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Diagnostics and Risk Assessment

PRINCIPAL INVESTIGATOR: Ganna Chornokur

CONTRACTING ORGANIZATION: H. Lee Moffitt Cancer Center and Research
Tampa, FL 33612

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13. SUPPLEMENTARY NOTES

14. ABSTRACT. The overall scope of the proposed postdoctoral training project is to provide protected time for the Primary Investigator (PI) to obtain a comprehensive training in the field of prostate cancer health disparity. The PI is a postdoctoral scientist whose long-term career goal is to contribute to the resolution of cancer-related health disparities by conducting innovative, high-impact research as an independent investigator. Within the scope of this grant, a comprehensive training consists of the two main parts: a training part and a research part. For the training part, PI is attending relevant seminars, conferences, takes classes, and writes manuscripts and grants. For the research part, we hypothesized that a combination panel (DETECT) of genetic, biochemical, socio-cultural and lifestyle population-specific biomarkers and factors will provide a valuable PCa screening and risk assessment tool. The PI has started with the genotyping of 528 DNA samples obtained from African American and European American men with prostate cancer and controls. It was found that two SNPs were statistically significantly associated with prostate cancer risk in African American, and one SNP – in European American men. Going further, the excessive prostate cancer risk associated with one of the SNPs in African American men was found in obese men only; it was not seen in either non-obese African American men, or European American men regardless of their body mass. The PI has proposed a concept of the increased risk in obese AAM which will be functionally tested in the year 2 of this award.

15. SUBJECT TERMS

African American, prostate cancer, risk factors, biomarkers, health disparity

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Introduction

The overall scope of the proposed postdoctoral training project is to provide protected time for the Primary Investigator (PI) to obtain a comprehensive training in the field of prostate cancer health disparity. The PI is a postdoctoral scientist / young investigator whose long-term career goal is to contribute to the resolution of cancer-related health disparities by conducting innovative, high-impact research as an independent investigator with competitive, peer-reviewed funding. PI aims to achieve her long-term career goal through an integrated 2-year research and training program in the comprehensive H. Lee Moffitt Cancer Center and Research Institute, with appropriate guidance of an experienced Mentor, Dr. Nagi Kumar, who is a nationally recognized expert in the chemoprevention of cancer and is a leader in health disparities research, and the team of Co-mentors (Drs. Park and Phelan). Within the scope of this grant, a comprehensive training agenda has been proposed; it consists of the two main parts: a training part and a research part (supplemental project). Specific progress to date on each of those parts is outlined in the body of this annual report. It is resumed with the “Key Research Accomplishments” and “Reportable Outcomes” sections that briefly summarize the main reportable outcomes emanating from this work.

BODY

A. Training Program. The specific activities of the PI’s career development plan are provided below.

1. Structured mentoring program coordinated by PI/primary mentor and co-mentor(s).

Dr. Chornokur maintains weekly and/or bi-weekly one hour meetings with her primary mentor, Dr. Nagi Kumar, and a co-mentor, Dr. Catherine Phelan. Meetings with a third co-mentor, Dr. Jong Park, is scheduled on as-needed basis. The same schedule will continue throughout the year #2 of this training award.

2. Gain proficiency and a better understanding of science used to develop and implement primary prevention intervention in minority populations.

- This task is being accomplished by: 1. regular meetings with the Mentoring team as described above; 2. conducting extensive bi-annual literature searches on the topics of chemoprevention of prostate cancer, prostate cancer racial health disparity, and other relevant literature (community outreach programs, for example); 3. being involved in the relevant research projects at the Moffitt Cancer Center (please see Table 1); 4. attending the relevant talks, ground rounds and seminars at Moffitt and USF (please see task 7); and 5. extensive networking (please see task 9). This comprehensive systematic approach has allowed Dr Chornokur to develop and submit two peer-reviewed grants (please see the task 6) and publications (please see the task 8). This schedule will continue in the year #2 of this award, likely leading to additional deliverables including the grant proposals and manuscripts.

3. Gain hands-on research experience in the implementation and conduct of research studies.

- Under the mentorship of Dr Phelan, the PI is currently involved in the two NIH and one DoD funded projects (aside from her own research study): 1. PC050873 (Phelan PI): Prostate Cancer in African-American Men: Serum Biomarkers for Early Detection Using Nanoparticles; 2. 1R01 CA149429-01 (Phelan PI): The Mitochondrial Genome and Ovarian Cancer Risk; and 3. 5 U19 CA148112-02 (Sellers PI): Follow-up of Ovarian Cancer Genetic Association and Interaction Studies (FOCI). The PI is involved in the two NIH funded clinical trials under the mentorship of Dr. Kumar: 1. R01 CA12060-01A1 (Kumar PI): Phase II, Randomized, Double-blind, Multi-centered Study of Polyphenon E in Men with High-grade Prostatic Intraepithelial Neoplasia (HGPIN) and Atypical Small Acinar Proliferation (ASAP); 2. P20 MD003375-01 (Kumar PI): Phase II Clinical trial of Purified Isoflavones in Prostate Cancer: Comparing Safety, Effectiveness and Mechanism of Action between African American and Caucasian Men. The PI is also involved in the following NIH funded R01 project under the mentorship of Dr. Park: R01CA128813 (Park PI): Genetic & epigenetic analysis of

angiogenesis genes in recurrent prostate cancer. The summary of these projects, along with specific PI's activities, are shown in the Table 1.

Table 1. Research projects that the PI is currently involved with through her Mentors.

Project	Primary hypothesis, goals and/or objectives	PI's involvement, tasks etc
PC050873 Prostate Cancer in African-American Men: Serum Biomarkers for Early Detection Using Nanoparticles	In this study our objective is to set up a prostate cancer case-control study in order to develop new serum biomarkers for early detection of prostate cancer using Nanotechnology. It also sought to investigate whether any bio-behavioral risk factors are associated with prostate cancer in African American men.	The PI was involved in this study while doing her PhD work in Biomedical Engineering at the University of South Florida. The study is now closed for accrual, however, the data analysis and research dissemination continue. Specifically, under the mentorship of Dr Phelan, the PI collaborated with a statistician to investigate known bio-behavioral risk factors of prostate cancer, along with PSA levels, and risk of prostate cancer in African American / Black men. This work has generated intriguing pilot results that were presented by the PI as a poster at several relevant high-impact scientific meetings. The PI has also prepared a manuscript entitled "Risk Factors for Prostate Cancer in African American Men" that is now undergoing final revisions. This project, that is highly relevant to the PI's training and her own research work, provides plethora of vital skills needed to conduct an interdisciplinary health disparity research in prostate cancer. The latter includes review and understanding of the most up-to-date literature in the field, skills necessary to perform epidemiological and statistical analyses, and – the most importantly – understanding and interpretation of the findings. These skills will lay the foundation for the PI to start developing her own intervention and independent research in prostate cancer health disparity in the year 2 (as outlined in the task 5 of this award).
1R01 CA149429-01 The Mitochondrial Genome and Ovarian Cancer Risk	It was hypothesized that that inherited variation in mitochondrial-related genes is associated with ovarian cancer risk. The objective is to more comprehensively investigate the contribution of mitochondrial genome variation to ovarian cancer risk.	In this award, the PI is actively involved in the pathways and genes/SNPs selection, as well as analysis interpretation and dissemination. This includes extensive literature search on the topic, review of the molecular and biochemical mechanisms that may play a role in the development of ovarian cancer, and understanding the statistical analyses involved in the data management. Importantly, the PI is exposed to the opportunities and challenges of the multicenter, multi-institution, collaborative work that involves extraordinary big sample size. These experiences are vital for an independent health disparity researcher. In addition, the PI obtains basic understanding of ovarian cancer research through this project. While not explicitly health disparity related, this project may serve as a foundation for the PI's own future work in ovarian cancer health disparity.
5 U19 CA148112-02 Follow-up of Ovarian Cancer Genetic Association and Interaction Studies (FOCI)	Specific aims of this project include evaluating the role of candidate genes at susceptibility loci in ovarian cancer; determining the functional significance of top candidate SNPs; and performing detailed functional characterization of candidate genes and SNPs.	PI's involvement into this multicenter, multi-institution high-impact study is similar to the one described above (CA149429-01). However, it allows for an even broader understanding of all ovarian cancer research, mitochondria related or not. PI attends the regular monthly-scheduled conference calls where the findings, challenges, manuscripts and cofrence presentations, future funding opportunities and current progress are being systematically discussed. Similarly to CA149429-01, this work is not disparity-related, however, it exposes the PI to a unique research experience that is vital to a transdisciplinary health disparity researcher and would have been hard to impossible to obtain elsewhere.
R01 CA12060-01A1 Phase II, Randomized, Double-blind, Multi-centered Study of Polyphenon E in Men	Men with HGPIN who receive Polyphenon E containing 400mg of EGCG per day for 12 months will significantly decrease	PI attends the monthly research meetings where specific research-related progress is being discussed. PI is aware of the recruitment challenges and is involved in the interventions aimed at increasing the recruitment rates. In addition, the PI will shadow the project coordinator when she recruits and/or follows up new or existing patients. The PI is using this trial as an

with High-grade Prostatic Intraepithelial Neoplasia (HGPIN) and Atypical Small Acinar Proliferation (ASAP)	progression to CaP compared with men with HGPIN who take placebo.	opportunity to learn how to conceive and implement a chemopreventive intervention in prostate cancer.
1 P20 MD003375-01 Phase II Clinical trial of Purified Isoflavones in Prostate Cancer: Comparing Safety, Effectiveness and Mechanism of Action between African American and Caucasian Men	We hypothesized that supplementation with a constant dose of purified isoflavones (vs a placebo) will produce an increase in plasma levels of isoflavones which will be correlated with stabilization or reduction in surrogate markers of proliferation and thereby contribute to a decrease or stabilization of disease progression in men diagnosed with early stage prostate cancer.	PI's involvement into this clinical trial is similar to the one described above (CA12060-01A1). However, this projects links the PI to the Center of Equal Health (CEH), an NIH-funded initiative between USF and Moffitt to reduce and eliminate health disparities. The PI was funded through CEH for one year, and this funding has allowed the PI to develop the idea, apply for and get this training grant. The PI attends regular monthly CEH meetings and conference calls between Moffitt and USF to discuss the clinical trial. The PI also has access to the majority of CEH-organized activities, including the community outreach programs. These unique experiences without a doubt add to the PI's transdisciplinary training in prostate cancer health disparity.
R01CA128813 (Park PI): Genetic & epigenetic analysis of angiogenesis genes in recurrent prostate cancer.	The ultimate goal of this study is to identify biomarkers that can be used at the time of diagnosis to predict risk of recurrence and improve clinical treatment decision making. Central hypothesis is that genetic and epigenetic individual variation in genes involved in the angiogenesis pathway is associated with recurrence of prostate cancer.	The following important contributions to the PI's training and her own research project stem from this R01: 1. approximately 75% of all DNA samples used in the PI's supplemental project were collected within the scope of this R01; 2. the PI has both the laboratory access AND hands-on support from personnel involved into this study (Dr Park's lab). That includes sample storage and handling, genotyping, and help in interpreting the results; 3. PI is getting help in the data analysis from personnel in the Dr. Park's group that are involved into this study.

4. Initiate and complete a research supplement project.

- The Institutional Review Board (IRB) and Scientific Review Committee (SRC) approvals have been obtained by the PI. The copies of both approvals are attached in the appendices 1 and 2, respectively. At the end of year #1, specific aim 1 has been completed. Please see the section "Research plan" for more details.

5. To develop interventions and independent research questions based on the results from research study completed.

- As outlined in the training SOW (Table 2), this task will be completed in the year #2.

6. Gain extensive grant writing experience.

- PI has submitted the following two extramural peer-reviewed research grants: an NIH R03 on 02/2012 (1R03CA172753-01: Comparative race-specific chemopreventive effects of curcumin in prostate cancer), and a DoD hypothesis development award on 06/2012 (PC120156: Comparative race-specific chemopreventive effects of curcumin in prostate cancer). Although the two submitted are based on the same hypothesis and thus are not scientifically distinct, it is advantageous for the PI's grant writing experience to submit two grants to the different funding agencies. Importantly, the focus of the submitted grants is on the molecular mechanisms of prostate cancer health disparity, and the effectiveness of chemopreventive intervention against prostate cancer in Black and White men, and is thus directly relevant to the PI's training. Specific aims page for the aforementioned grants is shown in the appendix 3. For more details on these submissions. As a part of her grant

writing training, the PI has attended an NIH-organized grant writing workshop that was held during the annual AACR meeting (May 31, 2012, Chicago IL). She has also attended several scientific writing/ grant writing seminars (please see task 7, items B,J,K,L). Additional grant submissions (NIH PAR-12-094, in particular) are planned in the year #2 of this award.

7. To attend research and educational meetings.

- PI is an associate member at the American Association for Cancer Research (AACR). During the year 1, PI has attended (and presented her work, where indicated) at the following relevant research and educational meetings.

1. Joining FORCES Against Hereditary Cancer Conference (June 2011, Orlando FL). The poster presentation entitled "Risk of Gastrointestinal Cancers in Female BRCA1 and BRCA2 Mutation Carriers".
 2. Center for Equal Health Strategic Planning Retreat Meeting (September 2011).
 3. Annual AACR meeting (March-April 2012, Chicago IL). The poster presentation entitled "The Risk Factors for Prostate Cancer in African American Men".
 4. The First Florida Prostate Cancer Research Symposium (May 4-5 2012, Orlando FL). The poster presentation entitled "The Risk Factors for Prostate Cancer in African American Men".
 5. Moffitt's 2012 Scientific Symposium (May 10 2012, Tampa FL). The poster presentation entitled "The Risk Factors for Prostate Cancer in African American Men".
- The poster copies are included in the appendices 4 (BRCA) and 5 (prostate).

PI is also attending relevant scientific talks, ground rounds and seminars that occur at Moffitt and/or USF. Select, the most relevant presentations are shown below.

- A. Why Culture Matter in Eliminating Health Disparities, Collins Airhihenbuwa, PhD, June 3, 2011.
 - B. American Cancer Society-Funding Opportunities for Research and Training. Charles L. Saxe, PhD. Moffitt Cancer Center. August 1, 2011.
 - C. Fishers of Med: Evaluating a Digital Training Curriculum, Brian Rivers, PhD, MPH. August 31, 2011.
 - D. The Skin You're In: Making Progress in Eliminating Health Inequalities, Thomas LaVeist, PhD. November 4, 2011.
 - E. Medically Underserved Areas and Patient Navigation, Elizabeth Calhoun, Med, PhD. January 19, 2012.
 - F. A Biocultural Approach to Racial Disparities in Health: Genetics, Epigenetics, and the Biological Embedding of Psychosocial Stress, Amy Non, PhD. Candidate for Faculty Position in Biological Anthropology Seminar. January 23, 2012.
 - G. Minority Enrollment in Clinical Trials: Challenges and Best Practices, Mona N. Fouad, MD, MPH. February 13, 2012.
 - H. Participatory Research and Evaluation: Case for Building Practice-Based Evidence, Joseph Telfair, DrPH, MSW, MPH. Center for Equal Health External Advisory Board Meeting, February 16, 2012.
 - I. Planning and Implementing Lay Health Worker Interventions for Cancer Control: a Systematic Process to Increase Program Outcomes, Maria Fernandez, PhD. March 9, 2012.
 - J. Elements of Basic Science Grant Writing: A physician-scientist View, Eduardo Sotomayor, MD. MPDA Grant Writing Seminar. January 12, 2012.
 - K. Manuscript writing workshop: The Introduction, Methods, Results, and Discussion (IMRaD) Format, Jane D. Carver, PhD, MS, MPH. MPDA Career Development Seminar. February 21, 2012.
 - L. Enhancing Your Success as a Published Author, Jane D. Carver, PhD, MS, MPH. Cancer Epidemiology Career Development Seminar. March 21, 2012.
 - M. Socioeconomic Status and Tobacco Related Disparities. David Wetter, PhD, MS. May 11, 2012
 - N. Ethical Cancer Research & Uninformed Consent: The Henrietta Lacks Story. Organized by Moffitt Diversity Department. May 23, 2012.
 - O. Past Experiences – Lessons Learned (SELECT, CARET, Retinoids vs. Statins, COX-2 inhibitors): What Went Wrong? Where Do We Go From Here? Ernest Hawk, MD, PhD. May 29, 2012.
- Additionally, as required by her work, the PI maintains the Human Subjects (certification updated on 04/2012), Biosafety (04/2012) and Mandatory Moffitt education (05/2012) tests and trainings up to date.

8. *Scientific writing and research dissemination.*

- The following research articles have been published, accepted or submitted for publication during the year 1 of this award (06/2011 – 06/2012):
- 1. Shahnjayla Connors, Ganna Chornokur, Nagi Kumar. New Insights to the Mechanisms of Green Tea Catechins in the Chemoprevention of Prostate Cancer. *Nutrition and cancer*. 11/2011; 64(1):4-22; PMID: 22098273
- 2. Kumar NB, Crocker, T, Smith T, Pow-Sang, J, Spiess, PE, Connors, SK, Chornokur, G, Iravani Dickinson, S, Williams, CR, Salup, R, Bai, W. Prostate Cancer Chemoprevention targeting High Risk Populations: Model for trial design and outcome measures. *J Cancer Sci Ther*. 2012; PMID: 22422102
- 3. T.G. Kryshchak L.V. Borkovska O. Kolomys N.O. Korsunskaya V.V. Strelchuk, L.P. Germash, K.Yu. Pechers'ka, G. Chornokur, S.S. Ostapenko, C.M. Phelan, O.L. Stroyuk. The effect of bio-conjugation on aging of the photoluminescence in CdSeTe-ZnS core-shell quantum dots. *Superlattices and Microstructures* 51(3) 2012, 353–62
- 4. Manju Venugopal, Sunil K. Arya, Ganna Chornokur, Shekhar Bhansali. A Realtime and Continuous Assessment of Cortisol in ISF Using Electrochemical Impedance Spectroscopy // *Sens Actuators A Phys*. 2011 1;172(1):154-160. PMID: 22163154
- 5. Ganna Chornokur, Gang Han, Richard Tanner, Hui-Yi Lin, Jack Steel, Patrick Watson, Julio Pow-Sang and Catherine Phelan. Risk factors for prostate cancer in African American men. Undergoing final revisions. Please see appendix 6 for a copy of this manuscript.

Please see the section 7 for the list of attended meetings and poster presentations.

9. *Interactions with established scientists, networking, and peer linkages.*

- This training activity is being achieved through: 1. working with collaborators (inside and outside of the mentoring team) to write joint grant submissions; 2. contributing to manuscripts written by other scientists; 3. networking and learning from peers and colleagues at the research meetings; 4. participating in the USF/Moffitt Center for Equal Health; and 5. attending the “networking with experts” lunches that follow bi-monthly ground rounds at Moffitt.

10. *Additionally, as requested by the peer-review committee*, Dr. Chornokur has audited the “Cancer epidemiology” course at USF that was taught by two Moffitt Cancer Epidemiology Assistant Members. She has also completed the 5-weeks “Biostatistics 101” course (certificate awarded), designed and taught by the Moffitt Biostatistical core. The audit of “Cancer biology 2” course is planned in the year 2 of this award (Fall 2012).

Deliverables and Evaluation. PI will be evaluated annually by Mentor, co-Mentor and other faculty. Annual evaluations will assist the Mentor in refining this training program.

- Successful annual evaluation is a part of this training grant, as well as a requirement a Moffitt Cancer Center sets for every postdoctoral scientist. This extensive evaluation process includes a rating of the postdoc's behavioral criteria (teamwork, responsibility, adaptability etc), as well as professional accomplishments and progress within the past year. It also includes an outline of the major professional goals and career targets set for the next year. These goals are set up by a postdoc herself, and approved (with modifications, if needed) by her Mentor(s). To comply with this requirement, PI was evaluated by the team of her mentors in December-January 2011/2012 (the PI's anniversary date at Moffitt). Based on this evaluation, PI has gotten an overall score of 4.2 out of 5 that corresponds to the “Surpasses” mark on the evaluation scale used. A list of professional goals for the next year was also set and approved. These goals either meet or exceed the goals set up within the scope of this training grant. The copy of a complete evaluation is included in the appendix 7.

Table 2. Career Development Experiences and Timeline (training SOW).

Career Development Experiences / Timeline in Months	1-4	5-8	9-12	13-16	17-20	21-24
1. Structured mentoring program coordinated by the primary mentor through regularly scheduled weekly one-hour face-to-face meetings	x	x	x	x	x	x
2. Gain an understanding of the scientific paradigm used to develop, propose and implement bio-behavioral studies in minority populations	x	x				
3. Hands-on research experiences in scientific studies		x	x	x	x	x
4. Initiate and complete the research project	x	x	x	x	x	x
5. Begin developing bio-behavioral interventions and initiate her independent research plan for an independent position						x
6. Hands-on grant writing experiences			x	x	x	x
7. Research and educational meetings/journal club/grand rounds(1 per week)	x	x	x	x	x	x
8. Scientific writing and research dissemination			x	x	x	x
9. Interactions with established scientists, networking, and peer linkages	x	x	x	x	x	x

Summary of the training program progress: all tasks up to date as proposed in the training SOW.

B. Research Project. Specific progress to date is outlined below.

Specific research progress. We have initially proposed to prospectively recruit men into this study; however, based on the challenges associated with recruitment of African American men and seeking the most efficient training program in the limited time available to the PI, the Mentoring committee decided to augment this approach to use the retrospectively collected samples available from Drs. Phelan and Park. This augmented project is being carried out through the following specific aims.

1. **Specific Aim #1.** Evaluate different role(s) of genetic variations between AAM and EAM using the panel of select genetic markers. This will be achieved by an analysis of 600 germline DNA samples (300 AA and 300 EA), with each racial group containing 180 cases and 120 controls.
2. **Specific Aim #2.** Assess the genotype/phenotype correlations using the total of 120 AA samples (60 cases and 60 controls). This will be achieved by plasma analysis for expression of the most significant gene(s)/SNP(s), identified within the specific aim #1.
3. **Specific Aim #3.** To evaluate the feasibility of using the comprehensive DETECT approach in AAM as a PCa screening and risk assessment tool. Statistical measures to analyze the data obtained in the Aims #1-2, in addition to the medical charts and bio-behavioral questionnaire data, will be used. This will be achieved by: **3a.** Estimating the associations between the individual DETECT markers and PCa risk. **3b.** Establishing combined associations of selected (in sub-aim 2a.) markers and PCa. **3c.** Building and evaluating a prediction model of PCa risk based on results in Aim 2a and 2b.

While making the decision to augment the project, The Mentoring committee was guided by the following advantages of the new project versus the old one, keeping in mind the best interest of the PI and the scientific integrity of the project:

1. the new project allows to test the same hypothesis (**We hypothesize**, that a combination panel (DETECT) of genetic, biochemical, socio-cultural and lifestyle population-specific biomarkers and factors will provide a valuable PCa

screening and risk assessment tool) but offers substantial time-saving opportunity. Give the very limited training time, the PI will be better off using this time to advance her other training activities. The Mentoring committee realizes that the “hands-on” patient recruitment experience is very valuable for the PI; to accomplish this, the PI will shadow a clinical coordinator that is recruiting patients in Dr. Kumar’s R01 CA12060-01A1 clinical trial (please see Table 1 for details). This will be accomplished in the year #2 of this award. In summary, the PI will still get the “hands on” patient recruitment experience while saving valuable training time allowing the in-depth focusing on other training activities.

2. the new project allows to substantially increase the sample size (120 versus 600 samples total), thus increasing the power to detect weaker associations. For example, at the 0.05 level of significance, the sample size of 600 will detect an odds ratio of approx 1.8 or higher with the power of 80%, while the sample size of 120 will only detect an approximate odds ratio of 3 or higher.
3. the new project allows for a comparison between African American and European American men that would not have been possible using an old format. The Mentoring committee considered this research experience to be of value for the PI’s training, since plethora of health disparity work is based on the aide-by-side comparison between the different racial and ethnic groups.
4. the new project allows the PI to get hands on research experience in the concept of functional health disparity work, thus placing a special emphasis on the importance of gene-environment interactions in the development of cancer health disparities. The Mentoring committee considers this particular aspect of health disparity work to be of the outermost importance for the PI.

Specific progress. Aim #1: *Evaluate different role(s) of genetic variations between AAM and EAM using the panel of select genetic markers. This will be achieved by an analysis of 600 germline DNA samples (300 AA and 300 EA), with each racial group containing 180 cases and 120 controls.*

- SNP selection. PI has performed extensive literature search, that allowed her to select 10 short nucleotide polymorphisms (SNPs) that were: 1. reported positively associated with prostate cancer (increased risk) in African American (desirable) and/or White men; 2. functional (i.e. possibly having an influence on the gene expression); 3. reported Minor allele frequency (MAF) at least 15% in both African / Black and European / White men. Based on these criteria, the following SNPs were selected (Table 3).

Table 3. Short description of the SNPs selected for the Aim #1 of this study. W: White men; AA: African American men; OR: odds ratio;

SNP	Functional (Y/N) and gene	notes	ref
Rs4430796 G/A, Transition Substitution W:0.47(A) AA:0.34(A)	Possibly Y. TCF2 gene intronic region, possible effect on transcription	OR = 1.4	1
Rs7501939 T/C, Transition Substitution W:0.49(T) AA:0.48(C)		OR = 1.44	
Rs1859962 G/T, Transversion Substitution W:0.5(G) AA:0.2(G)		OR = 1.21 Associated with both overall, and familial/aggressive PCa in white men	
Rs10993994 C/T, Transition Substitution W:0.34(T) AA:0.2(C)	Y; MSMB gene encodes PSP94; reduced promoter activity	OR = 1.3	2, 3

rs822396 A/G, Transition Substitution W:0.15(G) AA:0.2(G)	Y; ADIPOQ	OR = 3	4
Rs4263970 C/T, Transition Substitution W:0.45(C) AA:0.47(T) Rs4612601 A/G, Transition Substitution W:0.45(A) AA:0.5(G)	Y: EPHB2	OR= 1.31 OR = 1.35 Sporadic PCa in AAM only	5
rs4962416 C/T, Transition Substitution W:0.23(C) AA:0.23(C)	Y: CTBP2 gene	OR = 1.17 – 1.63 in AAM	6
Rs627839 G/T, transversion substitution W:0.45(T) AA:0.46(T)	Y: RNASEL	OR = 3.98 in White men (PCa specific death)	7
Rs2070874 G/T, transition substitution W:0.2(T) AA:0.45(T)	Y: IL4	OR = 2.16 in White men (PCa specific death)	7

- Merging of the databases and creating the data dictionary. Because the samples came from two different and independent studies (Drs. Phelan and Park PIs), the PI had to create a merged data dictionary to be used in her study. This task was successfully accomplished. The data dictionary can be found in the appendix 8.
- The Institutional Review Board (IRB) and Scientific Review Committee (SRC) approvals were successfully obtained by the PI. The copies of both approvals are attached in the appendices 1 and 2, respectively.
- Sample selection. The PI has selected the samples for her study on the basis of matching. She has performed a pair wise extensive matching of cases and controls by race and ethnicity, age (+/- 2 years in most cases), Gleason score, TNM stage (cases), and PSA (where available).
- Genotyping was carried out by the PI in the Dr. Park's molecular biology laboratory. Applied Biosystems primer and PCR supplies were used to genotype the individual SNPs in all the samples.
- Data analysis was carried out using the SAS software and p-values < 0.05 were considered statistically significant.

Results. 528 germline DNA samples were successfully genotyped. That includes 259 samples obtained from African American men (136 cases and 123 controls), and 269 samples obtained from Non-Hispanic White men (147 cases and 142 controls). Each genotyping plate included 5-10% of duplicate samples, and concordance rates for all the genotyping experiments were 99% or more. Once the genotyping was completed, the dominant, recessive and additive age-adjusted unconditional logistic regression models were fitted to explore the associations of individual SNPs with prostate cancer. We have analyzed the results for all men combined (cases vs controls), as well as African American (AAM) and European American (EAM) men separately.

Although we cannot reveal the rs-numbers for the significant SNPs at this time, the genotyping analysis has provided the following results:

1. African American men carrying two copies of the rs* SNP have more than twofold increase in prostate cancer risk (OR 2.42; CI: 1.31-4.47; p=0.0046), and this increase in risk appears to be highly statistically significant. 24% of men are homozygous for the risk allele in our study. However, heterozygous men

also appear to be at the statistically significantly increased risk (OR 1.56; CI 1.08-2.27; $p=0.0193$), albeit to a lesser extent. About 47 % of men were heterozygous in our study. Hence, the rs* SNP appears to be a risk factor for prostate cancer in African American men.

2. African American men carrying two copies of the wild allele of rs** SNP have decreased prostate cancer risk (OR 0.57; CI: 0.34-0.97; $p=0.0383$). However, heterozygous men also appear to be at the statistically significantly reduced risk (OR 0.67; CI: 0.46-0.99; $p=0.0431$). About 50% of men were homozygous of the wild allele, and 37 % of men were heterozygous in our study. Hence, the wild allele of the rs** SNP appears to be protective of prostate cancer in African American men.
3. European American men carrying two copies of the wild allele of rs*** have increased prostate cancer risk (OR 1.69; CI: 1.02-2.8; $p=0.0415$). However, heterozygous men also appear to be at the statistically significantly increased risk (OR 1.52; CI: 1.02-2.26; $p=0.0384$). About 50% of men were homozygous of the wild allele, and 40 % of men were heterozygous in our study. Hence, the wild allele of the rs*** SNP appears to be a risk factor of prostate cancer in White men.
4. We used the SNAP software to determine if the rs* and rs** were in a linkage disequilibrium (LD) in Black men. However, they were not ($r^2=0.145$). Hence, we conclude that in African American men, the effects of those SNPs are independent of each other.
5. We have used the SNAP software to further look for SNPs that are in a strong ($r^2 \geq 0.8$) and/or moderate LD ($r^2 \geq 0.5$) with rs* and rs** in African American men, and rs*** in European American men. The results are shown in the Table 5. From these results, we conclude that the effects of our SNPs of interest, if indeed real, are coming from the SNPs itself and not from any other SNPs in the LD region.

Table 5. SNPs reported being in LD regions with our SNPs of interest.

SNP of interest	$r^2 \geq 0.8$	$r^2 \geq 0.5$	Disease and comments
Rs* in AAM	none	rs11***** ($r^2=0.61$) rs80***** ($r^2=0.549$)	None reported being associated with prostate cancer or any other disease.
Rs** in AAM	none	none	NA
Rs*** in EAM	rs49***** ($r^2=1.00$) rs49***** ($r^2=1.00$) rs12***** ($r^2=1.00$) rs12***** ($r^2=0.92$) rs11***** ($r^2=0.92$) rs12***** ($r^2=0.83$)	14 additional SNPs	rs12*****: slightly increased risk for prostate cancer in EAM (OR=1.1); no other known associations.

We have also started looking at the bio-behavioral risk factors that were previously reported being associated with prostate cancer. The results are shown in the Table 6. Additional variables will be analyzed in the year #2 of this award.

Table 6. Age-adjusted association between select anthropometric and behavioral variables and prostate cancer in men stratifying by race and combined. **Bold** denotes statistically significant associations; *italics* denotes statistically marginally significant associations.

	AAM	EAM	All
Height: OR (95% CI); p-value	0.98 (0.9-1.05); 0.544	0.92 (0.85-0.99); 0.0434	0.95 (<i>0.898-1.001</i>); 0.0549
BMI: OR (95% CI); p-value	1.06 (1.008-1.114); 0.022	0.98 (0.93-1.023); 0.332	1.02 (0.98-1.05); 0.374
Smoking: OR (95% CI); p-value	1.01 (0.99-1.03); 0.118	1.00 (0.99-1.01); 0.959	1.002 (0.99-1.01); 0.565

Since our results indicated that BMI might be positively associated with prostate cancer in African American men, we decided to look for possible associations between BMI and significant SNPs: rs* and rs**. Although our numbers were small, the results are shown in Table 7.

Table 7. rs7501939 and rs4430796 as risk factors for prostate cancer in African American men stratified by the body weight/BMI. Statistically significant associations are shown **in bold**.

	Non-obese AAM: BMI<30; 55 cases and 69 controls	Obese AAM: BMI≥30; 79 cases and 49 controls	All AAM
Rs*	1.09 (0.64-1.83); 0.763	2.14 (1.2-3.8); 0.0103	2.42 (1.31-4.47); 0.0046
Rs**	0.84 (0.49-1.43); 0.513	0.67 (0.37-1.2); 0.181	0.57 (0.34-0.97); 0.0383

Similarly, we have also tested the association of rs*** and prostate cancer in White men by obesity status. No statistically significant association was seen in either non-obese (p=0.3) or obese (p=0.8) men of European descent.

As could be seen from data shown in Table 7, we were either underpowered to detect the effect of obesity in the rs** carriers, or there's no apparent association. Interestingly, the ORs (point estimates) were still in the protective range (less than 1.0) in both groups; however that observation did not attain statistical significance perhaps due to decreased sample size in both groups.

Interestingly, the rs* remained a significant risk factor for prostate cancer in obese AAM even considering a small sample size, and the excessive risk was still more than twice. However, rs* no longer appeared to be a risk factor for prostate cancer in the non-obese AAM.

Short description of the gene(s) that contain rs* and rs**.

The genes(s) containing rs* and rs** are broadly implicated in the glucose, insulin and fatty acid metabolism, and were previously linked to diabetes and prostate cancer risk in the predominantly White populations. They were also reported being associated with some other cancers, including ovary. Studies involving men of African descent are lacking. Our results indicate that these genes may be implicated in the prostate cancer risk in obese Black men, possibly through the disrupted glucose and/or fatty acid metabolism. In the carriers of the risk alleles, there may be active obesity-related (and/or associated diabetes related) mechanisms that trigger/hasten the development of prostate cancer. In the non-obese (non-diabetic?) men, the rs* alone may not be sufficient to increase the PCa risk. Please see schematic illustration of this hypothesis (Figure 1). Please note that at this time, the PI is specifically interested in the mechanisms that increase prostate cancer risk. Hence, the focus is on the rs*. However, the rs** may be related to the same pathway(s). The authors are hopeful that future studies, specifically in the year 2 of this proposal, will shed light on the aforementioned associations, leading to both the increased and decreased prostate cancer risk.

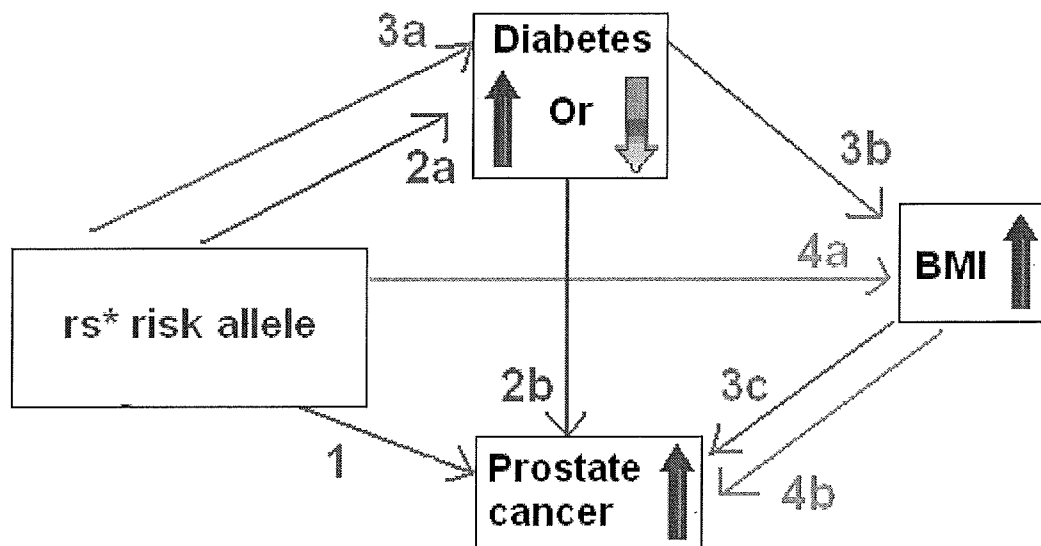


Figure 1. Possible pathways involved in the increased prostate cancer risk in rs* African American carriers. 1 (blue line): direct association; 2a and 2b (magenta lines): association mediated through increased or decreased diabetes risk; 3a, 3b and 3c (grey lines): association mediated through increased or decreased diabetes risk and associated BMI increase; 4a and 4b (green line): association mediated through increased BMI.

Short description of the gene(s) that contain rs***.

Rs*** is located in the gene that encodes a transcriptional factor that is involved in the cell energetic balance and metabolism. It has also been linked to angiogenesis. Multiple SNPs within this gene were reported being implicated in prostate cancer risk (very slight increase in risk), however, the results were inconsistent.

Specific progress. Specific Aim #2. *Assess the genotype/phenotype correlations using the total of 120 AA samples (60 cases and 60 controls). This will be achieved by plasma analysis for expression of the most significant gene(s)/SNP(s), identified within the specific aim #1.*

- This task will be completed in the year #2 of this award.

Specific progress. Specific Aim #3. *To evaluate the feasibility of using the comprehensive DETECT approach in AAM as a PCa screening and risk assessment tool. Statistical measures to analyze the data obtained in the Aims #1-2, in addition to the medical charts and bio-behavioral questionnaire data, will be used. This will be achieved by: 3a. Estimating the associations between the individual DETECT markers and PCa risk. 3b. Establishing combined associations of elected (in sub-aim 2a.) markers and PCa. 3c. Building and evaluating a prediction model of PCa risk based on results in Aim 2a and 2b.*

- This is a statistical (data analysis) aim that is being accomplished in both years of this award. Specifically, the tasks # 3a and 3b are in progress (Tables 4-7). The task #3c will be completed in the year #2 of this award.

Summary of the research progress: Aim #1 – completed; Aim #2 – pending completion in the year 2; Aim #3 – partially completed; pending full completion in the year 2.

Key Research Accomplishments

1. 528 germline DNA samples were successfully genotyped. That includes 259 samples obtained from African American men (136 cases and 123 controls), and 269 samples obtained from Non-Hispanic White men (147 cases and 142 controls).
2. Based on the genotyping results, three SNPs showed statistically significant associations with prostate cancer. In African American men: rs* risk-allele (OR 2.42; CI 1.31-4.47; p=0.0046) and rs** risk-allele (OR 0.57; CI 0.34-0.97; p=0.0383). In European American men: rs*** risk-allele (OR 1.52; CI 1.02-2.26; p=0.0384).
3. Select anthropometric variables were statistically significantly associated with prostate cancer in our cohort of men. In African American men: BMI (OR 1.06; CI 1.008-1.114; p=0.022). In European American men: height (OR 0.92; CI 0.85-0.99; p=0.0434).
4. Interestingly, rs* risk-allele appeared to be a risk factor for prostate cancer in obese (BMI ≥ 30) African American men only (OR 2.14; CI 1.2-3.8; p=0.0103). It was no longer a risk factor in the non-obese African American men.
5. Neither rs** nor rs*** showed statistically significant associations with BMI and/or height.
6. Based on the aforementioned data, the PI has proposed a following hypothesis to be tested in the year #2 of this award.

In obese (diabetic?) AAM, there may be active obesity-related mechanisms that alone do not lead to increased PCa risk; however, the presence of the rs risk-allele may either cause additional risk-increasing mechanisms, or enhance the ones related to obesity, leading to more than twofold increased PCa risk. In the non-obese (non-diabetic?) men, the rs* risk-allele alone may not be sufficient to increase the PCa risk.*

Reportable Outcomes

1. Grants submitted:

- NIH R03 1R03CA172753-01: Comparative race-specific chemopreventive effects of curcumin in prostate cancer; submitted on 02/2012;
- DoD hypothesis development PC120156: Comparative race-specific chemopreventive effects of curcumin in prostate cancer; submitted on 06/2012.

2. Posters presented:

- Joining FORCES Against Hereditary Cancer Conference (June 2011, Orlando FL). The poster presentation entitled "Risk of Gastrointestinal Cancers in Female BRCA1 and BRCA2 Mutation Carriers".
- Center for Equal Health Strategic Planning Retreat Meeting (September 2011).
- Annual AACR meeting (March-April 2012, Chicago IL). The poster presentation entitled "The Risk Factors for Prostate Cancer in African American Men".
- The First Florida Prostate Cancer Research Symposium (May 4-5 2012, Orlando FL). The poster presentation entitled "The Risk Factors for Prostate Cancer in African American Men".
- Moffitt's 2012 Scientific Symposium (May 10 2012, Tampa FL). The poster presentation entitled "The Risk Factors for Prostate Cancer in African American Men".

3. Manuscripts (published, accepted for publication or submitted):

- Shahnjaya Connors, Ganna Chornokur, Nagi Kumar. New Insights to the Mechanisms of Green Tea Catechins in the Chemoprevention of Prostate Cancer. *Nutrition and cancer*. 11/2011; 64(1):4-22; PMID: 22098273
- Kumar NB, Crocker, T, Smith T, Pow-Sang, J, Spiess, PE, Connors, SK, Chornokur, G, Iravani Dickinson, S, Williams, CR, Salup, R, Bai, W. Prostate Cancer Chemoprevention targeting High Risk Populations: Model for trial design and outcome measures. *J Cancer Sci Ther*. 2012; PMID: 22422102
- T.G. Kryshchak L.V. Borkovska O. Kolomys N.O. Korsunskaya V.V. Strelchuk, L.P. Germash, K.Yu. Pechers'ka, G. Chornokur, S.S. Ostapenko, C.M. Phelan, O.L. Stroyuk. The effect of bio-conjugation on aging of the photoluminescence in CdSeTe-ZnS core-shell quantum dots. *Superlattices and Microstructures* 51(3) 2012, 353–62
- Manju Venugopal, Sunil K. Arya, Ganna Chornokur, Shekhar Bhansali. A Realtime and Continuous Assessment of Cortisol in ISF Using Electrochemical Impedance Spectroscopy // *Sens Actuators A Phys*. 2011 1;172(1):154-160. PMID: 22163154
- Ganna Chornokur, Gang Han, Richard Tanner, Hui-Yi Lin, Jack Steel, Patrick Watson, Julio Pow-Sang and Catherine Phelan. Risk factors for prostate cancer in African American men. Undergoing final revisions. Please see appendix 6 for a copy of this manuscript.

4. Classes / courses taken or audited:

- Cancer Epidemiology (Moffitt Cancer Center and University of South Florida);
- Biostatistics 101 (Moffitt);
- NIH grant writing workshop (AACR Annual Meeting);
- Human Subjects Protection refresher course (Moffitt Cancer Center and University of South Florida);
- Biosafety refresher course (Moffitt Cancer Center and University of South Florida);
- Moffitt annual Mandatory education test (Moffitt).

Conclusions

Both the training program and the research supplemental project are up to date, as described in the SOW in the original proposal.

On the training part, the PI uses every opportunity available to her to advance her knowledge and expertise in prostate cancer health disparity. The main training activities include, but are not limited to, regular meetings with the Mentoring team; gain hands-on research experience in the implementation and conduct of research studies; writing and submitting grants and manuscripts; attending relevant high-impact scientific meetings and conferences; making presentations; taking relevant courses and classes; and attending local seminars, ground rounds, and/or workshops focused on the topics of cancer (including prostate cancer), health disparities, community outreach and molecular biology/genetics.

On the research part, the PI has successfully genotyped 528 germline DNA samples obtained from AAM and EAM with prostate cancer and controls. For the genotyping experiments, she has selected 10 functional SNPs previously reported being associated with increased prostate cancer risk. It was found that two SNPs were statistically significantly associated with prostate cancer risk in AA, and one SNP – in EA men. Going further, the excessive prostate cancer risk associated with one of the SNPs in AA men was found in obese men only; it was not seen in either non-obese AAM, or EAM of any body mass. The PI has proposed a concept of the increased risk in obese AAM which is going to be functionally tested in the year 2 of this award.

A “so what section”: prostate cancer health disparity has a recognized genetic basis. Studies aimed to tease out the impact of low penetrance genetic variants/ SNPs, such as this one, have a potential to substantially reduce the magnitude of the disparity by focusing the majority of screening, early detection and prevention efforts on the high-risk populations. It may, however, be challenging to translate the genetic data from bench to bedside due to the inherent complexity of the gene-gene, as well as gene-environment interactions. In this study, we have selected the functional SNPs that are significantly associated with prostate cancer risk in Black and White men. Further, we are attempting to build and test the model of risk that starts with the SNPs of risk, their impact on protein expression, cell biology, organ-specific function, and finally, an organism as a whole. We strongly believe that this comprehensive approach will finally allow us to shed light on the important question of the individual’s genetic variance and its impact on prostate cancer risk.

References

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3. Ahn J, Kibel AS, Park JY, et al. Prostate Cancer Predisposition Loci and Risk of Metastatic Disease and Prostate Cancer Recurrence // *Clin Cancer Res* 2011;17:1075-1081
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5. Robbins CM, Hooker S, Kittles RA, Carpten JD. *EphB2* SNPs and Sporadic Prostate Cancer Risk in African American Men // *PLOS one* May 2011 | Volume 6 | Issue 5 | e19494.
6. Thomas G, Jacobs KB, Yeager M, et al. Multiple loci identified in a genome-wide association study of prostate cancer // *Nat Genetics* 2008 40(3).
7. Lin DW, FitzGerald LM, Fu R, et al. Genetic Variants in the *LEPR*, *CRY1*, *RNASEL*, *IL4*, and *ARVCF* Genes Are Prognostic Markers of Prostate Cancer-Specific Mortality. *Cancer Epidemiol Biomarkers Prev*; 2011; 20, 1928.

Appendices

1. IRB approval
2. SRC approval
3. Specific aims of the submitted R03
4. BRCA GI poster
5. Prostate AAM poster
6. Prostate AAM manuscript (unpublished at this time)
7. Moffitt postdoctoral evaluation
8. Merged data dictionary



DIVISION OF RESEARCH INTEGRITY AND COMPLIANCE
Institutional Review Boards, FWA No. 00001669
12901 Bruce B. Downs Blvd., MDC035 • Tampa, FL 33612-4799
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7/21/2011

Ganna Chornokur
H Lee Moffitt Cancer Center
12902 Magnolia Dr.

RE: **Exempt Certification** for IRB#: Pro00004885

Title: Comprehensive Population-Specific Marker Panel for Early Prostate Cancer
Diagnostics and Risk Assessment

Dear Dr. Chornokur:

On 7/21/2011, the Institutional Review Board (IRB) determined that your research meets USF requirements and Federal Exemption criteria as outlined in the federal regulations at 45CFR46.101(b):

(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

As the principal investigator for this study, it is your responsibility to ensure that this research is conducted as outlined in your application and consistent with the ethical principles outlined in the Belmont Report and with USF IRB policies and procedures. Please note that changes to this protocol may disqualify it from exempt status. Please note that you are responsible for notifying the IRB prior to implementing any changes to the currently approved protocol.

The Institutional Review Board will maintain your exemption application for a period of five years from the date of this letter or for three years after a Final Progress Report is received, whichever is longer. If you wish to continue this protocol beyond five years, you will need to submit a continuing review application at least 60 days prior to the exemption expiration date. Should you complete this study prior to the end of the five-year period, you must submit a request to close the study.

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

A handwritten signature in cursive script, appearing to read "Janelle Perkins".

Janelle Perkins, PharmD, Chairperson
USF Institutional Review Board

August 24, 2011

Ganna Chornokur, PhD
H. Lee Moffitt Cancer Center & Research Institute
University of South Florida
12902 Magnolia Drive
Tampa, FL 33612

Dear Dr. Chornokur:

The Scientific Review Committee (SRC) has reviewed your response to its critique of amendment version dated 07/05/2011 to your research protocol entitled, **"Comprehensive Population-Specific Marker Panel for Early Prostate Cancer Diagnostics and Risk Assessment"** (MCC 16701). The revised amendment version dated 08/15/2011 is approved as written for use at the Moffitt Cancer Center pending approval of the Institutional Review Board (IRB).

The use of tissue and data for research purposes is essential to advancing the scientific field; however because of safety, privacy, and security reasons, such research use is highly regulated by the federal government. Accordingly, the use of such tissue must be in accordance with the applicable Institutional Review Board (IRB) policy. Any changes or deviations that you wish to carry out on your approved study must be reported to the SRC Coordinator for determination of whether additional Scientific Review Committee (SRC) and IRB approvals are needed. This approval does not guarantee access to tissue samples.

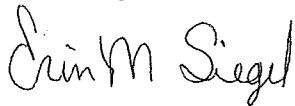
It is your responsibility to ensure that all Moffitt staff (pathology, tissue core, data management, etc.) are informed and aware of the details of the project. The committee encourages the use of in-services for those projects that are complex or require special attention.

All changes made to protocols approved by the SRC must be submitted to the Protocol Review and Monitoring System office. Changes made to the protocol document require SRC review and approval. Minor changes (i.e. changes to personnel, non-scientific changes, changes that do not affect patient participation) will be expedited through the SRC review process.

If this project is not being managed by the Clinical Trials Office or Clinical Research Unit, then it is your responsibility to follow through with all requirements for submission to the IRB. All IRB approvals are required to be documented in Oncore, and all associated regulatory documentation (signed applications, IRB approval letters and IRB approved consent forms, etc.) are to be saved in the appropriate study folder in the e-binders directory at J:\ebinders.

Oncore is the Cancer Center's mechanism for submission and review of materials requiring Scientific Review (SRC) and Protocol Monitoring (PMC). If you need access to Oncore, please contact Jeryl Madden, Oncore Administrator, at 745-6964 for assistance.

Sincerely,

A handwritten signature in cursive script that reads "Erin M Siegel".

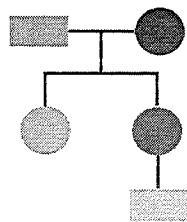
Erin Siegel, PhD, MPH
Chair, Scientific Review Committee

SPECIFIC AIMS:

The American Cancer Society estimates that about 240,890 new cases of prostate cancer (PCa) occurred in the US during 2011 and 33,720 men died due to this disease. While PCa remains the most common type of solid malignancy, and the second-leading cause of all cancer death in men, African American men (AAM) have 1.6 times the incidence, and more than twice the mortality rate of PCa, compared to European American men (EAM) [1]. Although the reason(s) for this striking racial disparity are not well understood, recent research have identified the overactive survival mechanisms, that may predispose AAM to a more biologically aggressive disease. Despite advances in the screening, early detection and treatment of PCa, the mortality and morbidity burden in AAM from the disease remains high. With the current uncertainty and complexity with regard to timing and frequency of screening for high risk populations, there is a pressing need for PCa control beyond early screening and detection. It is well recognized that the most promising approach to cancer control is a national commitment to prevention. Notably, PCa constitutes an ideal chemopreventive target due to existence of well defined premalignant lesions, as well as a generally long period of tumor dormancy in the localized stage [2;3].

Epidemiological and laboratory studies have demonstrated that several plant-derived botanicals influence multiple biochemical and molecular cascades that inhibit mutagenesis, proliferation, induce apoptosis and suppress the formation and growth of human cancers, modulate genetic and epigenetic pathways, thus targeting several hallmarks of carcinogenesis. Among these promising agents, curcumin (diferuloylmethane, an Indian dietary spice) was found to delay initiation and slow down PCa progression in the epidemiological and molecular studies [4-6], and animal models [7;8]. Curcumin exerts its multitargeted anticancer activity on myriad of cellular pathways that are essentially antiproliferative and proapoptotic [9-10]. Curcumin has been shown to inhibit proliferation in several prostate cancer cell lines, such as LNCaP, DU-145, and PC3 [9;11]. Curcumin has also been shown to induce cell cycle arrest in G1/S [12] and G2/M [13] phases in LNCaP and PC3. Additionally, curcumin induces apoptosis in LNCaP, DU145 and PC3 [12;14]. Curcumin inhibits NFκB activity in LNCaP and DU145 [14]. Lastly, curcumin inhibited invasiveness and reduced the MMP2 and MMP9 expression in DU145 [7]. Interestingly, AA-derived PCa tumors were found to have over expressed signaling receptors (including AR and EGFR) [15-16] and significantly greater proliferation rates can be observed in AA-derived prostate tumors relative to EA-derived tumors. Similarly, key anti-apoptotic protein BCL-2 is up-regulated [17-18], NFκB pathway is more active [19] in AAM-derived PCa tumors, whereas elevated expression of MMP9 has also been observed, increasing their invasive capacity [20]. These characteristics observed in AA-derived prostate cancer cell lines compared to EA-derived cell lines suggest that AAM and EAM PCa tumors treated with curcumin may exhibit different proliferation rates, demonstrate different cell cycle profiles, apoptosis rates, NFκB activities, and invasion capacities. Since curcumin specifically targets these molecular processes critical to prostate carcinogenesis, at the public health level, these data provide first clues that AAM may have even better response to curcumin in terms of PCa chemoprevention. However at present, the effect(s) tumor biological differences exert on the chemoprevention of PCa with curcumin in AAM are unknown. Given the increased burden of PCa in AAM and potentially high effectiveness of PCa chemoprevention in reducing the disease burden, there is a dire need to establish and compare the effectiveness of PCa chemoprevention with curcumin in AAM and EAM, in order to inform the design of future chemopreventive trials in this exceptionally high risk population. With the availability of several commercially standardized formulations of curcumin and excellent safety profile, curcumin is an attractive compound to be tested for PCa chemoprevention. Our long term goal is to optimize the effectiveness of chemopreventive intervention against PCa in AAM and EAM. The objective of the proposed work is to determine whether chemopreventive effects of curcumin differ in AAM and EAM PCa cell lines. Our central hypothesis is that chemopreventive effects of curcumin, as measured by the changes in the main carcinogenic events - cell proliferation, cell cycle/ apoptosis and invasion/ metastasis - differ in AAM and EAM due to the underlying differences in tumor biology. We propose the following specific aim to test our hypothesis.

Specific aim 1 :To compare the chemopreventive effects of curcumin, as measured by the changes in the main carcinogenic events - cell proliferation, cell cycle/ apoptosis and invasion/ metastasis, in the well-characterized PCa cell lines, derived from AAM and EAM prostate tumors. Our successfully completed project is expected to contribute to evidence-based, clearly documented chemopreventive effects of curcumin in AAM and EAM derived PCa cell lines, as measured by the markers of cell proliferation, cell cycle/ apoptosis and invasion/metastasis. These mechanistic data are of a critical importance for designing a chemopreventive clinical trial of curcumin in men with PCa. Because AAM consistently carry increased burden of PCa, evidence based, specifically tailored chemopreventive intervention would offer tremendous public health benefit not only to that particular racial group, but to racially and ethnically diverse U.S. population as a whole.



Risk of gastrointestinal cancers in female BRCA1 and BRCA2 mutation carriers



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Background: It is estimated that 10-15% of all cancers are directly attributed to specific genetic alterations that are passed among generations and are known as "cancer syndromes". Among the latter, Hereditary Breast and Ovarian Cancer Syndrome (HBOC) that is characterized by deleterious mutations in the BRCA1 and BRCA2 genes is the most prominent and described. While the increased risk of female breast and ovarian cancers in female BRCA1 and BRCA2 mutation carriers is well known, the risk of gastrointestinal (GI) (colon, rectum, colorectum, pancreatic, stomach, liver and gallbladder/bile duct) cancers is a subject of much debate. Previously, an increased risk of colorectal and liver cancer was seen in BRCA1 carriers, while increased risk of gallbladder/bile duct cancers were attributable to BRCA2. However, no significant associations were reported in other studies, and thus the data is inconclusive. Because BRCA1 and BRCA2 mutation carriers may constitute up to 4% in certain ethnic groups (notably, Ashkenazi Jews), accurate penetrance estimates are important for the counseling and management of cancers in this particularly vulnerable group.

Study goal and methods: In this work, we thought to estimate the incidence of GI cancers in 4536 female BRCA1 and BRCA2 mutation carriers that were followed for a mean of 4 years (range 1 month to 11 years). Incidence rates were compared with population-specific incidence rates and relative risks (RRs) to carriers together with 95% confidence intervals (CIs) were estimated by use of a maximum likelihood approach.

Study population: Eligible women who carried deleterious BRCA1 or BRCA2 mutations were recruited at the participating study sites from United States, Canada, Europe and Israel from 1992 to 2003. Written informed consent was obtained and the study was IRB approved. The members of the cohort were followed up until: 1. the date of completion of the follow-up questionnaire; 2. the development of cancer; 3. age 75 years; or 4. death. All cancers were confirmed by pathology reports. The majority of women were of a Non-Hispanic White (Caucasian) ancestry.

Results: There were 4559 women (xx carried BRCA1, xx carried BRCA2 mutation, and 37 (0.4%) carried both) with the mean age at entry 47.3 years (range 30-74 years). The women were observed for 4 years. 13 GI cancers developed in BRCA1 (mean age 53.5 years), and 6 – in BRCA2 mutation carriers (mean age 57.3 years). Detailed characteristics of BRCA1/2 female mutation carriers who developed GI cancers is presented in Table 1. The RRs for colon, rectal, stomach, pancreatic and gallbladder/bile duct cancers, by the BRCA1 or BRCA2 carrier status are presented in Figure 1. For comparison, the RRs observed in the general population are shown as 1.

Pt #	GI cancer	Stage	Age at dx	BRCA1 or BRCA2	Mutation	Prior cancer(s)
1	Liver			BRCA1	exon 16 C4808G	breast
2	Colon			BRCA1	exon 11 1559insA	none
3	colon			BRCA1 and BRCA2	exon 16 5083del19, exon 11 5946delCT	breast
4	Rectal			BRCA1	exon 11 Q494X	Ovarian, HNC
5	Colon			BRCA1	exon 11 4184del4 (delTCAA)	none
6	Rectal			BRCA2	exon 11 6024delTA (1943 ter)	Breast, ovarian
7	Bile duct			BRCA2	missing	ovarian
8	Colon			BRCA1	exon 15 4693delAA	Breast, skin
9	Colon			BRCA1	exon 20 5382insC (1829 ter)	Breast, ovarian
10	colon		-	BRCA2	exon 11 5804del4	Breast, skin
11	Rectal			BRCA1	exon 11 1048delA	Breast, ovarian
12	rectal			BRCA1	exon 11 Q491X	none
13	colon			BRCA1	exon 20 5382insC (1829 ter)	breast
14	pancreas	????	????	BRCA1	??????	??????
15	pancreas	????	????	BRCA1	??????	??????
16	pancreas	????	????	BRCA1	??????	??????
17	pancreas	????	????	BRCA2	??????	??????
18	pancreas	????	????	BRCA2	??????	??????

Table 1. Detailed characteristics of BRCA1/2 mutation carriers who developed GI cancers.

Conclusion: our results establish important differences in the site-specific cancer risks, associated with BRCA1 and BRCA2 mutations. BRCA1 mutations are associated with the modestly increased risk of colon, rectum, colorectum, pancreatic, liver and gallbladder/bile duct cancers, while BRCA2 mutations are associated with increased risk of rectal, pancreatic and gallbladder/bile duct cancers, but decreased risk of cancers of colon and colorectum. Our results suggest decreased risk of stomach cancer in both the BRCA1 and BRCA2 female mutation carriers. However, additional research is needed to accurately document the site-specific penetrance estimates in these specific populations.

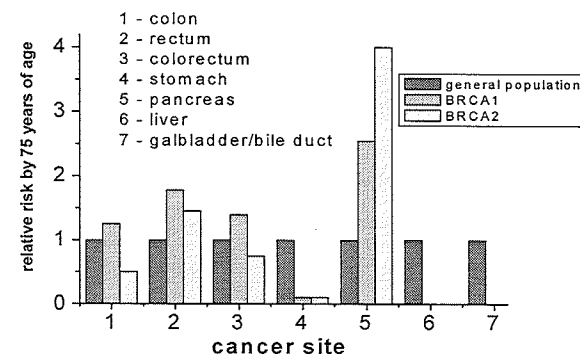
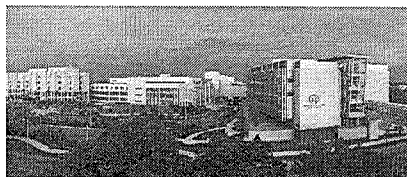


Figure1. The RRs for GI cancers by the BRCA1 or BRCA2 carrier status. The general population risk is taken as 1.

Discussion: Although we have observed an increase in the RRs of the most GI cancers in the BRCA1, and some GI cancers in the BRCA2 female mutation carriers, these increases were modest ranging from 1.25 (RR of colon cancer in BRCA1 carriers) to 4 (RR of pancreatic cancer in the BRCA2 carriers). Our findings are in agreement with, to date, the largest studies of cancers in BRCA1 and BRCA2 carriers by Thompson et al [1], Ford et al [2] and the Breast Cancer Linkage Consortium [3]. The authors have reported modest increases in pancreatic (BRCA1: RR=2.26; BRCA2: RR = 3.51), gallbladder and bile duct (BRCA2: RR=4.97), colon (BRCA1: RR=2.03) and liver (BRCA1: RR=4.06) cancer incidences, and possibly other abdominal/GI cancers. One of our intriguing findings is the absence of stomach cancers, although modestly increased stomach cancer RRs (1.1-4) were previously reported in BRCA1/2 mutation carriers [3-5]. However, the incidence of stomach cancer in white females in the developed countries is very low (about 4.5 per 100,000) and thus the absence of stomach cancers in the cohort of 5000 women comes at no surprise. Large cohorts of women and/or longer follow-up times may be needed to accurately estimate the RR of stomach cancer.

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Risk Factors for Prostate Cancer in African American Men

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Rationale

In the United States, African American/ Black men experience 1.6 times the incidence and 2.4 times the mortality rates of prostate cancer (PCa), and present with more advanced stages, as compared with Caucasian American men (Figures 1 and 2).

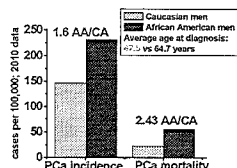


Figure 1. Incidence, mortality and age at prostate cancer diagnosis by race.

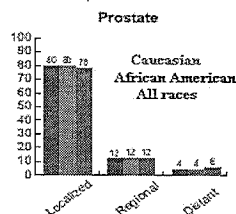


Figure 2. Stage at prostate cancer diagnosis by race (Jemal et al, 2010).

Population-wide screening with Prostate Specific Antigen (PSA) blood test has not been definitely proven to reduce prostate cancer mortality. Of approximately 1 million prostate biopsies performed every year in the U.S., around 70-80% are unnecessary, leading to increased anxiety and other potential side effects such as bleeding and infections in healthy men.

Hence, the need for an effective diagnostic and/or screening test, with higher sensitivity and specificity towards lethal prostate tumors has been recognized, specifically in the high risk population of African American / Black men. In an attempt to address this need, we have investigated known risk factors of prostate cancer, along with PSA levels, and risk of prostate cancer in African American / Black men.

Subjects

Recruitment took place at Moffitt and community hospitals/physician practices, prior to initiation of treatment from 03/2008 till 03/2010. Eligible subjects self-classified as African American men and were 40-80 years old. Cases were defined as men having biopsy-confirmed prostate cancer. Controls were defined as men having no evidence of prostate cancer on biopsy and/or low PSA levels. All men signed an informed consent form and provided a blood sample for DNA, serum and plasma, risk factor questionnaire data and access to their medical records.

Statistical Analysis

The following statistical analyses were performed.

- Descriptive statistics for discrete and continuous variables;
- Pearson's Chi-square test (Fisher's exact test) for independence;
- Wilcoxon rank-sum test for comparing cases and controls;
- Univariable and multivariable logistic regression models (with backward elimination and Hosmer-Lemeshow goodness-of-fit test);
- Spearman's correlation and Kendall's Tau correlation for age versus PSA, BPH and smoking.

Results

A total of 35 cases and 70 controls were analyzed. Some continuous (Table 1) and categorical (Table 2) variables were statistically significantly different between cases and controls. Since the cases in our study were on average 8 years older than controls, we explored if there was a correlation between age versus PSA, and age versus BPH. Significant positive correlation between PSA and age ($p=0.0045$), and BPH and age ($p=0.0122$) was found; however, including age as a covariate had no effect on the univariate (Table 3) or multivariable (Table 4) logistic regression models. Hence, we have concluded that age difference did not significantly affect our results.

In the univariate model, six factors were associated with prostate cancer (Table 3). However, only PSA and BPH were significantly associated with prostate cancer in the multivariate logistic regression model (Table 4).

Table 1. Descriptive statistics for continuous variables.

Variable	Control mean (SD; n)	Case mean (SD; n)	p-value
Age at diagnosis, years	54.12 (9.13; 68)	59.40 (9.24; 35)	0.0071
Cigarettes smoked per day	10.29 (10.16; 34)	18.88 (13.79; 16)	0.011
PSA, (ng/ml)	1.24 (1.32; 31)	6.51 (8.14; 25)	<0.001

Table 2. Descriptive statistics for categorical variables.

Variable	Controls: % yes (number responded out of 70)	Cases: % yes (number responded out of 35)	p-value
Abnormal PSA results	5.5 (55)	94 (32)	<0.001
Diagnosis of BPH	23 (69)	59 (34)	<0.001
Diagnosis of PIN	10 (70)	89 (35)	<0.001
Diagnosis of prostatitis	2 (70)	26 (35)	<0.001

Table 3. Odds ratios and p-values from univariate logistic regression per diagnosis of prostate cancer*.

Variable	Odds ratio point estimate; (95% CI)	P-value
Cigarettes smoked per day	1.066; (1.005, 1.130)	0.034
PSA, (ng/ml)	2.828; (1.672, 4.781)	<0.001
Positive PSA result (y/n), ever	350.998; (46.826, >999)	<0.001
Ever diagnosed with BPH	5.429; (2.041, 14.437)	<0.001
Diagnosed of PIN on biopsy	69.316; (16.007, 300.173)	<0.001
Ever diagnosed with prostatitis	20.180; (2.377, 171.351)	0.006

Table 4. Summary of the multivariate logistic regression per diagnosis of prostate cancer*.

Variable	Standard Error	Odds Ratio (95% CI)
PSA, (ng/ml)	0.5474	4.340; (1.484, 12.689)
Ever diagnosed with BPH	1.2921	14.248; (1.132, 179.310)

* Both models adjusted for age.

Conclusions

In our study, PSA and BPH were significantly associated with prostate cancer in the multivariate logistic regression model. Despite the limitation of a small sample size, our data is in agreement to a recent report (Pettaway et al, 2011) in which African Americans with BPH were observed to have a much greater risk of developing prostate cancer than similar Caucasian men, highlighting differences in the biology of prostate cancer between populations. Additional studies with increased sample size are needed to further explore these differences.

References

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Risk factors for prostate cancer in African American men

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Abstract

Background. African American / Black men have 1.6 times the incidence and 2.4 times the mortality rate of prostate cancer, compared to Non-Hispanic White men. Thus, prostate cancer constitutes one of the most striking racial health disparities, the causation of which is not well understood.

Main hypothesis. We hypothesized that select clinical and/or bio-behavioral risk factors are associated with prostate cancer in African American men.

Participants and Methods. 105 African American / Black men aged 34-80 (35 cases and 70 controls) were recruited. Univariable and multivariable logistic regression models were built to test the marginal and joint effects of the variables when predicting the cancer status.

Results. In the univariable regression models, prostate specific antigen (PSA; $p < .001$), smoking (cigarettes/day; $p = 0.011$), diagnosis of benign prostatic hyperplasia (BPH, yes/no; $p < .001$), diagnosis of prostatitis (yes/no; $p < .001$) and prostatic intraepithelial neoplasia (PIN, yes/no; $p < .001$) were independently associated with the prostate cancer diagnosis. However, only PSA (OR = 2.495) and diagnosis of PIN (OR = 26.723) remained significant in the age-adjusted multivariate logistic regression model.

Conclusions. Our results suggest that, as expected, PSA levels are associated with prostate cancer in African American / Black men. A history of PIN is also associated with prostate cancer in African American men. Despite the limitation of a small sample size, our results highlight the differences in the biology of prostate cancer between populations and underscore the need for developing appropriate risk-reduction strategies, specifically targeting high-risk groups.

Introduction

In the United States, prostate cancer is the leading non-cutaneous cancer diagnosed in men and the second leading cause of all cancer deaths in men, preceded by only the lung cancer [1]. However, the prostate cancer burden is not the same across all racial and ethnic groups. An African American / Black man faces an average lifetime PCa risk of 1 in 5, compared to an approximate risk of 1 in 7 for a Non-Hispanic White man. Thus, prostate cancer constitutes to be one of the most striking racial health disparities, for which men of African descent are burdened with 1.6 times the risk of being diagnosed with the disease and 2.4 times the risk of dying from it, compared to Non-Hispanic White men [2]. The overall burden of prostate cancer from disease onset to progression and survival continues to be disproportionate for African American men [3] despite steady nationwide improvements in screening, early detection and treatment of this particular malignancy. Population-wide screening with Prostate Specific Antigen (PSA) blood test has not been definitely proven to reduce prostate cancer specific or all-case mortality [4]. Further, PSA is known for its notoriously high false positive rates approaching 75-80% [5], leading to unnecessary biopsy-related side effects, such as bleeding and infections, in healthy men. Hence, the need for an effective diagnostic and/or screening test, with higher sensitivity and specificity towards lethal prostate tumors has been recognized, specifically in the high risk population of African American / Black men. In an attempt to address this need, we have investigated known risk factors of prostate cancer, along with PSA levels, in African American / Black men. The results of our study may contribute to the identification and validation of novel markers of prostate cancer detection that can improve specificity of the more common surrogate markers such as PSA for screening and early detection of prostate cancer in the high risk population of African American men.

Participants and methods

Participants. The study was approved by the University of South Florida Institutional Review Board (IRB#104213), and was open for recruitment from March 2007 till December 2009. "Cases" were defined as African American men with biopsy-confirmed PCa. "Controls" were defined as African American men with low PSA and/or no evidence of PCa on biopsy. The African American ancestry was self-reported. The cases and controls were recruited during the initial PCa screening of all consecutive, unselected patients at three institutions: 1. Lifetime Cancer Screening and prevention Center at the H. Lee Moffitt Cancer Center and Research Institute; 2. the Moffitt Cancer Center Hospital, Tampa Bay Radiation Oncology centers, and 3. 30th Street Medical Associates (a community clinic). Written informed consent was obtained from each participant. Participants were asked to complete a comprehensive questionnaire addressing general health risk factors, family history, and donate a blood sample.

Men were excluded if they did not self-identify as African American / Black, were outside of the 30-80 year old range, were in poor physical or mental health, were diagnosed with other cancers (non-melanoma skin cancer was acceptable), or did not speak English well enough to read and understand the informed consent. Of note, the participation rates for both cases and controls were above 90%.

Clinical data collection. The clinical data was extracted from medical records by study personnel. Operative and pathology reports are obtained by study personnel from the office of the diagnosing physician. From these reports, PCa stage, grade, histologic type, size of tumor and extent of surgical treatment were verified. Data abstracted from these reports was reviewed in conjunction with review of pathology slides from the surgical specimen by a single pathologist, who verified disease grade and histologic type. The results from the operative and pathology results then determined whether a study volunteer is classified as 'case' or 'control'.

Blood collection and analyses. Two vials of blood were collected from each participant; Ten ml of blood were drawn (by the phlebotomist or nurse) into each tube prior to intervention or treatment. Both tubes were processed and stored at the Tissue Procurement Core at the Moffitt Cancer Center that served as the main study site. P53 and OPG analyses were carried out using standard commercially available ELISA kits.

Bio-behavioral data collection. Self-reported comprehensive, bio-behavioral questionnaires were administered to each participant at the time of recruitment. The majority of questions were either categorical (yes/no, or not sure/unknown) or continuous (i.e. height and weight), requiring participants to enter the value(s). Since participants were given an option to not answer/skip any question, some of the variables have missing values. However, overall only a small fraction of all data is missing.

Statistical analyses.

Frequency and percentages of the discrete variables were computed. Pearson's Chi-square test and Fisher's exact test were used to test the independence between discrete variables and cancer status as being positive (case) or negative (control). Fisher's exact test is used if one or more subgroup frequencies is less than 5. Mean and standard deviation were reported for continuous variables. Wilcoxon rank-sum test was used to compare the distributions of each continuous variable between the case and control groups. Univariable and multivariable logistic regression models were built to test the marginal and joint effects of the variables when predicting the cancer status. Point and interval estimates of the odds ratio as well as the p-value of each of the variables were reported. Backward elimination procedure with preselected significance level of 0.05 was used to select significant variables in the multivariable logistic regression [6]. Hosmer-Lemeshow goodness-of-fit test was used to evaluate the goodness-of-fit of the multivariable model [7]. Spearman's correlation and Kendall's Tau correlation were used to estimate the possible

correlations between age versus PSA, BPH and smoking. All p-values less than 0.05 were considered significant. Statistical analyses were conducted using Statistical Analysis System (SAS) software, version 9.2 (SAS Institute, Cary, NC).

Results

A total of 110 African American men were recruited. Of those, 35 were classified as cases, and 70 – as controls. Tables 1-3 show the continuous (Table 1) or categorical (Table 2 and 3) characteristics of men by case or control status. Among the continuous variables, age at diagnosis, cigarettes smoked per day, and PSA value were significantly different among cases and controls. The amount of sitting hours was marginally significant. Among the categorical variables, an abnormal PSA result, ever diagnosed with BPH, PIN or prostatitis were significant. Allergies (yes/no), and the use of cholesterol lowering medications within the last year (yes/no) were marginally significant. The rest of variables of interest did not differ between cases and controls.

Table 1. Descriptive statistics for continuous variables.

Variable	Control mean (SD; n)	Case mean (SD; n)	P-value
Age at diagnosis, years	54.12 (9.13; 68)	59.40 (9.24; 35)	0.0071
Current Weight, pounds	213.89 (52.62; 70)	220.31 (36.56; 35)	0.303
Weight at 18, pounds	160.04 (24.61; 67)	164.71 (35.43; 34)	0.883
Age diagnosed with BPH	56.29 (8.28; 14)	49.05 (19.97; 20)	0.661
Age diagnosed with PIN	59.50 (9.07; 6)	57.90 (9.85; 30)	0.640
Age started smoking	17.49 (4.13; 35)	17.59 (5.03; 17)	0.438
Total years smoked	19.76 (13.13; 34)	22.76 (12.70; 17)	0.379
Cigarettes smoked per day	10.29 (10.16; 34)	18.88 (13.79; 16)	0.011
Vigorous physical activity hours, weekly	4.00 (2.00; 12)	4.10 (2.28; 10)	0.973
Moderate physical activity days, weekly	4.44 (2.14; 27)	3.38 (1.75; 16)	0.112
<i>Sitting hours, weekly</i>	<i>5.00 (3.30; 43)</i>	<i>6.35 (3.79; 31)</i>	<i>0.096</i>
The number of lifetime sexual partners	16.23 (19.54; 31)	19.38 (23.20; 24)	0.878
PSA, (ng/ml)	1.24 (1.32; 31)	6.51 (8.14; 25)	<.001
P53, (U/ml)	23.93 (45.31; 9)	4.58 (0.91; 5)	0.285
OPG, (pg/ml)	290.27 (105.25; 31)	317.30 (101.87; 25)	0.335

Table 2. P-values of for categorical variables.

Variable	p-value
Country of birth (US vs other)	0.306
Marital status	0.124
Education	0.228
Ever received an abnormal PSA result	<.001
Diagnosis of BPH	<.001
BPH treated by TUR	0.972
Diagnosis of PIN	<.001
Diagnosis of PIA	0.439
Diagnosis of prostatitis	<.001
Vasectomy	0.364
Aspirin use	0.648
NSAID use	0.886

Variable	p-value
Other medications	0.348
Antidepressants	0.477
Heart disease medications	0.782
Hugh blood pressure medications	0.328
<i>Cholesterol lowering medications</i>	<i>0.067</i>
Osteoporosis medication	0.155
Thyroid medication	0.477
Diabetes medication	0.622
<i>Allergies (Yes/No)</i>	<i>0.072</i>
Smoking now	0.498
Ever smoked	0.988
Total tobacco-years	0.855
Ever tired to quit smoking	0.627
Fam. Hist. of any cancer (Yes/No)	0.272
Fam. Hist. of female cancer (Yes/No)	0.182
Fam. Hist. of male cancer (Yes/No)	0.422
The number of lifetime sexual partners	0.938

Table 3. Frequency tables of significant categorical variables.

Variable	Level	Frequency in Control Group	Frequency in Case Group
Ever received an abnormal PSA result			
	No	52	2
	Yes	3	30
Diagnosis of BPH			
	No	53	14
	Yes	16	20
Diagnosis of PIN			
	No	63	4
	Yes	7	31
Diagnosis of Prostatitis			
	No	69	26
	Yes	1	9

In the univariable regression models, PSA (ng/ml; $p<.001$), smoking (cigarettes/day; $p=0.011$), diagnosis of benign prostatic hyperplasia (BPH, yes/no; $p<.001$), diagnosis of prostatitis (yes/no; $p<.001$) and prostatic intraepithelial neoplasia (PIN, yes/no; $p<.001$) were independently associated with the prostate cancer diagnosis (Table 4). However, only PSA and diagnosis of PIN remained significant in the age-adjusted multivariate logistic regression model, where significant and marginally significant factors were included (Table 5). This result implies potential correlations among predictors and multicollinearity that worth further investigation with a larger sample size.

Table 4. p-value and odds ratio from univariable logistic regression[#]

Variable	Odds ratio point estimate; (95% CI)	P-value
Cigarettes smoked per day	1.066; (1.005, 1.130)	0.034
PSA, (ng/ml)	2.828; (1.672, 4.781)	<.001
Ever received an abnormal PSA result	350.998; (46.826, >999)	<.001
Diagnosis of BPH	5.429; (2.041, 14.437)	<.001
Diagnosis of PIN	69.316; (16.007, 300.173)	<.001

Variable	Odds ratio point estimate; (95% CI)	P-value
Diagnosis of prostatitis	20.180; (2.377, 171.351)	0.006

Table 5, Summary of the multivariable logistic regression model*#

Parameter	Chi-Square test statistics	P-value	Odds ratio and 95% confidence interval
PSA, ng/ml	5.7876	0.0161	2.495 (1.85-5.256)
Diagnosis of PIN on biopsy	9.3155	0.0023	26.723 (3.24-220.38)

*The Hosmer-Lemeshow test gives p-value 0.973 indicating that this multivariable model fits the data well.

#Both models adjusted for age

Discussion

Results of our study suggest that, in African American / Black men, accuracy of PSA screening test may be improved by adding select known biological and bio-behavioral risk factors. As expected, PSA test results were statistically significantly associated with PCa status (Tables 1, 4 and 5). The major finding of our work is that the diagnosis of Prostatic Intraepithelial Neoplasia (PIN and HGPIN) is another clinical factor that statistically significantly associates with PCa in our cohort of African American men in the age-adjusted multivariable logistic regression model. Thus, adding the diagnosis of PIN may improve the accuracy of PSA screening test for PCa in African American men. This finding comes at no surprise since PIN, especially high-grade (HGPIN) is an established PCa risk factor [8-9]. Although the majority of PIN/HGPIN studies involved predominantly Non-Hispanic White men, Powell et al [10] have analyzed prostate autopsies obtained from African American and Non-Hispanic White men that died of causes other than PCa. Interestingly, the authors reported significantly higher prevalence of PIN and HGPIN in African American men 40-49 years old (but not the younger men), compared to Non-Hispanic Whites (46% vs 29%, respectively). Based on the observed results, the authors have hypothesized that the 40-49 years age range may be the beginning of PCa racial disparity, as more African American men that harbor HGPIN go on to develop cancer. Thus, the diagnosis of PIN/HGPIN may increase the accuracy of PSA screening test. Additional sufficiently powered studies are needed to explore if diagnosis of PIN/HGPIN can aid in PCa detection, as well as delineate an especially high-risk group of African American men that are likely to benefit of chemopreventive intervention for PCa (statins, green tea/curcumin/lycopene supplementation etc).

Benign Prostate Hyperplasia (BPH) is significantly associated with the diagnosis of PCa in African American / Black men. While the connection between BPH and PCa is controversial [11], our data corroborates the findings reported by Pettaway et al [12], who found that African American men diagnosed with BPH were more than twice as likely to be diagnosed with PCa, compared to their Non-Hispanic White counterparts (HR = 2.21 (C.I. 1.47–3.33)). Additionally, the incidence of BPH seems to be higher in men of African descent [13]. Taken together, this provocative data suggests that increased burden of PCa in African American men may be explained, at least partially, by the higher prevalence of BPH in that population.

In our unselected consecutive sample of African American men, cases were on average 5 years older compared to controls. This is expectable since the risk of being diagnosed with PCa increases with age [14]. Interestingly, our cases were, on average, 8 years younger at diagnosis, compared to the average US-wide age at the time of PCa diagnosis (59 vs 67 years [15], respectively). This is in concordance with the trend of African American men being younger at diagnosis, compared to the Non-Hispanic White men [15-16]. Thus, the results of our study add to the evidence supportive of considering PCa screening at the younger age in men of African descent.

In agreement with the previously published evidence obtained in predominantly Non-Hispanic White [17-18] as well as African American [19] men, a medical history of prostatitis was statistically significantly associated with PCa in our cohort. Positive association between PCa and prostatitis is attributed to the chronic inflammation in the prostate gland [20-21]. Interestingly, we did not observe a statistically significant association between Proliferative Inflammatory Atrophy (PIA) and PCa. While there is significant biological evidence that PIA is likely to be a precursor for PCa [20-23], the epidemiological studies on this topic are lacking. The null association of PIA with PCa in our study may be explained by the small sample size, as only a few men reported being diagnosed with this condition. Sufficiently powered epidemiological studies are needed to explore a biologically plausible causative association between PIA and PCa.

Among the behavioral variables, the number of cigarettes smoked per day was modestly, albeit significantly, associated with the increased PCa risk (OR 1.066; (1.005-1.130), p=0.034). In our sample, cases smoked on average, 18.9 cigarettes per day, while controls smoked 10.3 cigarettes per day (p=0.011). The previous literature published on the topic of smoking and PCa has offered inconsistent results with mostly null [24-25] or a modestly elevated risk [26] associations reported. Huncharek et al [27] have conducted a comprehensive meta-analysis of 24

prospective cohort studies with the goal of estimation the casual relationship between prostate cancer and smoking. The authors concluded that there was modest, but significant association with the amount of cigarettes smoked in a day or in a year (RR=1.22; 95% CI=1.01, 1.46), but no association was observed for a current smoker status (RR=1.04; 95% CI=0.87, 1.24). This data is in agreement to our findings. Of note, the studies reviewed by Huncharek et al [27] focused mainly on European and Asian populations, and the fraction of African descent participants was small. To date, information on smoking and PCa in African American men remains scarce. Taioli et al [28] have reported that African American men who are smokers and are homozygous for the glutathione-S-transferases (GMST1) deletion, are under modestly increased risk for PCa (OR = 1.28 (1.01–1.56)), while in never smokers, this mutation was protective (OR: 0.66, 95% CI: 0.46–0.95). The authors have suggested that cigarette smoking contains many substrates for GSTM1; therefore, it is expected that a loss of GSTM1 function will affect the accumulation of genotoxic compounds from tobacco smoke. Interestingly, holds true for African American (and not Caribbean or African) men. This effect was explained by the fact that African American men smoke, on average, considerably more compared to Caribbean or African men; however, the sample size in the study was relatively small thus not allowing to draw a definite conclusion. Similar findings were reported by Lavender et al [29], who found a modest (OR≤2) but statistically significant association between select polymorphisms in glutathione S-transferase (GST) genes and smoking, underscoring the importance of gene-environment interactions in considering an individual's risk of cancer. Our results suggest a trend of association between the number of sitting hours and PCa (p=0.096). Sitting during work and/or leisure time is known to modestly increase the risk for PCa. Orsini et al [30] have reported that men who sat only half or less of their work day were at 20% reduced risk for PCa, compared to men who sat the whole day. This study was done in Sweden and thus included men of mainly Non-Hispanic white / European descent. Although the number of sitting hours did not attain statistical significance in our sample, our results are suggestive of a potential association of PCa with sitting. Interestingly, we did not observe a statistically significantly decreased risk of PCa with physical activity, either vigorous or moderate. Physical activity was reported to reduce PCa risk in both Non-Hispanic white [31] and Black [32] men. It is possible that our physical activity results were not reliable due to over reporting, especially given that the majority of men were either overweight or obese (average BMIs 29.7 in controls and 30.4 in cases). It is thus possible that sitting served as an indirect inverse proxy for physical activity; or else, sitting by itself has PCa promoting ability. The authors are hopeful that future studies will address this important knowledge gap. A potentially interesting finding was that the use of cholesterol lowering medications of any class was marginally associated with PCa (p=0.067). This is especially important since only a handful of men in our study were taking an anti-cholesterol medication. This finding is in agreement with the reports that found decreased risk of PCa in men who took statins [33-34]. Unfortunately, participants in our study did not specify the kind of medication they were taking to control the blood cholesterol levels. However, since statins are currently widely used, we can infer – with a certain level of certainty – that the majority of men in our cohort were taking statins. An alternative explanation to our findings was reported by Mondul et al [35-36], according to which men with lower blood cholesterol levels had decreased risk of PCa in general, regardless of whether they were on medication or not. Interestingly, this effect was even more pronounced in men with higher BMIs. Given that the majority of men in our study were either overweight or obese (average BMI 29.7 controls and 30.4 cases), our findings are in agreement with those reported by Mondul et al [35], suggesting that lower cholesterol levels may be protective of PCa in African American men. This conclusion also agrees with Moses et al [37], who reported that increased low density lipoprotein (so-called “bad” cholesterol) was positively associated with biopsy-confirmed PCa in African American, but not in Non-Hispanic White men. An interesting and somewhat unexpected trend suggested by this study was a potential association with allergies with PCa (p=0.072). A handful of studies that explored this connection resumed with controversial results with increase in PCa risk [38], decrease in PCa risk [39] and no association [40] all being reported. Unfortunately, our questionnaires did not ask men to specify the allergen(s); however, it is feasible to hypothesize that allergy to potential PCa-protective nutrients and foods, such as tomatoes and tomato-based products, may predispose a man to PCa due to reduced consumption of lycopene or other protective nutrients. It is also feasible that allergies expose an organism to chronic elevated levels of inflammation, thus increasing the risk of cancer. It might be possible that there is a yet undiscovered biological mechanism that makes men of African descent with allergies more vulnerable to PCa. Finally, our findings may be due to chance especially given the small sample size.

In summary, only PSA and BPH were statistically significantly associated with PCa in the age-adjusted multivariate logistic regression model in our cohort of African American men. Our data highlights the difference in PCa biology between populations, and suggests that African American men with BPH might be under increased risk for PCa, compared to their Non-Hispanic white counterparts. Future studies are needed to explore these findings in light of developing the risk-reduction strategies appropriate for the high-risk population of African American men with BPH.

Limitations. Results from this study should be interpreted in light of limitations. We are aware that the small sample size is a potential limitations of this study. For example, quite a few entries in Table 3 are smaller than 5. A consequence of such a small sample is the wide confidence intervals of the significant categorical variables in Tables 4 and 5. However, given the underrepresentation of African American / Black men in PCa studies and the increased burden of this malignancy on Black men, we believe our results suggest the differences in prostate cancer biology between populations and underscore the need to conduct sufficiently powered studies to further explore those differences.

Another possible limitation in this study was that we did not access the dietary patterns. It might be possible that the number of sitting hours is a proxy for unhealthy lifestyle in general and may be confounded by the high-fat, low vegetable dietary patterns. However, the rest of statistically significant variables in the study do not seem to be confounded by diet and thus could be reliably accessed in the absence of dietary information.

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**Post Doc
Anniversary Evaluation - 2011/12**

Employee Identification

Name: Ganna Chornokur	Employee ID: 4459845
Title/Rank: POST DOC FELLOW	Hire Date: 12/30/2009
Department #: 25609	Department: Cancer Epidemiology
Emp Status: 50	

PART I: BEHAVIORAL CRITERIA

DO NOT ADJUST SECTION WEIGHT.
SECTION WEIGHT MUST REMAIN 50%

Behavioral Criteria

Score: 4.1 / 5.0 (50%)

Customer Focus: Commitment to Providing Outstanding Customer Service **Score: 3.6 / 5.0 (0%)**

Conveys a positive image of Moffitt to customers. Is dedicated to superior customer service and satisfaction. Develops and maintains positive relationships with both internal and external customers. Demonstrates dignity and respect to internal and external customers.

- ☐ 4.6 – 5.0: Far Exceeds
- ☒ 3.6 – 4.5: Surpasses
- ☐ 2.5 – 3.5: Successfully Meets
- ☐ 1.0 – 2.4: Does Not Meet

Comments:

Teamwork: Work, as Part of a Group, to Achieve Results **Score: 4.6 / 5.0 (0%)**

Shares equally in the department's success and failures. Works effectively and constructively to find mutually beneficial solutions for all concerned parties. Shares knowledge and expertise with others to ensure the success of team and individual efforts. Supports co-workers by maintaining attendance requirements. When appropriate, works in partnership with staff, faculty and/or patient and family advisors to improve processes or care.

- ☒ 4.6 – 5.0: Far Exceeds
- ☐ 3.6 – 4.5: Surpasses
- ☐ 2.5 – 3.5: Successfully Meets
- ☐ 1.0 – 2.4: Does Not Meet

Comments:

Adaptability: Demonstration of Creativity, Innovation, Flexibility & Willing Acceptance of Challenge **Score: 4.6 / 5.0 (0%)**

Demonstrates willingness to adapt to changing individual and institutional roles, needs and environment. Exhibits a problem solving attitude; constantly seeks ways to improve processes, increase efficiency, find solutions to current situations or to develop new methods and procedures.

- ☒ 4.6 – 5.0: Far Exceeds
- ☐ 3.6 – 4.5: Surpasses
- ☐ 2.5 – 3.5: Successfully Meets
- ☐ 1.0 – 2.4: Does Not Meet

Comments:

Responsibility: Acting Responsibly in All Matters **Score: 3.6 / 5.0 (0%)**

Accepts accountability for actions, choices and outcomes; assumes nothing; answers for own conduct and obligations.

- ☐ 4.6 – 5.0: Far Exceeds
- ☒ 3.6 – 4.5: Surpasses
- ☐ 2.5 – 3.5: Successfully Meets
- ☐ 1.0 – 2.4: Does Not Meet

Comments:

Commitment to Excellence: Striving to do the Best Every Day

Score: 3.6 / 5.0 (0%)

Consistently provides quality product/services. Commits to the principle of continuous improvement in the workplace. Projects pride in their work as exhibited in day-to-day interactions with staff, co-workers, patients and all those they come in contact with. Commits to the principles of patient and family-centered care: dignity & respect, information sharing, participation and collaboration.

- ☐ 4.6 – 5.0: Far Exceeds
- ☒ 3.6 – 4.5: Surpasses
- ☐ 2.5 – 3.5: Successfully Meets
- ☐ 1.0 – 2.4: Does Not Meet

Comments:

Culture of Safety: Promotion of safety & prevention of injury must be the first consideration

Score: 4.6 / 5.0 (0%)

Maintains awareness and follows safety policies and procedures applicable to assigned duties. Commits to the principle of continuous improvement in the workplace. Uses sound judgment including reasonable awareness of potential hazards before acting. Promptly reports errors and/or events and/or situations of actual or potential harm.

- ☒ 4.6 – 5.0: Far Exceeds
- ☐ 3.6 – 4.5: Surpasses
- ☐ 2.5 – 3.5: Successfully Meets
- ☐ 1.0 – 2.4: Does Not Meet

Comments:

PART II: ACCOMPLISHMENTS/PROGRESS WITHIN THE PAST YEAR:

POST DOC: In the areas below, describe your accomplishments relative to the specific area.

Work Accomplished toward goals

Work

State the project title, broad project goals and the specific progress made in the last year. If multiple projects are underway, evaluate progress with each project, identify the

relevant obstacles and include a timeline for completion.

1. MCC16701. We hypothesize, that a combination panel (DETECT) of genetic, biochemical, socio-cultural and lifestyle population-specific biomarkers and factors will provide a valuable PCa screening and risk assessment tool. The goal of this study is to evaluate a feasibility of using DETECT as a reliable approach to estimate the risk and/or detect PCa early in AAM ultimately eliminating the disparity in PCa morbidity and mortality.

Specific progress to date.

- SRC and IRB approvals were obtained. This was actually the hardest, the longest, and the most painful process so far.
- Since active recruitment was associated with great financial, time, organizational and participation barriers, we have substituted the prospective sample collection with retrospectively collected samples in the Drs. Phelan and Park studies. The strength of this approach is that I will analyze 600 samples in total (300 African American). Thus, much greater statistical power could be achieved, compared with just 120 samples in total. In addition, Caucasian samples will also be analyzed, allowing for an interracial comparison between biomarkers.
- The data dictionary to combine the epidemiological data for the two studies has been completed.
- Sample selection and supply ordering have been completed.
- The nearest future plans: genotyping.
- The timeline for completion of the project: 09/2013, as specified by the grant.

2. MCC14648. We hypothesized that select clinical and/or bio-behavioral risk factors are associated with prostate cancer in African American men. 105 African American men aged 34-80 (35 cases and 70 controls) were recruited. Univariable and multivariable logistic regression models were built to test the marginal and joint effects of the variables when predicting the cancer status. Specific progress.

- The data collected during the accrual time of this protocol was analyzed and the most relevant variables were chosen for analysis.
- Statistical analysis was performed by biostatistician;
- Significant variables were identified and discussed;
- An abstract, based on the findings of this research, was submitted to the AACR 2012 meeting.
- A manuscript, based on the findings of this research, is in progress.
- Future plans: planning of a bigger study involving more African American men with prostate cancer and healthy controls.
- Timeline for completion: this secondary analysis of collected data is already completed. However, the manuscript will take another 3-6 months to be submitted.

3. MCC16112. We hypothesized that variation in the mitochondrial genome and nuclear genome-wide variation plays a role in ovarian cancer. The GOAL of this study is to more comprehensively investigate the contribution of mitochondrial genome variation to ovarian cancer risk.

Specific progress.

- The list of genes related to the pathways of cellular senescence, hormonal pathways, and chromatin remodelling have been assembled. This list yielded over 400 genes total.

- The list of SNPs related to the genes, identified within the mentioned above pathways, was assembled.
 - The selection of over 8000 of SNPs was analysed in the subset of ovarian cancer cases and controls. Several significant SNPs ($p < 0.05$) in different genes have been identified.
 - Future plans: writing a manuscript and/or an abstract to disseminate our findings.
- Timeline for completion: this specific part - within one year. The project however will not end until another 4 years.

1. Research

1

Human Subjects (list grants number, title and IRB # in which you participated):

1. PC101913 and MCC16701 : "Comprehensive Population-Specific Marker Panel for Early Prostate Cancer Diagnostics and Risk Assessment". Funding Agency: Department of the U.S. Army (DoD) Prostate Cancer Research Program; Chornokur PI.
2. W81XWH-06-1-0034 and MCC14648: "Prostate Cancer in African American Men: Serum Biomarkers for Early Detection Using Nanoparticles". Funding Agency: Department of the U.S. Army (DoD) Prostate Cancer Research Program; Phelan PI.
3. 1R01 CA149429-01 and MCC16112: "The Mitochondrial Genome and Ovarian Cancer Risk". Funding agency: NIH; Phelan PI.

2

Vertebrate Animals (list grants number, title and IACUC # in which you participated):

N/A

2. Training

1

Meetings attended (w/o presentation):

1. 10/10: ASCO-NCI-EORTC Annual Meeting on Molecular Markers in Cancer, Florida
2. Center for Equal Health/ P20 Strategic Planning Retreat Meeting; date: 09/29/2011

2

Workshops/Training completed in the last year (Research, Ethics, Human Subjects, Biosafety, Vertebrate Animals use-include date completed):

IRB and Bioethics completed ~2 years ago
Mandatory Education test: 05/2011

3

Optional Workshop/Training completed in last year (Communication Skills, Clinical Trials, Grant/Scientific Writing, technical Workshops, English as a Second Language):

EndNote training at USF library: approx date 12/2010;
Clinical trials, Grant/Scientific Writing completed ~2 years ago;

4

Other Training:

Cancer Epidemiology course: in progress;
Cancer Health Disparities course: in progress;
Biostats 101 lecture series: 10-11 2011 (Certificate of Completion Awarded);
01/11: 11-hour educational course, entitled "Cultural and Linguistic Competency: A 21st Century Response to Historical & Unending Inequities" (Certificate of Completion Awarded);
09/23/2011: "Feed your future"; 3-hour lecture series in recognition of Infant Mortality Month at USF.

3. Publications/Presentations

1

Peer-reviewed publications:

1. Shahnjaya Connors, Ganna Chornokur, Nagi Kumar. New Insights to the Mechanisms of Green Tea Catechins in the Chemoprevention of Prostate Cancer. Accepted to the International Journal of Nutrition and Cancer, 2011
2. G. Chornokur, Kyle Dalton, M. Borysova, and N. Kumar. Disparities at Presentation, Diagnosis, Treatment and Survival in African American Men, Affected by Prostate Cancer. "The Prostate", 71(9), 985-97, 2011
3. G. Chornokur, S. Arya, C. Phelan, R. Tanner and S. Bhansali. Impedance-based Miniaturized Biosensor for Ultrasensitive and Fast Prostate Specific Antigen Detection. Hindawi "Journal of Sensors", vol 2011, Article ID 983752, 7 pages
4. Manju Venugopal, Sunil K. Arya, Ganna Chornokur, Shekhar Bhansali. A Realtime and Continuous Assessment of Cortisol in ISF Using Electrochemical

Impedance Spectroscopy // Sensors and Actuators A, 2011

5. Sunil K. Arya, Ganna Chornokur, Manju Venugopal and Shekhar Bhansali. Antibody functionalized Interdigitated -electrode (ID E) based impedimetric cortisol biosensor // Analyst, 2010, 135, 1941 - 1946

6. S. Arya; G. Chornokur, M. Venugopal; and S. Bhansali. Dithiobis(succinimidyl propionate) Modified Gold Micro Array Electrode Based Electrochemical Immunosensor for Ultrasensitive Detection of Cortisol // Biosensors and Bioelectronics 2010 25(10), 2296-2301

2

Other (non peer-reviewed) publications:

N/A

3

Manuscripts that are in preparation or under review:

1. Ganna Chornokur and Catherine M Phelan. Global ovarian cancer disparities: a review.

2. Catherine M. Phelan, Robert Royer, Shiyu Zhang, Song Li, Kelly Metcalfe, Aletta Poll, Ping Sun, Ganna Chornokur, Steven A. Narod. Risks of gastrointestinal cancers in female BRCA1 and BRCA2 mutation carriers.

3. Ganna Chornokur, Gang Han, Richard Tanner, Julio Pow-Sang, and Catherine Phelan. Biomarkers of prostate cancer in African American men.

4. Meghan E. Borysova, Ganna Chornokur, Kyle J. Dalton, and Dawood H. Sultan. Prostate Cancer Health Disparities throughout the Cancer Control Continuum.

4

Abstracts/Posters/Talks presented (Indicate authors, title, date, venue):

06/2011, Orlando, FL: Joining FORCES Against Hereditary Cancer Conference – presenter. The poster presentation entitled “Risk of Gastrointestinal Cancers in Female BRCA1 and BRCA2 Mutation Carriers”.

03/2011, Tampa, FL: The Moffitt Research Institute Scientific Retreat Conference – presenter. The poster presentation entitled “Comprehensive Population-Specific Bio-Behavioral Marker Panel for Early Prostate Cancer Diagnostics and Risk Assessment: a DETECT study”.

10/2010, Miami, FL: 3rd AACR conference “The Science of Health Disparities” – presenter. The poster presentation entitled “Comprehensive Population-Specific Marker Panel for Prostate Cancer Screening”.

Abstract submitted for poster presentation (acceptance status is yet unknown):

Submission date 11/2011. Conference: Chicago, IL 03/2012: Annual AACR meeting - presenter. The abstract entitled "Risk Factors of Prostate Cancer in African American Men".

4. Honors and Awards

1

Open Comment:

N/A

5. Grants/Proposals

Include PI, Agency, Date, Total Cost

1

Proposals funded:

11/2010: The recipient (Principal Investigator) of the 2-year Health Disparity Training Award: "Comprehensive Population-Specific Marker Panel for Early Prostate Cancer Diagnostics and Risk Assessment". Funding Agency: Department of the U.S. Army (DoD) Prostate Cancer Research Program; Start Date: 08/2011.
Total cost: ~115,000

2

Proposals submitted:

N/A

3

Proposals in preparation/planning:

Chemopreventive Effects of Curcumin In Prostate Cancer Cell Lines, Derived from African American and European American Men: R03 proposal in preparation.

6. Teaching (if applicable)

1

List teaching responsibilities. Include individuals mentored: student name, program, dates:

I am currently mentoring a USF PhD student, Edikan Archibong. Edikan's primary department is Biomedical and Chemical Engineering and she's pursuing research in biosensors in cancer. As she has just started in August 2011, her final topic is still in preparation. However, she is learning cancer biology in general and methods (including ELISA) in particular, and I am her immediate mentor in this process. Edikan will be conducting research in Dr. Phelan/Alvaro's labs at Moffitt, as well as at the Engineering department at USF.

7. Service and Administration (if applicable)

1

National level:

N/A

2

Local (Moffitt/USF) level:

N/A

3

Research group or lab level:

N/A

8. Career Progress

1

Career goals:

My long-term career goal is to contribute to the resolution of cancer-related health disparities by conducting innovative, high-impact research as an independent investigator with competitive, peer-reviewed funding.

This broad, long-term goal is being achieved through methodologically

organized series of the following structured activities:

1. Structured mentoring program coordinated by the mentoring team. This includes weekly meetings with Dr. Phelan; bi-weekly meetings with Dr. Kumar; meetings with Dr. Park and biostatisticians on as-needed basis.
2. Become Familiar with the Major Studies and Findings in the Area of cancer disparity. This is achieved by regular attendance of relevant Moffitt ground rounds and USF lecture series; systematic review of the cutting edge literature in cancer health disparities field; and attendance of relevant conferences, seminars and classes.
3. Gain Expertise in Methodologies Needed to Conduct Transdisciplinary cancer disparity research. This is achieved by gaining experience in the cutting edge laboratory (i.e. genotyping) as well as bio-behavioral (i.e. community participatory research) techniques.
4. Be Able to Critically Review and Evaluate Research in Cancer disparity. This is achieved through attendance of journal clubs, as well as through discussions with my Mentoring team and writing my own review manuscripts that were published and are getting ready for submission to high impact peer-reviewed journals.
5. Gain an Understanding of Fundamental Issues Regarding the Ethical Conduct of Research, and responsible conduct of human research. This was achieved through attending Bioethics for researchers class (certificate awarded), as well as IRB certification (certificate awarded), and by discussions with my Mentors who are engaged in clinical trials and other human subjects' research.
6. Attend and present at relevant research and educational meetings. Please see the previous sections for details on the meetings and presentations.
7. Scientific writing and research dissemination. Please see the previous sections for details on the published manuscripts and manuscripts in preparation.
8. Applying for peer-reviewed research funding. A training grant was funded by the DoD; in addition, an R03 submission is in preparation. Please see the details in the previous sections.
9. Contribute to raising a new generation of students interested in cancer research. This is achieved by mentoring a PhD student. Please see details in the previous section.

2

How are you making necessary connections:

1. Regular attendance of Moffitt ground rounds, including designated meeting with the speaker (only in case of the most relevant topics / similar research interests);
2. Regular attendance of relevant seminars and lectures given at USF, including meeting with the speaker (only in case of the most relevant topics / similar research interests);
3. Attending and presenting at the high impact conferences, including the AACR and ASCO meetings;
4. Being introduced to the Moffitt scientists/members by my Mentor(s);
5. Active collaboration with several Moffitt cores, including biostatistics and survey cores.

3

List jobs applied to or Interviews which have taken place (Optional):

N/A.

I have started the execution of my funded 2-year proposal just a few months ago. I consider successful completion of this proposal to be an important step in my career, and since Moffitt is an ideal environment for this purpose, I am NOT looking for other jobs at this time.

4

Other career oriented accomplishments/concerns:

N/A

PART III: NUMERICAL EVALUATION

EVALUATOR: Assign a score to each area (see rating scale below).
Weights on areas may be adjusted but must be whole numbers only.
Weights of 8 areas must add up to 50%

Rating Scale

4.6 – 5.0: Far Exceeds- Outstanding performance that always exceeds expectations and is demonstrated for an extended period of time.

3.6 – 4.5: Surpasses - Very strong performance that exceeds expectations in most situations and meets expectations in all others.

2.5 – 3.5: Successfully Meets- Consistently meets performance expectations.

1.0 – 2.4: Does Not Meet - Indicates inconsistent performance, meeting some, but not all skill requirements. Immediate and substantial improvements must be made.

Work Accomplished
towards goals

Score: 4.6 / 5.0 (7%)

Score 1-5. If not applicable, change weight to zero

Score: 4.6 / 5.0 (0%)

Training

Score: 4.5 / 5.0 (7%)

Score 1-5. If not applicable, change weight to zero

Score: 4.5 / 5.0 (0%)

Publications

Score: 4.6 / 5.0 (6%)

Score 1-5. If not applicable, change weight to zero

Score: 4.6 / 5.0 (0%)

Honors and Awards

Score: 4.0 / 5.0 (6%)

Score 1-5. If not applicable, change weight to zero

Score: 4.0 / 5.0 (0%)

Grants/Proposals

Score: 4.5 / 5.0 (6%)

Score 1-5. If not applicable, change weight to zero

Score: 4.5 / 5.0 (0%)

**Teaching
(if applicable)**

Score: 4.0 / 5.0 (6%)

Score 1-5. If not applicable, change weight to zero

Score: 4.0 / 5.0 (0%)

**Service and
Administration
(if applicable)**

Score: 3.6 / 5.0 (6%)

Score 1-5. If not applicable, change weight to zero

Score: 3.6 / 5.0 (0%)

Career Progress

Score: 4.6 / 5.0 (6%)

Score 1-5. If not applicable, change weight to zero

Score: 4.6 / 5.0 (0%)

Summary Score

Score: 4.3 / 5.0 (50%)

Summary of Numerical Evaluation area. Area weight should equal 50%

Numerical Evaluation Comments

Evaluator comments related to the numerical evaluation:

OVERALL SCORE (FINAL SCORE) **Score: 4.2 / 5.0 (100%)**

The Overall Score is made up of the Numerical Evaluation and Behavioral Competencies areas

PART IV: NEW GOALS

POST DOC: Propose goals and expectations for the next year. Identify potential obstacles and propose solutions.

EVALUATOR: Populate the Approved Goals areas as applicable, using the Proposed Goals as a guide.

Post Doc's Proposed Goals: Research/Scholarship

Main focus: Continue the execution of MCC16701 (DoD DETECT training grant); aim 1 should be completed and analysed and aim 2 should be initiated.

Also, continue the MCC16112 and MCC14648 as it related to data analysis and research dissemination.

Approved Goals: Research/Scholarship

Main focus: Continue the execution of MCC16701 (DoD DETECT training grant); aim 1 should be completed and analysed and aim 2 should be initiated.

Also, continue the MCC16112 and MCC14648 as it related to data analysis and research dissemination.

Post Doc's Proposed Goals: Training

- Continue regular attendance of relevant workshops, Moffitt Ground rounds and USF lectures;

- Audit the following classes: Cancer biology III; tentative: health disparities (subject to availability);
- Clinical: shadow research coordinators from Dr. Kumar's group as they recruit patients into the clinical trials;
- Tentative: phlebotomy course;
- Tentative: grant writing workshop(s) (subject to availability).
- Tentative: shadow an MCC prostate cancer physician (subject to availability).

Approved Goals: Training

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- Audit the following classes: Cancer biology III; tentative: health disparities (subject to availability);
- Clinical: shadow research coordinators from Dr. Kumar's group as they recruit patients into the clinical trials;
- Tentative: phlebotomy course;
- Tentative: grant writing workshop(s) (subject to availability).
- Tentative: shadow an MCC prostate cancer physician (subject to availability).

Post Doc's Proposed Goals: Publications/Presentation

Publications: at least two 1-author publications in the relevant peer-review journals accepted for publication.

Presentations: at least two poster and/or oral presentations at the high-impact scientific meetings / conferences. Possible meetings may include AACR meeting 03/2012 (abstract submitted), AACR Cancer health disparity meeting 09-10/2012, relevant prostate cancer meetings and/or other high Impact health disparity meetings to be held in 2012.

Approved Goals: Publications/Presentation

Publications: at least two 1-author publications in the relevant peer-review journals accepted for publication.

Presentations: at least two poster and/or oral presentations at the high-impact scientific meetings / conferences. Possible meetings may include AACR meeting 03/2012 (abstract submitted), AACR Cancer health disparity meeting 09-10/2012, relevant prostate cancer meetings and/or other high Impact health disparity meetings to be held in 2012.

Post Doc's Proposed Goals: Honors and Awards

AACR Scholar-in-Training Awards: Available to early-career scientists presenting a meritorious proffered paper at the AACR Annual Meeting.
I have applied for this award at the time of abstract submission.

Approved Goals: Honors and Awards

AACR Scholar-in-Training Awards: Available to early-career scientists presenting a meritorious proffered paper at the AACR Annual Meeting.
I have applied for this award at the time of abstract submission.

Post Doc's Proposed Goals: Grants/Proposals

At least one NIH R03 proposal submitted and/or
at least one DoD proposal submitted (other than the training grant).
Focus: prostate cancer health disparities

Approved Goals: Grants/Proposals

At least one NIH R03 proposal submitted and/or
at least one DoD proposal submitted (other than the training grant).
Focus: prostate cancer health disparities

Post Doc's Proposed Goals: Teaching

Continue mentoring Edikan Archibong.
Tentative: mentoring other students, including Summer Interns like SPARK/LINK.

Approved Goals: Teaching

Continue mentoring Edikan Archibong.
Tentative: mentoring other students, including Summer Interns like SPARK/LINK.

Post Doc's Proposed Goals: Service and Administration

At this point, I don't have any goals in this area.

Approved Goals: Service and Administration

At this point, I don't have any goals in this area.

Post Doc's Proposed Goals: Career

To continue my transition to an Independent researcher by the means of:

1. Enhancing my research skills:
 - a. Molecular methods
 - b. Biobehavioral components
 - c. Learning about Cancer disparities
 - d. Writing publications
 - e. Presenting my research
2. Gaining career development skills:
 - a. Grant submissions (R03, DoD Idea development)
 - b. Forming research collaborations
 - c. Management of the limited funds, available through the DoD training grant, and budgeting

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 - c. Management of the limited funds, available through the DoD training grant, and

budgeting

New Goals Overall Comments (Optional):

Evaluator may use this area to make comments related to new goals:

Overall, Ganna is doing very well. We need to start Ganna's entrance into service and administration and increase her teaching.

Post Doc Final Comments (optional):

Evaluator Final Comments (optional):

Employee:

Ganna Chornokur G.C. (electronic signature for the evaluation of
Ganna Chornokur)

Date:

01/03/2012 09:15 AM

Manager:

Catherine Phelan C.P. (electronic signature for the evaluation of
Ganna Chornokur)

Date:

01/03/2012 10:08 AM

Variable	Dr Phelan's study	Dr Park's study
Case	Part 7, #1: Yes, table, row "prostate cancer"	Part III, A: Yes - prostate
Control	Part 7, #1: No	Part III, A: No
Age	2012 – Part 1, #4 year only	2012 – the DOB year only (top of the 1 st page)
Age at diagnosis (cases only)	Part 7, #1 table, column "What was your age when you were told you have this type of cancer", row "prostate cancer".	Top of the 1 st page: [date of current diagnosis, year] – [DOB, year]
Race/ethnicity: - Black/Non-Hispanic or African American	Part 1, #1: No; and Part 1, #2: Black or African American	Part I, C: No; and Part I, D: Black or African American
- White/Non-Hispanic or Caucasian	Part 1, #1: No; and Part 1, #2: White	Part I, C: No; and Part I, D: White
Education: - Some High school	Part 1, #6: less than 6 th grade; 6 th – 8 th grade; 9 th – 10 th grade;	Part I, E: grade school/junior high school; some high school
- High school graduate	Part 1, #6: 11 th – 12 th grade; GED or equivalent;	Part I, E: high school graduate
-Some college	Part 1, #6: some college; vocational school	Part I, E: some college/ technical/ vocational school certificate
- College graduate	Part 1, #6: graduate college	Part I, E: college graduate
- Postgraduate	Part 1, #6: postgraduate or professional school	Part I, E: post-graduate degree
Relationship status: - Married/living with a partner	Part 1, #5: cohabitating/living together; married	Part I, A: married/living with partner
- Widowed/ divorced/ separated/ single	Part 1, #5: Widowed; divorced/separated; single	Part I, A: widowed; divorced; separated; single
- Refuse to answer	Part 1, #5: Refuse to answer	Not an option
Personal history of cancers (other than prostate cancer): - Yes	Part 7, #1: Yes, table, all rows besides prostate cancer. Please specify the cancer type	Part III, A: Yes – a. If yes, what area of the body and what was the diagnosis? Please specify the cancer type
- No	Part 7, #1: No	Part III, A: No
If yes to <u>Personal history of cancers</u> , please specify the age at diagnosis	Part 7, #1: table, column "what was your age when you were told that you had this type of cancer?"	Part III, A, b. In what year was your diagnosis and how old were you?
Family history of cancers - Yes	Part 8, #6: Yes	Part III, C: table is filled
- No/ Don't know	Part 8, #6: No; don't know	Part III, C: table is empty
If yes to family history of cancers, what was the cancer site/type?	Part 8, #6, table – yes to the "type of cancer" column; AND/OR Part 8, #7, table – yes to the "type of cancer" column. Please specify the type(s).	Part III, C: table, column "type (site) of cancer". Please specify the cancer type(s).
If yes to family history of cancers, what blood relative(s) got it?	Part 8, #6, table – column "please indicate who has had this type of cancer"; AND/OR Part 8, #7, table – column "please indicate who has had this type of cancer" Please specify the relative(s).	Part III, C: table, column containing the relatives (mother, father, sister, brother, grandmother, grandfather). Please specify the relative(s).
What of these conditions do you have? - Depression - Heart disease - High blood pressure - High cholesterol - Thyroid issues - Diabetes None of the above	Part 3, # 3: "yes" marked for one or more of the following: antidepressants, medication for heart condition, cholesterol lowering medication, thyroid medication, treatment of adult onset diabetes. Please document which of the above. Part 3, # 3: "yes" marked for one or more	Part II, table: column "yes" checked for one or more of the following: diabetes, heart disease, thyroid problems, high blood pressure, depression. Please document which of the above. Part II, table: column "yes" checked for

	of the following: osteoporosis prevention; chemoprevention treatment; none of the above	chronic bronchitis, asthma, asbestosis, epilepsy, stroke, osteoarthritis, rheumatoid arthritis; AND/OR the column "no" checked for everything (else).
Were you born in the US? - Yes - No	Part 1, #3: the box "United States" is checked Part 1, #3: the box "other" is checked	Part I, F: yes Part I, F: no
If No to "Were you born in the US", specify the country.	Part 1, #3: the box "other" is checked. Please list the specified country.	Part I, F: a. "If no, in what country were you born?" Please list the country.
If No to "Were you born in the US", how many years have you lived in the US?	Part 1, #3: "In you were born in another country, how many years have you lived in the United States?" Please list the number.	Part I, F: b. "In what year did you come to live in the United States?" Please list the following: 2010 – [the # in the Part I, F: b.].
Occupation - Refuse to answer	Part 1, #7: what is your occupation, current or former? Please list the occupation provided. Part 1, #7: "refuse to answer" box is checked	Part VIII, A: "what occupation or job have you worked at the longest?" Please list the occupation provided. Not an option
Height	Part 1, #8.1.: "how tall are you".	Part IV, C: "how tall are you"
Weight at diagnosis	Part 1, #8.2.: "how much do you currently weigh"	Part IV, B: "your current weight"
BMI	$BMI = (\text{weight, pounds}) * 703 / \text{height, inches}^2$	
Physical activity during the last year, hrs per week: - Vigorous - Moderate - Walking No physical activity	Part 9, #1 [days per week] * Part 9, #2 [hours and minutes per day] Part 9, #3 [days per week] * Part 9, #4 [hours and minutes per day] Part 9, #5 [days per week] * Part 9, #6 [hours and minutes per day] Part 9, # 1-6, options "no activities" and/or "don't know/not sure" checked.	Part IV, H: table, rows jogging or running, swimming, bicycling, aerobics, column "hours per week" Part IV, H: table, rows racket sports, team sports, dancing, column "hours per week" Part IV, H: table, row walking, column "hours per week" Part IV, H: table – no activities checked
NSAIDs on a regular basis - Aspirin - Ibuprofen - No Aspirin - No Ibuprofen	Part 3, #1: 1 per week; 2-5 per week; 6 or more per week; 1-3 per month are checked Part 3, #2: 1 per week; 2-5 per week; 6 or more per week; 1-3 per month are checked Part 3, #1: never is checked Part 3, #2: never is checked	Part V, B: table, "Yes" by any of the Aspirin products is checked Part V, B: table, "Yes" by any of the Ibuprofen products is checked Part V, B: table, "No" by all of the Aspirin products is checked Part V, B: table, "No" by all of the Ibuprofen products is checked
Have you ever smoked (chewed, snuffed etc) tobacco products? - Yes - No	Part 5, #1(b): Yes Part 5, #1(b): No	Part VI, A: Yes Part VI, A: No
If yes, are you smoking (chewing, snuffing etc) tobacco products now? - Yes - No	Part 5, #1(a): Yes Part 5, #1(a): No	Part VI, A(1): table, raw "do you still smoke (chew etc)?" – Yes to any or all tobacco products Part VI, A(1): table, raw "do you still smoke (chew etc)?" – No to <u>all</u> tobacco products
How old were you when you started smoking (chewing, snuffing etc) tobacco products?	Part 5, #1(c): note the age	Part VI, A(1): table, raw "how old were you when you started smoking (chewing) regularly?" – note the age(s) for any or all tobacco products
On average, how many cigarettes (cigars etc) did you smoke (chew etc) per day?	Part 5, #1(e): note the number	Part VI, A(1): table, raw "on average, how many cigarettes did/do you smoke per

[illegible]