT, soft agar assay) were performed in order to prove the type of effect that Polyphenon E had on the various types of cancer cell lines. It was proven that the drug reduced the proliferation rate of all the cell lines regardless of the expression of the androgenic receptor. (Fig 1, 2) It was also shown that increasing drug concentrations caused more instances of programmed cell death in each of the cell lines. (Fig 4, 5) The C7 and the C7 Kras tests proved that the drug had more of an affinity to cause programmed cell death and reduce the proliferation rates in cancer cells compared to the normal cells. (Fig 3, 6)

After it was proven that the drug caused cell death in the various cancer cell lines it was important to find out the mechanisms of apoptosis that were occurring. The Bcl-

xL and the PARP pathways are proven to be expressed in the different cell lines with the exception of C7. The western blot analysis of cell lines showed a halt in the Bcl-xL (Fig 9) protein expression pathway was a mechanism of apoptosis LNCaP in the higher concentrations of the drug (10uM and 30uM). In the PARP protein expression pathways, the 10uM and the 30uM concentrations of the drug showed another mechanism of apoptosis in the LNCaP and the C7 Kras cell lines. (Fig 11)

Polyphenon E has shown proficiency in causing apoptosis in androgen receptor expressing and non expressing prostate cancer cell lines along with having a greater affinity toward cancer cells opposed to normal cells which was shown by the expression of the PARP protein. The drug can be very effective in the fight against cancer for the previously stated reasons, though more research is needed to find the exact mechanisms that cause apoptosis in the various cell lines.

FUTURE STUDIES

More protein expression experiments need to be done in order to see if Polyphenon E inhibits any other apoptosis pathways or even inhibits some protein expression pathways normal cell need for cell survival. A catalog of the proteins that Polyphenon E effects needs to be made so a comparison can be done on how apoptosis occurs in the different cancer cell types of the body. Polyphenon E is shown to cause a marked reduction in anti-apoptotic proteins of different cancer cell lines, so it must also be studied whether it could potentially inhibit expression of various proteins of the surrounding normal cells or whether it causes an over expression of proteins that could be detrimental to the cells.

Drug combination and interaction studies need to be done in order to find out if there are any drugs can be found to make Polyphenon E more potent and drugs that might cause it do turn ineffective or even detrimental to normal cell survival. As far as the mass distribution of the drug, this is an important matter due to amount of drugs that are going through people's system and the potential for toxic interactions. Also, if a drug can be combined with Polyphenon E that could increase its potency, the protein expression pathways that the drug combination needs to be found so that a "cocktail" therapy would be able to be developed.

Also, the more pathway inhibition studies need to be done in order to find out the exact breakdown in the PARP and the Bcl-xL pathways that is caused by the drug. It needs to be found whether it causes a breakdown in the transcription or translation portion of protein expression or even in the folding. Once all of these matters have been researched extensively, it can be concluded that Polyphenon E is as crucial to the fight against cancer as hoped.

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