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Evaluating the Role of Genetic Markers in Prostate Cancer Progression: A Multiethnic Cohort Experience

PRINCIPAL INVESTIGATOR:
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13. SUPPLEMENTARY NOTES

14. ABSTRACT Most prostate cancer (PCa) research has focused on risk, little is known about predictors of progression and even less about how these factors differ by ethnicity/race. Strong racial disparities in mortality have shown that African-Americans are twice as likely to die from PCa compared to Caucasians; very little data are available in Hispanics. Our overall goal is to identify markers related to PCa progression in a multiethnic cohort of 773 Caucasians, 361 African-Americans, and 246 Mexican-Americans, for whom we have already collected information. We have abstracted medical records for 1200 patients and are requesting copies of outside medical records for those who received care outside our institution, as well as continuing to abstract medical records. Additionally, we are matching our database with the National Death Index to update vital status. We are multi-plexing the genotyping assays to optimize the utilization of our archived specimens, and all DNA extractions have been completed. Our research may help explain ethnic/racial disparities in PCa progression and provide direction towards eliminating these disparities and may guide future studies to develop ethnic/racial specific interventions to improve outcome in the most common cancer in American men.

15. SUBJECT TERMS
Prostate cancer, race, ethnicity, prognosis

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INTRODUCTION:

There is a paucity of information regarding markers/factors associated with prostate cancer (PCa) outcome in the United States, especially how these factors differ among racial/ethnic groups. African-American men are more likely to have poorer outcome relative to age and stage-matched Caucasian patients; and very little is known about prognosis and even less about factors that could predict progression among Hispanics. The overall goal of our research project is to identify molecular, epidemiological and clinical markers related to prostate cancer (PCa) progression in a multiethnic cohort of 1,380 PCa patients (773 Caucasians; 361 African Americans, and 246 Mexican Americans).

BODY:

Task 1 **Patient Follow-up.** (Months 1-30)

a. Update patient follow-up data by checking clinical schedules and medical charts for updated information. Using a validated medical abstraction form, all patient charts will be abstracted.

b. Signed medical releases of information will be requested for care received outside of our institution. Copies of medical records will be requested.

c. Death certificates will be obtained for all participants identified as deceased.

d. Patients' self-reported recurrences (and subsequent treatments) and secondary cancers will be verified.

e. Data will be entered into existing databases.

In the second year of this grant, we have completed medical record abstractions for 1200 prostate cancer patients who have received follow-up care at our institution. Institutional patient records for each participant are being abstracted using the standardized form attached as Appendix A. The most recent clinical follow-up date at our institution is determined; this date is used as the "last date of contact" at the University of Texas MD Anderson Cancer Center (UTMDACC). In addition to baseline treatment information, we have abstracted follow-up information, such as each prostate specific antigen (PSA) level and date, adjuvant care received, prostate-related care (including care related to complications following treatment (i.e., incontinence, impotence)), as well as additional cancer diagnoses. Institutional medical records are available electronically, and abstractions are performed using a paper form and are being entered into an existing clinical database. We are continuing to abstract institutional medical records for the remaining patients and expect to be done with the abstractions in the 6 months.

For patients for whom we do not have recent follow-up information at UTMDACC, we are continuing to conduct telephone interviews to request these data. The greatest challenge we continue to face is locating and contacting these individuals we last spoke with several years ago. We are utilizing several options for obtaining updated contact information; including general internet searches, reverse address searches, and credit records. The Acxiom Insight Collection service, an internet-based paid subscription database, continues to be the most useful tool for us. To-date, we have successfully completed 120 follow-up interviews by phone. The protocol to verify potentially valid contact information includes calling the individual at least 5 times at different times of the day, as well as on weekends, if needed; the calls are conducted using the telephone script included as Appendix B. In addition, if these call attempts are not successful, we send a letter to the patient at the last known valid address (with address correction requested) explaining that we are trying to follow-up with them regarding their participation in a study and requesting that they contact us at their earliest convenience. Updated health and risk factor information is collected by trained interviewers, using a standardized questionnaire modified for this project (Appendix C).

Patients who are receiving follow-up care outside of UTMDACC are asked to sign a medical record release form (Appendix D) to allow us to obtain copies of the relevant records from their healthcare providers. Outside medical records are abstracted using the same standardized forms as used for UTMDACC records. Clinical recurrences and related treatments are noted on the abstraction forms and verified by the study clinical personnel. We are continuing to update vital status using data from the National Death Index.

Task 2 **Evaluate Constitutional Markers of Genetic Susceptibility.** (Months 1-30)

a. Genotyping assays for all genes will be established, tested and validated by the Department of Epidemiology Genotyping Core (Months 1-24).

We are refining our methodology to more efficiently multi-plex the assays for the remainder of the genotyping and conserve resources.

b. Biological samples for all participants will be located and retrieved from study archive freezers (Months 1-3).

Using our laboratory tracking database, biological samples for this study have been identified, located and retrieved from our freezer facility. Samples that will be used have been mapped and transferred to the genotyping facility. All specimens are stored at -80° in on-site freezers until analyses are conducted.

c. DNA will be extracted from banked specimens (Months 1-12).

DNA has been extracted from all of the banked specimens. DNA quality has been tested for the extracted samples to ensure the success of the analyses.

Extracted DNA has been successfully used for the genotyping assays performed and reported below.

d. DNA samples will be plated for genotyping analyses – half the samples will be done in Year 2 and the other half will be done in Year 3 (Months 13 & 25)

All samples have been quantified and standardized in preparation for final plating, which will be done immediately prior to genotyping. Maps for plating samples have been created with a mix of each racial/ethnic group on each plate.

e. Genotyping will be done for half the samples in Year 2 (Months 13-24) and the other half in Year 3 (Months 25-30).

To-date, we have completed preliminary genotyping 611 cases for MMP-1, 615 for e-cadherin, 433 for beta-2-adrenergic receptor, and 725 for cyclin D1. In our preliminary analyses, we have found significant differences with respect to genotypic frequency between racial/ethnic groups for MMP-1, beta-2-adrenergic receptor and cyclin D1. However, due to recent improvements in technology, we have changed our genotyping methodology; and we will commence with multi-plexed genotyping in Year 3. In addition, we are collaborating with several multi-ethnic consortiums (led by Tim Rebbeck at University of Pennsylvania, Brian Henderson at the University of Southern California, and Ros Eeles at the Institute of Cancer Research Royal Cancer Hospital-London) to conduct genome-wide association studies, particularly in African-Americans.

Task 3 **Final Analysis and Preparation of Reports.** (Months 30-36) – N/A

KEY RESEARCH ACCOMPLISHMENTS:

There are no key research accomplishments to report at this time; we are still in the process of collecting follow-up data. No interim analyses have been performed, nor were any planned to be conducted at this time-point.

REPORTABLE OUTCOMES:

Currently, there have been no manuscripts, abstracts, presentations, patents or licenses applied for based on this award. Additionally, there have not been any degrees supported by this award; no cell lines, tissue or serum repositories developed; no informatics applied for based on work from this award; no employment opportunities applied for and/or received based on experience/training supported by this award. Preliminary data (numbers of participants with follow-up information) have been included in 2 recent grant proposals: U01- Genome-wide association study of prostate cancer in African Americans (Henderson), funded; U19 –Trans-disciplinary cancer genomics research: post-GWA initiative (Henderson/Eeles), pending.

CONCLUSION:

Our research may help explain ethnic/racial disparities in PCa progression and provide direction towards eliminating these disparities. Additionally, our results may guide future studies to develop ethnic/racial specific interventions (i.e., behavioral, clinical) to improve outcome in the most common cancer in American men.

REFERENCES: N/A

APPENDICES:

APPENDIX A:

Medical record abstraction form

Medical Records Abstraction Form

Name

_____

Address

_____

_____

_____

MDACC# _____

MDA registration date _____/_____/____

Date of birth ____/_____/_____

Age at diagnosis _____years

Phone number _____

Ethnicity

☐ White ☐ Hispanic → ☐ African-American ☐ Asian ☐ Other _____	☐ Mexican ☐ Cuban ☐ S. American ☐ Other _____

Vital status ☐ Living ☐ Deceased → Date of death ____/____/____

Place of death _____

Cause of death _____

Last date of contact _____/_____/_____ Place of contact_____

Height: _____cm
_____ft/inches

Weight: _____kg
_____Ibs

Prostate cancer diagnosis

Date of diagnosis ____/_____/_____

Place of diagnosis: MDACC ☐ Yes ☐ No

Diagnostic tests ☐ Biopsy ☐ POS ☐ NEG ↓

☐ TURP ☐ POS ☐ NEG Where_____

☐ Chest x-ray ☐ POS ☐ NEG _____

☐ Bone scan ☐ POS ☐ NEG _____

☐ CT scan ☐ POS ☐ NEG

☐ Other _____ ☐ POS ☐ NEG When ____/_____/_____

Comments _____

Clinical stage of diagnosis

☐ Organ confined disease

☐ Regional disease

☐ Metastatic disease → date of confirmation ____/____/____

Sites: ☐ Bones ☐ Liver ☐ Adrenal gland ☐ Kidney ☐ Brain

☐ Other _____

TNM stage

T1 → ☐ x ☐ 0 ☐ a ☐ b ☐ c **T2** → ☐ a ☐ b ☐ c **T3** → ☐ a ☐ b **T4**

N → ☐ x ☐ 0 ☐ 1 ☐ 2 ☐ 3

M → ☐ x ☐ 0 ☐ 1 Summary _____

Comments _____

_____

Laboratory results

Post-treatment values

Most recent post-treatment PSA value _____ng/ml Date _____/_____/_____

Follow-up PSA Values _____ ng/ml Date _____/_____/_____

Follow-up PSA Values _____ ng/ml Date _____/_____/_____

Follow-up PSA Values _____ ng/ml Date _____/_____/_____

Follow-up PSA Values _____ ng/ml Date _____/_____/_____

Follow-up PSA Values _____ ng/ml Date _____/_____/_____

Follow-up PSA Values _____ ng/ml Date _____/_____/_____

Follow-up PSA Values _____ ng/ml Date _____/_____/_____

Follow-up PSA Values _____ ng/ml Date _____/_____/_____

Initial post-treatment PSA value _____ ng/ml Date _____/_____/_____

Pre-treatment values

Highest pre-treatment PSA value_____ ng/ml Date ____/_____/_____

Initial pre-treatment PSA value _____ ng/ml Date ____/_____/_____

Comments: _____

_____

Pathology report **Pathology report #: _____**

Specimen type ➲ ☐ **Prostatectomy**

MDACC grade ⇐ ☐ I ☐ II ☐ III ☐ IV ☐ other _____

Seminal Vesicle involvement ☐Yes ☐No **S/Margins** ☐ Positive ☐ Negative

Combined Gleason score

☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 _____

Dominant focus size /size _____cm Prostate volume _____ cm

Tumor locations ☐ Peripheral zone ☐ Central zone ☐ Transitional zone ☐ AFM zone

Comments_____
_____

Pathology report **Pathology report #: _____**

Specimen type ⇐ ☐ **Biopsy**

MDACC grade ⇐ ☐I ☐ II ☐ III ☐ IV ☐ other _____

Combined Gleason score

☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

Dominant focus size /size _____cm Prostate volume _____ cm

Tumor locations ☐ Peripheral zone ☐ Central zone ☐ Transitional zone ☐ AFM zone

Comments_____
_____

History of prostate cancer screening

☐ No

☐Yes → Type of screening test ☐ Prostate-specific antigen (PSA)

☐ Digital rectal examination (DRE)

☐ Trans-rectal ultrasound (TRUS)

☐ Other _____

Presence of urinary symptoms ☐ Yes ☐ No

Coments: _____
_____

Prostate cancer treatment received

☐ Radical prostatectomy Type → ☐ Radical Retropubic Prostatectomy (RRP) Date _____/_____/_____

☐ Radical perineal prostatectomy (RPP)

☐ Nerve-sparing

☐ Pelvic lymphadenectomy

☐ Orchiectomy → Date _____/_____/_____

☐ Cryosurgery → Date _____/_____/_____

		Onset of treatment	End of treatment
☐ Radiotherapy (EBRT)	→	Date _____/_____/_____	Date _____/____/____
☐ Brachytherapy	→	Date _____/_____/_____	Date _____/____/____
☐ Hormonal therapy	→	Date _____/_____/_____	Date _____/____/____
☐ Immunotherapy	→	Date _____/_____/_____	Date _____/____/____
☐ Surveillance	→	Date _____/_____/_____	Date _____/____/____
☐ Chemotherapy	→	Date _____/_____/_____	Date _____/____/____
☐ Other (specify) _____		Date _____/_____/_____	Date _____/____/____

Comments _____
_____

Complications of treatment

Urinary
Incontinence ☐ No
☐ Yes → Uses sanitary pad ☐ No
☐ Yes → number /day_____

Treatment received_____

Post-treatment status (1yr.) Number of pads/day _____ Date ____/____/____

Impotence ☐ No
☐ Yes → Treatment received _____
Post-treatment status (1yr.)_____

Urinary retention ☐ No
☐ Yes Treatment received _____

Other_____
_____
_____

Comorbid conditions prior to diagnosis of prostate cancer

☐ No ☐ Yes

↓

☐ Diabetes (IDDM, NIDDM)	Date of diagnosis ___/___/___
☐ Hemorrhage	Date of diagnosis ___/___/___
☐ Hypertension	Date of diagnosis ___/___/___
☐ Peptic ulcer disease	Date of diagnosis ___/___/___
☐ Congestive heart failure	Date of diagnosis ___/___/___
☐ Pancreatitis	Date of diagnosis ___/___/___
☐ Myocardial infarction	Date of diagnosis ___/___/___
☐ Cholelithiasis	Date of diagnosis ___/___/___
☐ Stroke	Date of diagnosis ___/___/___
☐ Alcoholism	Date of diagnosis ___/___/___
☐ Chronic obstructive pulmonary disease	Date of diagnosis ___/___/___
☐ Lupus erythematosus	Date of diagnosis ___/___/___
☐ Other _____	Date of diagnosis ___/___/___

Other pertinent information

Recurrence of prostate cancer

☐ No

☐ Yes → Date of diagnosis _____/_____/_____

Place of diagnosis _____

Type of treatment _____

Basis of diagnosis _____
_____
_____

Diagnostic tests			
	☐ Biopsy	☐POS	☐NEG
	☐ TURP	☐POS	☐NEG
	☐ Chest x-ray	☐POS	☐NEG
	☐ Bone scan	☐POS	☐NEG
	☐ CT scan	☐POS	☐NEG
	☐ Other _____	☐POS	☐NEG

Conditions diagnosed after diagnosis of prostate cancer

☐ No ☐ Yes
↓

Date of diagnosis _____/_____/_____
Type of disease _____

Place of diagnosis _____
Type of treatment received_____

Date of diagnosis _____/_____/_____
Type of disease _____

Place of diagnosis _____
Type of treatment received_____

Comments _____
_____

Last clinic visit Date _____/_____/_____

Notes

APPENDIX B:

Follow-up telephone recruitment script

SCRIPT 1 (Speaking to person who answers phone) –

Hello, my name is (INTERVIEWER'S NAME) and I am calling on behalf of MD Anderson Cancer Center, here in Houston. May I please speak with (PATIENT'S NAME)?

- NOT AVAILABLE – Verify (PATIENT'S NAME) lives at this residence. Ask "Is there a time that I could call back and speak with him?" OR "would you please ask him to call me (INTERVIEWER'S NAME) at (PHONE NUMBER) at his earliest convenience? Thank you for your assistance.

- YES – Thank you…(Wait for (PATIENT'S NAME) come to phone) Hello, my name is (INTERVIEWER'S NAME) and I am calling on behalf of MD Anderson Cancer Center, here in Houston. You participated in one of our prostate cancer studies a few years ago, and we are conducting a follow-up study to see how you are doing. Would it be all right with you if I asked you a few questions about your health and updated your information?

  - NO – thank you for your time. If you change your mind and would like to participate, please contact me (INTERVIEWER'S NAME) at (PHONE NUMBER).

  - YES – I want to let you know that answering these questions is completely voluntary, and you may decide not to answer any or all of them. (Administer risk factor questionnaire (Appendix D))

Following each call, the interviewer logs each call made onto the tracking log for each file, documenting the date, time, phone number dialed, and with whom they spoke. These logs are maintained in the individual patient's study chart, kept in a locked office coded by study identification number.

APPENDIX C:

Follow-Up questionnaire

PROSTATE CANCER FOLLOW-UP STUDY

M.D. A *M.D. Anderson Cancer Center* *Department of Epidemiology*

STUDY NUMBER:_____ **D** **ATE OF PC DIAGNOSIS:** _____/_____/_____

MED RECORD/PATIENT #:_____

DATE OF BASELINE INTERVIEW: _____/_____/_____

PATIENT RECEIVING FOLLOW-UP CARE AT MDACC: __(1)YES __(2) NO

DATE OF MOST RECENT MDACC VISIT: ___/____/____

_____ **HOME PHONE:** (____)_____

FIRST NAME **M.I.** **LAST NAME**

_____ **WORK PHONE:** (____)_____

STREET ADDRESS

_____ **SSN:** _____

CITY **STATE** **ZIP CODE**

INTERVIEW DATE: _____/_____/_____ **INTERVIEWER'S INITIALS:** _____

WHO IS COMPLETING QUESTIONNAIRE? o **PATIENT** o **PROXY**

IF PATIENT IS DECEASED, DATE OF DEATH _____ **C OUNTY & STATE OF DEATH** _____

As you may remember, you participated in a study of prostate cancer. We are currently updating our information, and we wanted to see how you are doing. Do you have a few moments to talk to me now or when can I call you back?

1. Are you currently being followed-up for your previous prostate cancer? _____ YES (1) _____ NO (2)

2. Where are/were you receiving follow-up care? _____

3. When was your most recent follow-up visit? _____ (Date)

When was the last time you had (the following test(s))? What were the results?

Test	Most Recent Date	Result (most recent)	
4. Prostate Specific Antigen/ (PSA)			___ Normal (1) **go to Q.8** ___ Abnormal (2) **go to Q.5**
5. Ultrasound (TRUS)			
6. Biopsy or Transurethral Resection of Prostate (TURP)			
7. Other (specify)			

8. Have you received any prostate treatment since you were last seen at MD Anderson/Kelsey-Seyboldt/VAMC/Dr.
_____ (select provider) in _____ (fill in last date)?
____ (1)YES _____(2) NO → Skip to Q. 12

9. When and where were/are you receiving treatment? (*e.g., MD/Clinic Name, Address, Phone #*)

Office Note: Obtain signed medical release of information

_____

_____

10. What type(s) of treatment did you receive? (e.g., radiation, hormone shots, hormone pills, chemotherapy)

_____

_____

11. Why was the treatment necessary?

_____

_____

Have you ever been told by a doctor or another health care professional that you have any of the following conditions?

CONDITION	BEEN TOLD?	DATE/AGE DIAGNOSED	TREATMENT/MEDICATION NAME
12. Diabetes (or sugar in urine)	_____ (1) YES _____ (2) NO		
13. Hypertension (high blood pressure)	_____ (1) YES _____ (2) NO		
14. Angina (angina pectoris)	_____ (1) YES _____ (2) NO		
15. Heart attack (myocardial infarction)	_____ (1) YES _____ (2) NO		
16. Any other kind of heart condition or disease (not mentioned above) SPECIFY: _____	_____ (1) YES _____ (2) NO		

CONDITION	BEEN TOLD?	DATE/AGE DIAGNOSED	TREATMENT/MEDICATION NAME
17. High cholesterol	_____ (1) YES _____ (2) NO		
18. Arthritis TYPE: _____	_____ (1) YES _____ (2) NO		
19. Any other cancer(s)? SPECIFY	_____ (1) YES _____ (2) NO		
20. Any other condition(s)? SPECIFY	_____ (1) YES _____ (2) NO		

TOBACCO

Previous Smoking Status
____ Current ____ Former ____ Never

The next questions are about smoking.

21. Since your prostate cancer diagnosis, has your smoking status changed? ___(1)YES ___(2) NO → **Fmr/Never smoker** Go to Q.24 **Currt smkr** Go to Q.23

22. Are you currently smoking cigarettes? ____ (1)YES ____(2) NO → When did you stop? _____ (Year)

23. On average, how many cigarettes per day do you/did you smoke? _____

MEDICATION/SUPPLEMENT USE

The next questions are medications and supplement use

24. Have you taken any supplements, over the counter medications or prescription medications at least once a month since your diagnosis? This would include all vitamins, minerals, herbal and non-herbal supplements of any kind.

_____ (2) No, GO TO Q. 26

_____ (1) Yes, Fairly regularly _____ (3)Yes, but NOT regularly

25. Please list the names of any supplements (including vitamins, minerals and herbal supplements), over-the-counter medications or prescription medications that you have taken. Also include the number of pills or tablets taken daily, weekly, monthly or yearly?

For Office Use:	_____ code

Supplement, Over-the-counter or prescription medication	**Number per Day**	**Number per Week**	**Number per Month**	**Number per Year**	**Rarely / Never (✓)**	**How many years?**	**Dose**
Brand:_____ Name on bottle: _____							
Brand:_____ Name on bottle: _____							
Brand:_____ Name on bottle: _____							
Brand:_____ Name on bottle: _____							

DIET

The following questions are regarding diet changes

Since your diagnosis, have you changed your consumption of the following types of foods?

FOOD TYPE	INCREASED
26. Fat	____(1) increased ____(2) decreased ____(3) no change
27. Fruits	____(1) increased ____(2) decreased ____(3) no change
28. Vegetables	____(1) increased ____(2) decreased ____(3) no change
29. Fiber	____(1) increased ____(2) decreased ____(3) no change
30. Soy products	____(1) increased ____(2) decreased ____(3) no change

31. Are there any comments that you would like to add about your diet or about the way you have changed your diet?

_____

_____

FAMILY HISTORY

In this section, I would like to ask you some questions about your family

FAMILY HISTORY PRE-CODE:

Previously reported family members WITH cancer:

Sex	Relative	Side of Family	Type of Cancer	Sex	Relative	Side of Family	Type of Cancer

32. Previously, you told us that your _____ (insert previous history here) had cancer, have any other immediate family members been diagnosed with cancer? ____ YES (1) ____ NO (2) → Go to Q. 34

33. Would you please give us some information about these NEW family members diagnosed with cancer? (DON'T include those previously reported)

Rel Code	Sex	Relative	Rel UIN	When was he/she born?	What kind of cancer?	ICD-9	When was he/she diagnosed?	Is he/she still living?	When did he/she die?
								____(1) Yes ____(2) No	
								____(1) Yes ____(2) No	
								____(1) Yes ____(2) No	
								____(1) Yes ____(2) No	
								____(1) Yes ____(2) No	

OCCUPATIONAL HISTORY

In this section, I would like to ask you some questions about your current occupation

34.

What is your job or occupation?	Years employed	Major duties	Equipment used (Any Chemicals?)	Work done by company	SIC	OCC
Current Job:	____To_____					
Spec						

If we need additional information from you in the future, can we contact you by telephone? ____ (1)YES ____ (2)NO

This is the end of our interview. I would like to thank you for your help with our research. If you have any questions that I or Dr. Strom can answer in the future, please feel free to contact us. We would also like to verify that we have your current address correctly recorded. We have your current address as: ***READ ADDRESS FROM FILE RECORD***

Is this address correct? _____(1) YES _____ (2)NO *(If NO, please provide correct information below)*

_____ _____
First Name Middle Name Last Name

_____
Street Address

_____ _____
City State Z ip Code

Also, so that we may keep contact with you, would you please give me that name, address, and telephone number of a person who does not live with you who will know your whereabouts in the future:

_____ _____
First Name Middle Name Last Name

_____
Street Address

_____ _____
City State Z ip Code

Thank you once again for your time and help with our research project. If we have any more questions in the future, we hope we can call you again.

INTERVIEW ASSESSMENT

Date of interview: ____/____/____ Interviewer's Initials: _____

Time Interview began: _____ Time Interview ended: _____

1. Respondent's cooperation was:

   _____ Very Good (1)

   _____ Good (2)

   _____ Fair (3)

   _____ Poor (4)

2. The quality of the interview was:

   _____ Highly Reliable (1)

   _____ Generally Reliable (2)

   _____ Questionable (3)

   _____ Unsatisfactory (4)

Please write comments about the interview: _____

_____

_____

_____

APPENDIX D:

Medical release of information form

AUTHORIZATION FOR DISCLOSURE OF HEALTH INFORMATION

(1) I hereby authorize _____ to disclose the following information from the health records of:

Patient Name: _____
Last First MI. Date of Birth MDA #

Address:_____
_____
Street City State Zip Code
Phone

covering the period of healthcare from _____ to _____.

(2) Information to be disclosed:

- ❑ Complete Health Record
- ❑ Primary Medical Evaluation
- ❑ Progress Notes
- ❑ X-Ray Reports
- ❑ Discharge Summary
- ❑ Consultation Reports
- ❑ Laboratory Tests
- ❑ Radiotherapy Notes
- ❑ Chemotherapy Notes
- ❑ Nurse's Notes

❑ Other (specify) _____

I understand that this will include information relating to (check if applicable):

- ❑ Acquired Immunodeficiency Syndrome (AIDS) or infection with HIV (Human Immunodeficiency Virus)
- ❑ Psychiatric care
- ❑ Treatment for alcohol and/or drug abuse

(3) This information is to be disclosed to: Dr. Sara Strom

Investigator's signature

UT MD Anderson Cancer Center

1515 Holcombe, Houston, Texas 77030

for the purpose of: **Medical Record completion for research protocol M91-004.**

(4) I understand this authorization may be revoked in writing at any time, except to the extent that action has been taken in reliance on this authorization. Unless otherwise evoked, this authorization will expire on the following date, event, or condition:

_____

(5) The facility, its employees, officers, and physicians are hereby released from any legal responsibility or liability for disclosure of the above information to the extent indicated and authorized herein.

Signed: _____
(patient) (date)

or _____
(Legal Representative)(Relationship to Patient) (date)

SUPPORTING DATA: N/A

USAMRMC Human Research Protection Office Continuing Review Submission Checklist

SUBJECT: "Evaluating the Role of Genetic Markers in Prostate Cancer Progression: A Multiethnic Cohort Experience," Submitted by Dr. Sara S. Strom, University of Texas, M D Anderson Cancer Center, Houston, Houston, TX, Proposal Number PC061038, Award Number W81XWH-07-1-0648, HRPO Log Number A-14108.

CONTINUING REVIEW OR TERMINATION DOCUMENTS TO SEND TO THE HRPO (If Applicable)

_X_ The continuing review summary report that was submitted to your IRB.

_X_ Local IRB approval letter with next expiration date.

_X_ Current copy of Protocol. Please list or track all Amendments that have occurred since the last time the protocol was submitted to HRPO.

_N/A_ Current consent form, if applicable. List or track all revisions that have occurred since the last time the consent form was submitted to HRPO.

THE FOLLOWING CHECKLIST IS PROVIDED AS A GUIDANCE REFERENCE REGARDING THE REQUIRED ELEMENTS TO BE INCLUDED IN A CONTINUING REVIEW REPORT, PLEASE ENSURE THAT APPLICABLE ITEMS ARE ADDRESSED IN THE CONTINUING REVIEW REPORT OR ATTATCHED IN A SEPARATE DOCUMENT:

__ Total number of subjects enrolled in the study (i.e., number recruited, enrolled, withdrawn by PI, discontinuation by subject, disenrolled [deaths, other])

__ Breakdown of participants by demographics as appropriate (e.g., groups/cohorts, gender, age, ethnicity, special populations)

__ Summary of SAEs, adverse events and unanticipated problems involving risks to subjects or others

__ Summary of withdrawals that have occurred, with reasons for withdrawal

__ Summary of complaints received

__ Summary of deviations that have occurred

__ Report includes a summary of research progress, including results obtained to date

__ Documentation of literature review update, including databases searched, dates of searches, key words and subject areas searched. Risk/benefit assessment or other protocol activities updated as necessary based on review of literature. Measures included to reduce or minimize any newly identified risks

__ Summary of any amendments, addendums, or modifications that have been made to the protocol since the initial approval (administrative, minor and major changes)

Name of individual to contact with questions regarding this report Sara S. Strom, PhD

Contact information (include email and phone number) sstrom@mdanderson.org 713-792-8274

Date (day month year) June 24, 2009

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

DATE: MAR 23, 2009

TO: Sara Strom Ph.D.
Box 189

FROM: Institutional Review Board IRB1
Office of Protocol Research
Box 198

SUBJECT: Expedited Continuing Review Approval of M91-004

Title: ECOGENETIC CASE-CONTROL STUDY OF PROSTATE CANCER

The above named and numbered protocol was reviewed using the expedited review process in accordance with the Institutional Review Board (IRB) Policy for Continuing Review of Research and the federal regulations governing human subjects research [45 CFR 46.109(e) and 21 CFR 56.109(f)].

On MAR 10, 2009, the IRB chair or designee expeditedly approved the continuation of this protocol. All research related activities may continue on this protocol for another 365 days.

If you have any questions regarding this matter, please call the Office of Protocol Research at (713)792-2933 or send an email to IRB CONTINUING REVIEW@mdanderson.org.

Thank you for your cooperation.

Institutional Review Board (IRB)
Continuing Review of Ongoing Clinical, Laboratory and Miscellaneous Protocols

Print Vers

Report Date: 02/25/09 **Due Date:** 03/06/09

The continuing review process is a requirement of this institution in compliance with federal regulations. The study Chairperson is responsible for updating the protocol status by providing the following information electronically to the Institutional Review Board for potential approval by the due date shown above. Direct your questions to the Office of Protocol Research at (713)792-2933 or send an email to IRB_ContinuingReview@mdanderson.org.

Protocol Number and Title: M91-004 - ECOGENETIC CASE-CONTROL STUDY OF PROSTATE CANCER

Study Chairperson: Sara Strom
E-mail: sstrom@mdanderson.org
NCI Support Grant Program: Epidemiology

For IRB1 Committee Review: 03/18/09
Last Continuing Review: 05/07/08

APPROVED 03/10/09

Sponsor/Supporter:

Notes

⚠ Currently the co-investigator and/or collaborator list for this protocol exists as shown. Please submit a revision to the Office of Protocol Research if the list appears incorrectly.

Collaborators	Co-investigators
[none]	Click here

Current Protocol Status (Date)

12/31/91 **Original IRB Approval**
11/13/08 **Informed Consent**
Waiver of informed consent: ☐ Yes ☑ No
11/15/95 **Active** (study in progress and accruing patients)
_____ **Request Close To New Patient Entry** (no new patient accrual, but patients continuing on treatment or still alive for follow up)
Date last patient entered 02/24/09
_____ **Request Termination** (no activity - all patients off study and no longer being followed)
NOTE: OFF DATE must be entered and a written summary must be attached that describes accrual, any toxicities and response data, and outcome(s) of research.

Is this a multicenter study? ☑ Yes ☐ No Maximum number of **multicenter** subjects approved 4500

Maximum number of **MDACC** subjects approved 3000 Registration required? ☑ Yes ☐ No Total accrual to date on PDMS 1647

The number of subjects where a translator was used during the informed consent process to verbally translate the consent document 0

Language(s) in which the consent was verbally translated:

Are all subjects off active intervention? ☑ Yes ☐ No
If yes, are subjects in long term follow-up? ☑ Yes ☐ No

Total AEs reported 0 AEs since last review 0 Number of treatment related deaths 0

Give a summary of the toxicity profile? ☑ Not Applicable If n/a, explain why. (Printout of adverse events not acceptable)
NA . Thi is not a treatment protocol

Give a summary of the response profile? ☑ Not Applicable If n/a, explain why.
NA

Who is monitoring the conduct of this study? Principal Investigator
No comment

Have any recent reports of preliminary analyses been prepared since the last review? ☐ Yes ☑ No
If yes, provide an attachment below

What is the result of an interim analysis or when is one planned? ☑ Not Applicable

Why should the study remain open?
We are still accruing patients

Please provide any additional comments or any overall synopsis of the study below.
No comment

Electronically signed by Sara Strom on 02/25/09 @ 17:46
Study Chairman (signature and date)

IRB Comments / overall
assessment

Electronically signed by Luis E. Fayad on 03/03/09 @ 16:15
IRB Chairman or Designee (signature and date)

☑ Approved ☐ Approved Contingent
☑ Expedited Review ☐ Full Review

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

DATE: APR 27, 2009

TO: Sara Strom Ph.D.
Box 189

FROM: Institutional Review Board IRB4
Office of Protocol Research
Box 198

SUBJECT: Expedited Continuing Review Approval of ID01-296

Title: EPIDEMIOLOGICAL, MOLECULAR AND CLINICAL MARKERS OF PROSTATE CANCER PROGRESSION

The above named and numbered protocol was reviewed using the expedited review process in accordance with the Institutional Review Board (IRB) Policy for Continuing Review of Research and the federal regulations governing human subjects research [45 CFR 46.109(e) and 21 CFR 56.109(f)].

On APR 11, 2009, the IRB chair or designee expeditedly approved the continuation of this protocol. All research related activities may continue on this protocol for another 365 days.

If you have any questions regarding this matter, please call the Office of Protocol Research at (713)792-2933 or send an email to IRB CONTINUING REVIEW@mdanderson.org.

Thank you for your cooperation.

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

DATE: JUN 20, 2008
TO: Sara Strom Ph.D.
189

FROM: IRB Coordinator
Office of Protocol Research
Unit 574

SUBJECT: Continuing Review Contingency Met
Continuing Review of Protocol ID01-296
EPIDEMIOLOGICAL, MOLECULAR AND CLINICAL MARKERS OF PROSTATE CANCER PROGRESSION

The M.D. Anderson Cancer Center Institutional Review Board (MDACC IRB4) chair or designee approved the above named and numbered protocol since the CONTINGENCY outlined by the committee at the <MAY 22,2008> meeting has been met as of <JUN 09, 2008>.

If you have any questions regarding this matter, please call the Office of Protocol Research at (713)792-2933 or send an email to IRB CONTINUING REVIEW@mdanderson.org.

Thank you for your cooperation.

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

DATE: MAY 29, 2008

TO: Sara Strom Ph.D.
Box 189

FROM: Institutional Review Board IRB4
Office of Protocol Research
Box 198

SUBJECT: Contingent, Expedited Continuing Review Approval of ID01-296, Entitled "EPIDEMIOLOGICAL, MOLECULAR AND CLINICAL MARKERS OF PROSTATE CANCER PROGRESSION"

The above named and numbered protocol was reviewed using the expedited review process in accordance with the Institutional Review Board (IRB) policy for Continuing Review of Research and the federal regulations governing human subjects research [45 CFR 46.109(e) and 21 CFR 56.109(f)].

On MAY 22, 2008, the IRB4 accepted the recommendations of the IRB chair or designee and approved the protocol contingent on the following:

Contingency 1: Please provide an update regarding the current sample size of the study.

Contingency 2: Please respond to this contingency by a generic memo from PDOL to "IRB Continuing Review" (contact 5-PDOL for assistance).

Please submit a response to the contingencies via PDOL, or if this protocol is hard copy, you may send your response to the Office of Protocol Research(OPR) at Unit 198.

Your reply must be received by <JUL 14,2008> or the protocol will not be in compliance with the IRB policy for Continuing Review of Research and will be closed to new patient registration. In addition, as principal investigator, you will be listed as non-compliant and will not be able to submit any new protocols for review until the contingencies have been met.

Should you have any questions regarding this matter, please contact OPR at (713)792-2933 or send an email to IRB CONTINUING REVIEW@mdanderson.org.

Thank you for your attention to this matter.

Institutional Review Board (IRB)
Continuing Review of Ongoing Clinical, Laboratory and Miscellaneous Protocols

Print Vers

Report Date: 03/20/09 **Due Date:** 03/06/09

The continuing review process is a requirement of this institution in compliance with federal regulations. The study Chairperson is responsible for updating the protocol status by providing the following information electronically to the Institutional Review Board for potential approval by the due date shown above. Direct your questions to the Office of Protocol Research at (713)792-2933 or send an email to IRB_ContinuingReview@mdanderson.org.

Protocol Number and Title: ID01-296 - EPIDEMIOLOGICAL, MOLECULAR AND CLINICAL MARKERS OF PROSTATE CANCER PROGRESSION

Study Chairperson: Sara Strom
E-mail: sstrom@mdanderson.org
NCI Support Grant Program: Epidemiology

For IRB4 Committee Review: 03/18/09
Last Continuing Review: 05/12/08

APPROVED 04/11/09

Sponsor/Supporter:

Notes

⚠ Currently the co-investigator and/or collaborator list for this protocol exists as shown. Please submit a revision to the Office of Protocol Research if the list appears incorrectly.

Collaborators — Click here
Co-investigators — Click here

Current Protocol Status (Date)

07/18/01 **Original IRB Approval**
_____ **Informed Consent**
Waiver of informed consent: ☑ Yes ☐ No

02/11/02 **Active** (study in progress and accruing patients)

_____ **Request Close To New Patient Entry** (no new patient accrual, but patients continuing on treatment or still alive for follow up)
Date last patient entered _____

_____ **Request Termination** (no activity - all patients off study and no longer being followed)
NOTE: OFF DATE must be entered and a written summary must be attached that describes accrual, any toxicities and response data, and outcome(s) of research.

Is this a multicenter study? ☐ Yes ☑ No Maximum number of **multicenter** subjects approved 0

Maximum number of **MDACC** subjects approved 1500 Registration required? ☐ Yes ☑ No

Total accrual to date on PDMS 0

Total accrual to date NOT registered in PDMS or CORe _____

Are all subjects off active intervention? ☑ Yes ☐ No
If yes, are subjects in long term follow-up? ☑ Yes ☐ No

Total AEs reported 0 AEs since last review 0 Number of treatment related deaths 0

Give a summary of the toxicity profile? ☑ Not Applicable If n/a, explain why. (Printout of adverse events not acceptable)
This is a follow-up study of patients consented under protocol M91-004. There was no clinical intervention for this protocol nor the parent one therefore there is no risk of toxicity associated with participation.

Give a summary of the response profile? ☑ Not Applicable If n/a, explain why.
This is a follow-up study of patients consented under protocol M91-004. There was no clinical intervention for this protocol nor the parent one therefore there is no response associated with participation.

Who is monitoring the conduct of this study? Principal Investigator
N/A

Have any recent reports of preliminary analyses been prepared since the last review? ☑ Yes ☐ No
If yes, provide an attachment below

What is the result of an interim analysis or when is one planned?
We found higher saturated fat consumption to be associated with increased risk of prostate cancer progression following prostatectomy, especially among obese men.

Why should the study remain open?
We are continuing to follow-up patients to evaluate for additional occurrences of disease progression.

Please provide any additional comments or any overall synopsis of the study below.
N/A

Optional attachments as supporting information: fat strom 2008.pdf

Electronically signed by Sara Strom on 03/20/09 @ 13:01
Study Chairman (signature and date)

IRB Comments / overall assessment

Electronically signed by Charlotte C. Sun on 04/11/09 @ 14:53
IRB Chairman or Designee (signature and date)

☐ Approved ☑ Approved Contingent
☑ Expedited Review ☐ Full Review

Protocol A-14108 (Proposal PC061038): Evaluating the role of genetic markers in prostate cancer progression: a multiethnic cohort experience (Sara S. Strom, PhD, PI)

Research Design. This proposal is a follow-up chart review study of a cohort of 1380 prostate cancer (PCa) patients for whom we have already collected baseline clinical and epidemiologic information and have banked specimens as part of studies conducted in our department. Patients will be identified by a unique alphanumeric study number that was sequentially generated as patients were invited to participate in the baseline study. Study numbers are linked to patient information in a password-protected secure FoxPro database maintained and backed-up on the departmental computer network. Access to this particular database is limited to study personnel. All hard copies of study records are maintained in the study office until patient follow-up abstractions are completed; once abstractions are completed, files are kept in our restricted-access file room. There are no randomization procedures for this study.

Study Population and Sample.

1. Target Population. The study population for this proposal is comprised of Caucasian, Mexican-American and African-American PCa patients enrolled in NIH/DoD funded PCa studies we have conducted for whom we have banked biological samples and baseline data. Since this proposal seeks to find explanations for racial/ethnic disparities between Caucasians, Mexican-Americans and African-Americans, men who did not self-classify as being a member of any of these racial/ethnic groups in their baseline interview will not be included this follow-up study. Age is limited to adults, as adenocarcinoma of the prostate is extremely rare in those under the age of 18 and may represent a different disease. Additionally, the study population is restricted to males as females are not at risk for developing PCa.

1. Sample Size Justification. Based on our sample size estimation and power calculations, with a sample size of 1380 (N = 773 Whites, N = 246 Hispanics, and N = 361 African Americans), we should have sufficient power to detect the relative risk estimates listed in Table 1 below. The population prevalence estimates used to calculate the minimum detectable hazard ratio (HR) listed in Table 1 were based on published genotypic frequencies and our preliminary data.

Table 1. Detectable Relative Risk Estimates (N = 773 Whites, N = 246 Hispanics, and N = 361 African Americans)

Characteristics of Interest	Detectable HR (White)	Detectable HR (Hispanic)	Detectable HR (African-American)
Obesity	1.35	1.72	1.56
Ever Smoker (current/past)	1.38	1.82	1.62
Family history of PC	1.41	1.82	1.64
MMP-1	1.36	1.72	1.56
MMP-9	1.38	1.75	1.58

VEGF	1.37	1.73	1.58
MMP-1 & Ever smoker	1.41	1.82	1.64

2. Sampling Method. The racial/ethnic composition of the patients in our cohort is representative of the racial/ethnic composition of PCa patients. A random sample of all PCa patients were recruited.

4. Inclusion and Exclusion Criteria. Men with adenocarcinoma of the prostate were included in the baseline protocol. Patients who had a prior history of any invasive cancer (excluding non-melanoma skin cancers) were excluded. Cases were restricted to residents of the United States.

5. Pregnant Women, Human Fetuses and Neonates Involved in Research. Not applicable.

6. Biomedical and Behavioral Research Involving Prisoners as Subjects. Not applicable.

Recruitment and Informed Consent Process.

1. Recruitment of Subjects. Patients who were identified to be eligible were invited to participate in the baseline protocol by a Research Interviewer. The study objectives and procedures were explained to each patient, and patients were given a copy of the UTMDACC Institutional Review Board approved consent form to review. There were no advertisements for this study.

2. Informed Consent Process. At the time of baseline enrollment, the interviewer reviewed the consent form and study procedures (i.e., interview, anthropometric measurements, and blood sample collection) with each participant; and each participant was given an opportunity to ask any questions that he may have prior to being asked to sign the consent form. The informed consent form fulfills the requirements set out by the UTMDACC Institutional Review Board. The patients were given the opportunity to refuse participation and were assured that such a refusal would in no way affect their treatment.

3. Intent to Benefit. Patients who were not capable of providing their own consent were not included in the baseline protocol since interviews with the patients' themselves was a significant source of the baseline data. Proxy interviews were not part of the baseline procedures.

4. Consent of Legally Authorized Representative. Not applicable.

5. Consent for Medical or Surgical Procedures. The informed consent form was signed by all participants and included a section outlining possible risks associated with participating in the baseline study. The risks associated with study participation were not greater than those associated with routine blood collection. These minor risks included pain, bleeding, bruising, and/or infection. The psychological risks posed may have led to anxiety engendered by questions pertaining to health and lifestyle habits. In our years of experiences with administering this questionnaire, we have not encountered any adverse effects or objections from respondents.

Data Collection. Data were collected using interviewer-administered questionnaires at baseline following obtaining informed consent, as described above. Follow-up data are collected through chart abstractions using a standardized form to be developed by the study personnel upon study commencement.

1. Screening Procedures. There are no screening procedures included in this protocol.

2. Laboratory Evaluations. Blood specimens are collected and banked as part of the baseline protocol.

    a. 25 mL of venous blood were collected in Vacutainer tubes with heparin (green-top tubes). Sample collections were scheduled in conjunction with patients' other blood collections whenever feasible. Patients were informed that the specimen collected for the baseline protocol is for research purposes, and no clinical information will be reported back to them on an individual basis.

    b. Evaluations to be made. As part of this protocol, we will extract DNA from stored whole blood and cell pellets for the genotyping analyses proposed.

    c. Storage. Whole blood and all separated blood components have been stored in several –80° freezers in our departmental Populations Science Laboratory. Multiple aliquots of each sample for each individual have been maintained and stored in separate freezers. Each specimen was labeled with the unique laboratory identifier number. Samples will be maintained for at least 10 years following study termination.

    d. Labs performing evaluations and special precautions. The analyses will be performed in the Genotyping Core in the Department of Epidemiology. We have extensive experience in collecting and archiving biological specimens, including blood, serum, and DNA. For quality controls of data obtained with PCR assays, we employ several measures to insure the quality and integrity of the DNA: 1) we use PCR workstations to protect our working area from the open environment; 2) we use the highest-quality reagents for all sample handling; 3) we have isolated our thermocyclers from our general work space to minimize contamination; and 4) we perform a daily decontamination procedure on the work area. To insure the accuracy of the data set, we routinely regenotype 10% of our sample sets at random. For difficult samples, we will repeat assays or samples will be sequenced for allele scoring. For all genotyping studies, data are reviewed and genotypes assigned by persons blinded to case status. For all PCR performed, samples are run with well-characterized control DNAs.

3. Clinical Assessments.

    a. Schedule of clinical evaluations and follow-up procedures. Not applicable

    b. A description of how adverse events will be recorded should be included when

appropriate. All unanticipated problems involving risk to subjects or others, serious adverse events related to participation in the study and subject deaths related to participation in the study will be promptly reported by phone (301-619-2165), by email (hsrrb@det.amedd.army.mil), or by facsimile (301-619-7803) to the USAMRMC, Office of Research Protections, Human Research Protection Office. A complete written report will follow the initial notification. In addition to the methods above, the complete report will be sent to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-ZB-PH, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

c. Disposition of clinical data. All hard copies of patient data, including questionnaires, consent forms, medical release forms and chart abstractions will be stored for a minimum of 10-years in our long-term storage file room. Access to this room is restricted and requires a security swipe badge for study personnel.

4. Methods used for data collection. Baseline data were collected by interviewer administered standardized questionnaire (Appendix 1). Data for the proposed study will be collected using a standardized abstraction form to be finalized by study personnel at study commencement.

Data Management.

1. Data Analysis. In this follow-up study, the primary endpoints are BF, clinical recurrence and death. Cases will be censored at time of follow-up, date of last contact or death, whichever is last. Time will be measured two ways: from diagnosis and from completion of treatment to the endpoints previously defined (see proposal). Based on published data, we expect a minimum of 413 failure or recurrences in study cohort (allowing for a 5% dropout rate). We expect that more than 30% of patients will be deceased at the end of the funding period.

   We will evaluate the associations between obesity, clinical markers (e.g., Gleason score, PSA at diagnosis, and clinical and pathological stage), epidemiological characteristics and genetic polymorphisms as predictors of time to disease progression using Cox proportional hazards regression modeling for each ethnic/racial group to calculate hazard ratios (HR). We will adjust for known clinical prognostic factors, specifically treatment received, through stratification of variables. We will adjust for known confounders, such as clinical parameters (i.e., Gleason score, clinical stage, etc.). Because the problem of multiple comparisons is always an issue in this type of study, we will concentrate on the most relevant risk factors and will control for type I errors using Bonferroni-type adjustments in our models. We will also consider permutation based p-values because Bonferroni corrections are in general conservative. Age will be treated as a continuous variable. BMI will initially be evaluated as a continuous variable, and graphical methods will be used to assess the actual form of its association. The standard cut-point of BMI $\geq$ 30 mg/kg^2 to define obesity and <30 mg/kg^2 as non-obese will be used. The family history analyses will focus on number of first-degree relatives with PCa. Smoking status will be classified as current, former, or never smoked. As shown in table 5, we will have sufficient power to test our primary hypotheses even when we stratify our data according

to different ethnic groups. These estimates in minimum detectable HR were based on published genotypic frequencies and our preliminary data.

2. Disposition of Data. All hard copies of patient data, including questionnaires, consent forms, medical release forms and chart abstractions will be stored for a minimum of 10-years in our long-term storage file room. Access to this room is restricted and requires a security swipe badge for study personnel. All electronic data are stored on our departmental network which is backed-up daily, and the data are stored in a restricted access partition with access limited to study personnel. All data will be stored for a minimum of 10 years following study termination.

3. Confidentiality. Respondents were assured that their confidentiality would be rigorously maintained by the project investigator and study personnel. All identifying information restricted to one page in the baseline questionnaire, which has been removed prior to data entry and stored in locked files in the Department of Epidemiology. Thereafter, respondents are identified only through identification number and results from this study will be reported only in the aggregate. The computer files are password-protected on a restricted access partition of the secure network to further ensure database security.

Risks/Benefits Assessment.

1. Risks. The possible risks associated with the baseline protocol were not different from those associated with routine blood collection and include pain, bleeding, bruising and/or infection. The psychological risks posed might lie in anxiety engendered by questions pertaining to current health and lifestyle habits. Fatigue related to completing the questionnaire was also feasible. However, in our years of experience in administering this baseline questionnaire we have not encountered any adverse effects or objections from respondents. There are no risks associated with the currently proposed protocol as patients will not be personally interviewed nor will any additional samples be required; it is simply a chart review, genotyping, and data analysis.

2. Precautions. For the baseline sample collection, precautions were taken to minimize the risk of injury by using trained/certified phlebotomists. All research interviewers were thoroughly trained in administering standardized questionnaires.

3. Special Care Needs. There are no specific special care needs associated with this protocol.

4. Benefits. There are no direct benefits for the individual participants. This study has the potential to identify factors that may explain racial/ethnic disparities in PCa prognosis.

Study Personnel

1. Biosketches for all key personnel have been previously submitted. Documentation that these personnel have been trained in Good Clinical Practices and Human Subjects Research is submitted under a separate cover.

2. Following are the roles and responsibilities for study personnel:
   Sara S. Strom, PhD, Principal Investigator will be responsible for the overall direction of this project and the integration of the epidemiological, clinical and laboratory components. She will work closely with Dr. Kuban to determine progression status for all participants. She will be responsible for data analysis, preparation of progress reports, and manuscripts for publication. She will supervise the study coordinator and research interviewers.
   Randa El-Zein, MD, PhD, Co-Investigator is an experienced molecular biologist who has collaborated with Dr. Strom on several different research grants. She will be responsible for overseeing and coordinating laboratory analysis with the Epidemiology Genotyping Core. She will work closely with Dr. Strom in laboratory data interpretation and manuscript preparation.
   Sanjay Shete, PhD, Co-Investigator will be responsible for developing the appropriate biostatistical approaches to analyze the data for each specific aim. He will work with Dr. Strom in interpreting analytic results and assist in model-building.
   Deborah Kuban, MD, Collaborator is the Deputy Chair of the Department of Radiation Oncology. She will provide clinical expertise in determining disease progression in patients treated with radiation, and will also assist in categorizing patients by treatment. She will work closely with Dr. Strom and other collaborators in determining progression status.
   Timothy McDonnell, MD PhD, Collaborator is an experienced urological pathologist. He has extensive experience in clinical research and will be responsible will provide clinical expertise in pathological staging for all patients. He will work closely with Dr. Strom and other researchers in the interpretation of results and writing of manuscripts.
   Mandy Chan, MS, Study Coordinator will be responsible for the day-to-day coordination and administration of study activities. She has extensive experience in all aspects of data collection. She will supervise the research interviewer and will be responsible for data quality, medical abstractions, and data management. She will coordinate sample retrieval with Dr. El-Zein, and will also maintain the genotyping data files. Additionally, she will assist Dr. Strom in the preparation of reports.
   Yessica Nunez, Research Assistant will be responsible for obtaining updated medical information from all institutions where patients have received PCa-related care. She will request all patients who have received care outside of UTMDACC to sign a release of medical information and will assist Ms. Chan (Study Coordinator) in abstracting medical records. Ms. Nunez will be responsible for data entry.

3. Conflict of Interest. The Investigators of this grant have no financial interest with a research sponsor nor any other significant financial interest that may reasonably appear to affect or be affected by the research.

4. Medical Monitor. Not applicable, this is a "not greater than minimal risk" protocol.

Modification of the Protocol. If changes in this protocol are indicated by the USAMRMC ORP HRPO, then we will submit a revision to our Institutional Review Board requesting their approval of the changes requested by the USAMRMC ORP HRPO. Following UTMDACC

Institutional Review Board approval, the revisions will be made to this protocol, and the revised protocol would be re-submitted to the USAMRMC ORP HRPO. Major modifications to the research protocol and any modifications that could potentially increase risk to subjects must be submitted to the USAMRMC ORP HRPO for approval prior to implementation. All other amendments will be submitted with the continuing review report to the USAMRMC ORP HRPO for acceptance.

Protocol Departure. Not applicable

Withdrawal from the Protocol.

1. Subjects may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. Patients were advised at the time informed consent was obtained that they may decide to discontinue participation at any time and that this decision would not affect the care they receive at our institution.

2. All participants in this study have already agreed to participate in our research. We do not anticipate withdrawals to occur from this protocol, as we will only be abstracting medical records.

Adverse Event Reporting. Since this study is a chart review and analysis of data and banked specimens, we do not anticipate any serious and /or unexpected or unanticipated events to occur.

Medical Care for Research Related Injury. Participants were provided with a copy of the informed consent form they signed that has the phone number of the UTMDACC Institutional Review Board Office in case of any questions about study-related injuries. Again, as this study is a chart review and analysis of data, we do not anticipate any research-related injuries to occur.

A copy of the approved continuing review report and the local IRB approval notification have been submitted to the USAMRMC ORP HRPO on the CDMRP website. A copy of the original baseline protocol, consent form and questionnaire are submitted as Appendix 1. A copy of the approved final study report and local IRB approval notification will be submitted to the USAMRMC ORP HRPO as soon as these documents become available.

This protocol ("Evaluating the role of Genetic Markers in Prostate Cancer Progression: A Multiethnic Cohort Experience" PC061038, Award Number W81XWH-07-1-0648, HRPO Log Number A-14108) recently received its annual review and approval by the University of Texas M.D. Anderson Cancer Center's Institutional Review Board (reviewed 05/21/08, approved 06/09/08). Please find attached copies of the review memo and the IRB's approval notice. No changes have been made to the protocol since the previous review. There is no consent for as this protocol was granted a waiver of informed consent. To date, we have completed medical record abstractions for 735 prostate cancer patients. These data are being entered into the clinical database. We are in the process of requesting copies of outside medical records for the men who received care outside of our institution as well as continuing to abstract institutional medical records for the remainder of the patient cohort. Additionally, we are preparing the CDC IRB application so that we can request vital status from the National Death Index. As proposed, death certificates will be procured for all deceased participants to determine immediate and underlying causes of death. Genotyping assays have been established and optimized in the departmental Genotyping Core, and DNA has been extracted from approximately 90% of the patients' archived whole blood.