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PRINCIPAL INVESTIGATOR: Dr. Amit Algotar

CONTRACTING ORGANIZATION: The University of Arizona

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14. ABSTRACT Current diagnostic modalities are inadequate to reliably differentiate between aggressive and indolent forms of prostate cancer (PCa). A significant number of men receive potentially unnecessary treatment along with associated morbidities. Identification of novel risk factors will allow for more reliable early diagnosis of PCa. Defective sensors of DNA damage and the resulting genetic instability likely are involved in the early development of PCa. The objective of this project is to determine if DNA damage and genetic instability are harbingers of PCa using prostate biopsy samples from men at high risk for this disease.					
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INTRODUCTION:

Current diagnostic modalities are inadequate to reliably differentiate between aggressive and indolent forms of prostate cancer (PCa). A significant number of men receive potentially unnecessary treatment along with associated morbidities. Identification of novel risk factors will allow for more reliable early diagnosis of PCa. Defective sensors of DNA damage and the resulting genetic instability likely are involved in the early development of PCa. The objective of this project is to determine if DNA damage and genetic instability are harbingers of PCa using prostate biopsy samples from men at high risk for this disease. Expression of ERG and/or PTEN and TMPRSS2/ERG translocation will be used as indicators for genetic instability. Association of DNA damage and genetic instability with indicators of disease aggressiveness (Gleason score and PSA velocity) will also be investigated. Formalin-fixed, paraffin-embedded prostate tissue biopsy slides from 150 men enrolled in a chemoprevention trial conducted at the Arizona Cancer Center. This trial was known as the negative biopsy trial (NBT) and the its primary aim was determine if selenium supplementation can reduce incidence of prostate cancer as compared to placebo. Primary analysis of this trial indicated no statistically significant effect of selenium supplementation on prostate cancer incidence. As a result, all the data, biological samples and biopsy tissue that were collected during the conduct of this trial could be used for subsequent research projects. The slides collected during NBT and identified for the current project will be processed for expression of markers of DNA damage and genetic instability using immunohistochemistry and fluorescence in-situ hybridization. Sensitivity, specificity, and area under the curve will be calculated to determine their utility as predictors of subsequent diagnosis of PCa.

Body:

Tasks completed during the course of first project year.

Block 1: Months 1-6, January 2012 to June 2012.

Task 1: Gaining clinical knowledge regarding prostate cancer

- In order to gain in-depth clinical knowledge regarding prostate cancer, Dr. Algotar attended the genitourinary oncology clinic with Dr. Frederick Ahmann, an expert genitourinary oncologist at The University of Arizona Cancer Center. Dr. Algotar also attended histopathologic evaluation of prostate biopsy and prostatectomy tissue with Dr. Nagle to learn about tissue acquisitions, tissue sectioning, tissue processing for H&E staining as well as barriers, pitfalls, troubleshooting and optimum procedures for each of the above steps. Additionally, Dr. Algotar was also able to accompany Dr. Nagle to learn how prostate cancer is detected in an H&E stained tissue section and how it is graded histopathologically.

Task 2: Preparing project documentation for scientific and human subjects review

- This has been completed. Please see appendix A.

Task 3: Training in laboratory techniques needed for this project

- 3a: Immunohistochemistry procedures, staining by hand, imaging under the supervision of Dr. Nagle's laboratory manager Kathleen McDaniel. This was done by using H2AX antibody and a fluorescence system for detection. Result interpretation carried out with Dr. Nagle.
- 3b: Immunohistochemistry procedures, staining by Ventana DiscoveryXT machine, imaging under the supervision of Dr. Nagle's laboratory technician Edward Abril using ERG antibody and colorimetric detection system. Result interpretation carried out with Dr. Nagle.

Task 4: Meetings and conferences

- Attended weekly mentoring meetings with primary and secondary mentors
- Attended six monthly mentoring committee meetings with mentoring committee
- Attended weekly meetings and seminars: Prostate Invasion and Metastasis Group, Prostate Cancer Translational Research meetings, Urology Grand Rounds, Cancer Prevention and Control Seminar, and Cancer Biology Seminar.
- Attended monthly meetings and seminars: Medical Oncology Genitourinary Conference, Frontiers in Medical Research and Hematology-Oncology Conference
- Attended quarterly meetings: Post-doctoral training workshop and AZCC/Ventana Medical Systems Quarterly Forum
- Department of Defense's Prostate Cancer Research Program organized "IMPACT" conference did not take place during this period, hence could not attend.

Block 2: Months 7-12, July 2012 to December 2013

Task 1: Courses

- Completed course title, "Oncogenes and Signal Transduction", Course number "CBIO 595A", Credits: 3

Task 2: Processing slides for immunohistochemistry (IHC)

- Identification, isolation, staining, processing, and statistical analysis of slides for ERG and PTEN markers (aim 1) and interpretation of these results with Drs. Stratton, Cress and Nagle. The goal of aim 1 was to determine if ERG-PTEN expression pattern in biopsy tissue can be used as predictors of prostate cancer diagnosis. A case-control study design was used in which men diagnosed with prostate cancer were considered to be the cases and those not diagnosed with prostate cancer were considered to be controls. The assay protocol was successfully optimized and implemented to stain study slides (figure 1).

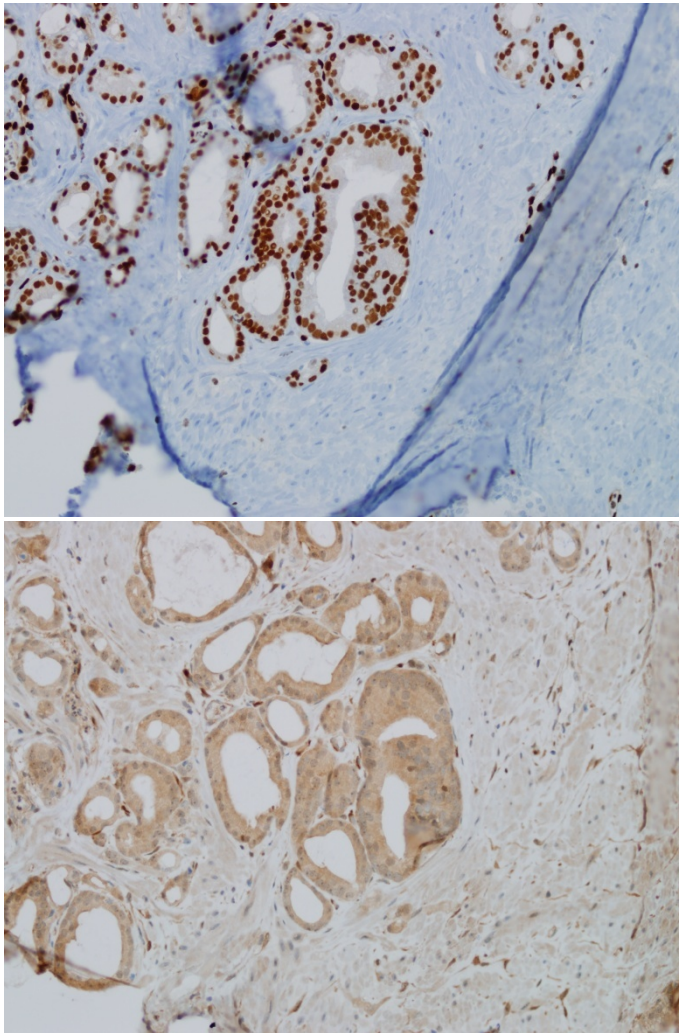


Figure 1: Prostate glandular tissue showing staining for ERG (top) and PTEN (bottom).

- All cases (N = 50) and a subset of control slides (N = 30) were stained. All cases except 1 demonstrated ERG+/PTEN+ expression. This distribution was much lower than had been anticipated and as a result did not reject the null hypothesis which was, there are no differences in the ERG/PTEN expression patterns between men diagnosed with prostate cancer and those not diagnosed with prostate cancer (Table 1). Since the null hypothesis could not be rejected, further staining of slides was stopped in order to conserve precious biological tissue. One explanation of this phenomenon could be the possibility that changes in ERG/PTEN expression pattern may be a late event and may not have taken place at the time of the biopsy. Second possibility is that due to archival, the tissue may have lost its epitope hence the antibody may not be able to bind to it.

Positive	Men diagnosed with prostate cancer	Men not diagnosed with prostate cancer
ERG	1	0
PTEN	50	30

- In light of these findings, an alternative hypothesis has been proposed. In this new hypothesis, prostate biopsy slides from men diagnosed with prostate cancer opting for active surveillance as their treatment modality are being stained for ERG/PTEN expression patterns to determine if ERG/PTEN expression patterns are associated with prostate specific antigen velocity, a commonly used marker of disease progression in men diagnosed with prostate cancer. This is a plausible hypothesis since ERG/PTEN expression has been associated with aggressive disease and high PSA velocity is an indicator of aggressive disease. We propose to investigate this hypothesis in sample of patients that participated in a Phase 2 clinical trial investigating the effect of selenium supplementation on prostate cancer progression. Results of this trial indicated that selenium did not have an effect on prostate cancer aggressiveness as measured by PSA velocity and hence biopsy tissue samples collected as part of the parent Phase 2 clinical trial can be used for this pilot project. The dataset and population are ideal for this pilot study since in this study PSA was measured every three months giving an accurate estimation of the subjects PSA velocity. The data from this trial demonstrates wide range of PSA velocities making this an ideal dataset to investigate this pilot project.
- Problems associated with conduct of this study: The service provide for IHC has had multiple instrument failures over past several months which has delayed this project. However this has now been resolved.

Task 3: Processing slides for fluorescence in-situ hybridization (FISH)

- The purpose of conducting FISH was to confirm translocation of the ERG gene. Since lack of ERG expression has consistently shown to be associated with absence of ERG translocation this was not performed. However, it can be pursued in the alternative hypothesis proposed above.

Task 4: Meetings and conferences

- Attended weekly mentoring meetings with primary and secondary mentors
- Attended six monthly mentoring committee meetings with mentoring committee
- Attended weekly meetings and seminars: Prostate Invasion and Metastasis Group, Prostate Cancer Translational Research meetings, Urology Grand Rounds, Cancer Prevention and Control Seminar, and Cancer Biology Seminar.

- Attended monthly meetings and seminars: Medical Oncology Genitourinary Conference, Frontiers in Medical Research and Hematology-Oncology Conference
- Attended quarterly meetings: Post-doctoral training workshop and AZCC/Ventana Medical Systems Quarterly Forum
- Was not invited to the Department of Defense's Prostate Cancer Research Program organized "IMPACT" conference, hence did not attend. The program officer explained that due to lack of funds and changes in rules, the IMPACT conference is going to be much smaller and hence not all awardees would be invited for it.

KEY RESEARCH ACCOMPLISHMENTS: Bulleted list of key research accomplishments emanating from this research.

- Identification and isolation of unstained slides needed for this project (N = 600) from a dataset consisting of more than 1500 slides. Additionally one H&E slide was also identified and isolated per subject (N = 225) to enable the pathologist to review if needed
- Staining, processing, and interpretation of these results of aim1 was done with Drs. Stratton, Cress and Nagle. Results indicated that the null hypothesis could not be rejected. This provides new insight into the role of ERG/PTEN in men high risk for prostate cancer. This led to the proposal of an alternative hypothesis which could further elucidate the role of ERG/PTEN in prostate cancer.
- Training in laboratory methods and procedures to conduct immunohistochemistry staining was obtained. This training consisted of conducting the staining by hand and also by using the Ventana Discovery-XT machine. Pros and cons of both these procedures were understood which will help with the conduct and interpretation of the current project and also subsequent projects.
- Clinical knowledge regarding presentation of patients and their concerns regarding advanced stage cancer was gained by attending the genito-urinary oncology clinics at The University of Arizona Cancer Center with Dr. Frederick Ahmann.
- "Oncogenes and Signal Transduction" strengthened Dr. Algotar's knowledge regarding cancer biology
- Meetings, conferences and seminars also contributed to strengthening Dr. Algotar's knowledge about cancer biology, epidemiology, research methods, especially with respect to prostate cancer.

REPORTABLE OUTCOMES: Provide a list of reportable outcomes that have resulted from this research to include:

- Manuscripts:
 - o Nagle R.B., **Algotar A.M.**, Cortez C.C., Smith K., Jones C., Sathyanarayana U.G., Yun S., Riley J., Nagy D., Dittamore R., Dalkin B., Brosh L., Pestano G. ERG Overexpression and PTEN Status Predict Capsular Penetration in Prostate Carcinoma. (Under review)
 - o **Algotar A.M.**, Stratton M. S., Ranger-Moore J., Ahmann F. R., Nagle R.B., Slate E., Hsu C.H, Clark L. C., Stratton S. P. Phase 3 clinical trial investigating the effect of selenium supplementation in men at high risk for prostate cancer. Prostate. 2012 Aug 10. doi: 10.1002/pros.22573
 - o **Algotar A.M.**, Thompson P.A., Ranger-Moore J., Stratton M.S, Hsu C.H., Ahmann F.R., Stratton S. P. Differences in characteristics of men with localised prostate cancer who demonstrate low, intermediate or high prostate-specific antigen velocity. Intern Med J. 2012 Apr;42(4):374-80. doi: 10.1111/j.1445-5994.2011.02473.x.
 - o **Algotar A.M.**, Hsu C.H., P. Singh, Stratton S. P. Selenium supplementation does not affect serum glucose levels in men at high risk for prostate cancer. (In press Journal of Diabetes)
- Book chapter:
 - o **Algotar A.M.**, Stratton M.S., Cress A.E. A new paradigm for prostate cancer prevention studies. Fundamentals of cancer prevention. Third edition. Springer publications. 2013.
- Patents:
 - o Pestano G., Nagle R.B., Cortez C., Vanpatten C., **Algotar A.M.** Expression of ETS related gene (ERG) & phosphatase & tensin homolog (PTEN) correlates with prostate cancer capsular penetration. (Pending)
- Grants applied:

Date applied	Sponsor	Project Title
5/1/2012	Department of Defense	Integrin $\alpha 6 \beta 4$ Mutations as predictors of prostate cancer in men at high risk for prostate cancer
5/1/2012	Department of Defense	PSA isoform kinetics as predictors of prostate cancer
2/15/2012	The University of Arizona Cancer Center Support Grant	Predictive utility of DNA damage and genetic instability towards prostate cancer diagnosis
6/4/2012	Better Than Ever Foundation	Pilot study to determine the clinical utility of PSA isoform kinetics as predictors for prostate cancer
12/16/2012	Patient Centered Outcomes Research	ERG-PTEN expression in biopsy tissue as predictions of aggressive prostate cancer

	Institute	
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CONCLUSION:

This project aims to determine if DNA damage and genetic instability are harbingers of prostate cancer using prostate biopsy samples from men at high risk for this disease. During the first year of this project, identification, isolation and staining of slides to investigate aim1 of this grant were carried out. Results of this stain did not allow for rejection of the null hypothesis. This gave investigators new insight into the role of ERG/PTEN expression in prostate cancer. Due to these results, an alternative hypothesis has been proposed and is planned to be investigated in year 2. During year 1, identification and isolation of slides needed for aim2 has also been accomplished. Staining of these slides will be carried out in year 2. In addition to the above mentioned laboratory activity, Dr. Algotar was able to strengthen his knowledge base regarding the clinical aspects of prostate cancer by accompanying Dr. Ahmann in the genitourinary oncology clinic. He was also able to learn laboratory staining techniques for ERG and PTEN under the supervision of Drs. Nagle and Cress. Dr. Algotar was also able to strengthen his knowledge base regarding cancer biology as a result of completing the class “Oncogenes and Signal Transduction” and interactions with experienced investigators during seminars and meetings.

REFERENCES:

APPENDICES:

Appendix A: NBT consent form and PHI release

SUPPORTING DATA: All figures and/or tables shall include legends and be clearly marked with figure/table numbers.

SUBJECT'S CONSENT FORM Page 1 of 6
PHASE III TRIAL OF SLENIUM FOR PROSTATE CANCER PREVENTION
(NEGATIVE BIOPSY TRIAL) HSC#: 99-11

I AM BEING ASKED TO READ THE FOLLOWING MATERIAL TO ENSURE THAT I AM INFORMED OF THE NATURE OF THIS RESEARCH STUDY AND OF HOW I WILL PARTICIPATE IN IT, IF I CONSENT TO DO SO. SIGNING THIS FORM WILL INDICATE THAT I HAVE BEEN SO INFORMED AND THAT I GIVE MY CONSENT. FEDERAL REGULATIONS REQUIRE WRITTEN INFORMED CONSENT PRIOR TO PARTICIPATION IN THIS RESEARCH STUDY SO THAT I CAN KNOW THE NATURE AND RISKS OF MY PARTICIPATION AND CAN DECIDE TO PARTICIPATE OR NOT PARTICIPATE IN A FREE AND INFORMED MANNER.

PURPOSE

I am being invited to participate voluntarily in a research study of the use of daily Selenium supplements in the prevention of prostate cancer. Selenium is an essential trace element that is required as part of a human diet. This double blind randomized study is designed to test the possibility that a supplement of Selenium may decrease the risk of developing prostate cancer. One previous trial in patients with a history of cancer of the skin observed a significantly lower risk of developing prostate cancer in patients who were in the Selenium supplemented group. The purpose of this study is to determine if Selenium supplementation will decrease the risk of developing prostate cancer. Two different dosages of Selenium will be used to try to determine which would be the most effective dose to use in the prevention of prostate cancer. This study does not use Selenium as a treatment option for the possible cure of prostate cancer.

SELECTION CRITERIA

I am being invited to participate because I have had persistently elevated Prostate-Specific Antigen (PSA) levels, or an abnormal rectal exam, and have had at least one negative biopsy for prostate cancer. I will be one of at least 700 individuals participating in this study being conducted under Investigational New Drug #29829 from the Food and Drug Administration.

STANDARD TREATMENT

Patients may take selenium supplements, which may be beneficial to preventing prostate cancer, without participating in this trial. If I decide not to participate in this study, I should continue monitoring my PSA level with my physician and wait for any possible changes. I will need to consult my regular physician to discuss these changes, should they occur. Participating in this trial will not limit my choice of treatments if I were to develop a rising PSA level or prostate cancer during this study.

PROCEDURE(S)

If I agree to participate, I will be asked to complete questionnaires about my health habits (such as smoking), use of vitamins or medicines, and history of medical problems at each visit. A blood sample of approximately 30 cc. (2 tablespoons) will be collected from me at the beginning of the study and at each of my regularly scheduled study visits. These visits are scheduled monthly for the first two months and then semiannually thereafter. The amount of Selenium in these blood samples will be measured in addition to the level of prostate specific antigen (PSA). My first, second and then yearly blood draw will be tested to ensure that my kidneys and liver are functioning within normal limits. Other analyses related to prostate cancer (including genetic testing) may be done on these samples in the future if warranted by

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PHASE III TRIAL OF SELENIUM FOR PROSTATE CANCER PREVENTION
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new scientific or medical information. In conjunction with the semiannual blood draw, and I will be asked to report any new illness requiring a physician's care, new medications that I am taking, and any hospitalizations that have occurred. If I am hospitalized or develop any significant new illness or a worsening of an existing illness I give my permission for the study investigators to obtain my medical records in order to determine the reasons for my hospitalization and the treatments which I received. This information will remain confidential. I will be monitored for all new illnesses and symptoms, since there is always the possibility for undescribed side effects to occur that can only be detected in double blind clinical trials. In addition, I will receive periodic telephone calls from study coordinators to discuss the trial and determine if I have any questions or concerns.

Most men with elevated PSA will have a biopsy in the next 4 years. Therefore, in the last year of the trial, I may be requested to have a biopsy, per the usual standard of care, performed by my urologist in order to determine if I have prostate cancer. As with all medical decisions, the final decision for future biopsies will be made by me and my physician.

At study entry, I will receive a 1 month supply of placebo tablets of Baker's yeast in order to determine if I have any problems taking the study tablets. Placebo tablets are made up of Baker's yeast (without the additional Selenium which is in the Selenium supplements) and are identical in size and appearance to Selenium tablets. After I am enrolled in the study I will be assigned by chance to one of three groups, two of which will take Selenium. One Selenium group will take 200 mcg daily in a yeast tablet, one group will take 400 mcg of Selenium daily in a yeast tablet, and the remaining group will receive a placebo yeast tablet. The group of patients taking the placebo tablets will serve as the control group for the study. I will take these tablets daily for up to five years. Neither I nor my physician will know to which supplementation group I was assigned, although this information may be given to my physician if it is medically necessary or in the event of an emergency. I will have a 2 in 3 chance (66%) of receiving Selenium supplements in this trial. I will receive a 6 month supply of tablets at randomization and semiannually thereafter.

Study personnel will obtain prostate tissue samples from all biopsies to examine biomarkers of prostate cancer. The samples will be obtained directly from the appropriate pathologist(s), and all information will remain strictly confidential.

RISKS

There are no known consequences to my health if I am in the placebo group since it contains Baker's yeast. There is a slight possibility that intolerance or allergic reaction to yeast will occur. If I am assigned to one of the Selenium groups, there is a risk that I could develop side effects including garlic breath, nail brittleness, and hair breakage. If I believe that I have developed these or other symptoms related to the Selenium supplementation, I will notify a study nurse as soon as possible at (520) 321-7798 or 1-800-243-6519. I may be asked to stop taking my tablets for a minimum of 30 days and have a special blood draw of approximately 17 cc (1 ¼ tablespoon). This sample will be analyzed for the amount of selenium in my blood and normal functioning of my kidney and liver. I will be eligible to restart my study tablets after my symptoms have resolved and my laboratory results have been confirmed to be within normal limits. These side effects have mainly been observed in approximately 10% of Chinese subjects

SUBJECT'S CONSENT FORM Page 3 of 6

PHASE III TRIAL OF SELENIUM FOR PROSTATE CANCER PREVENTION
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consuming a diet with over 1,000 mcg Selenium daily. With chronic or prolonged high Selenium intakes above those used in this trial, individuals have reported the development of "pins and needles" sensations, skin rash, irritability, weakness, nausea, or vomiting.

Recent analysis of a study using long-term supplementation with selenium to prevent the recurrence of non-aggressive skin cancers has provided data supporting a conclusion that selenium may increase the risk of developing a recurrence of a certain type of skin cancer- squamous cell carcinoma (SCC) that usually can be easily treated. Because of this finding I need to be aware that if I have had a SCC in the past, taking selenium might increase my chances of having it come back.

There may be some pain from the needle stick required to obtain my blood for evaluation, and some bruising at the needle site, or other minor complications from blood sample collection.

If I am diagnosed with prostate cancer during the course of this study I will notify a study nurse as soon as possible at (520) 321-7798 or 1-800-243-6519. I may be asked to have a final blood draw of 7cc (1/2 tablespoon). This sample will be analyzed for the selenium level in my blood.

BENEFITS

I may not receive any benefit from participation on this study, beyond the regular monitoring of my PSA, and kidney and liver functions.

CONFIDENTIALITY

My medical records will become part of my research file and will remain confidential, but the information will be available to, and will be analyzed by, the investigators and institutions participating in this study. Also, the Food and Drug Administration may inspect these records at any time. I will not, however, be personally identified in any publication of the results of this study.

I may be contacted periodically by the project investigators to obtain additional new information that may be important for the project. My doctor may ask me to withdraw from the study for scientific reasons or for my safety; for example, if I develop side effects or other medical problems.

Furthermore, study personnel will obtain Prostate Specific Antigen (PSA) test results from two years prior to my last negative prostate biopsy for inclusion in my research records. Also included in my research records will be copies of all pathology reports from all my biopsies and physician notes related to my prostate. Both PSA test results and pathology reports will be protected by the same confidentiality as my medical records, and will be used for research purposes only.

PARTICIPATION COSTS AND SUBJECT COMPENSATION

I will be responsible for the usual costs of treatment by my personal physician including regularly scheduled clinic visits (transportation, clinic fees, physician's fees, biopsies, bone scan and laboratory fees, etc.). I will not be charged for the supplement (tablets), the study blood draws, or the study laboratory tests relating to this research trial. I will not be paid for participating in this study.

PHASE III TRIAL OF SELENIUM FOR PROSTATE CANCER PREVENTION
(NEGATIVE BIOPSY TRIAL) HSC#: 99-11

LIABILITY

Side effects or harm are possible in any research program despite the use of high standards of care and could occur through no fault of mine or the investigator involved. Known side effects have been described in this consent form. However, unforeseeable harm also may occur and require care. I do not give up any of my legal rights by signing this form. In the event that I require or am billed for medical care that I feel has been caused by the research, I should contact the Principal Investigator, Frederick Ahmann, M.D. or Co-Principal Investigator, Steven P. Stratton, Ph.D. at 1-800-243-6519 extension 24. If I have questions regarding my rights as a research subject, I may call the Human Subject's Protection Program office, University of Arizona, Tucson, Arizona, 520-626-6721.

I can ask my urologist or the project coordinator at the Tucson Coordination Center any questions that I may have about the study. They will answer any further questions I may have at any time concerning the study, procedures, or any illnesses or injuries that may appear to be related to the study.

(NEGATIVE BIOPSY TRIAL) HSC#: 99-11

BEFORE GIVING MY CONSENT BY SIGNING THIS FORM, THE METHODS, INCONVENIENCES, RISKS, AND BENEFITS HAVE BEEN EXPLAINED TO ME AND MY QUESTIONS HAVE BEEN ANSWERED. I MAY ASK QUESTIONS AT ANY TIME AND THAT I AM FREE TO WITHDRAW FROM THE PROJECT AT ANY TIME WITHOUT CAUSING BAD FEELINGS OR AFFECTING MY MEDICAL CARE. MY PARTICIPATION IN THIS PROJECT MAY BE ENDED BY THE INVESTIGATOR OR BY THE SPONSOR FOR REASONS THAT WOULD BE EXPLAINED. NEW INFORMATION DEVELOPED DURING THE COURSE OF THIS STUDY WHICH MAY AFFECT MY WILLINGNESS TO CONTINUE IN THIS RESEARCH PROJECT WILL BE GIVEN TO ME AS IT BECOMES AVAILABLE. THIS CONSENT FORM WILL BE FILED IN AN AREA DESIGNATED BY THE HUMAN SUBJECT'S PROTECTION PROGRAM WITH ACCESS RESTRICTED TO THE PRINCIPAL INVESTIGATOR, FREDERICK AHMANN, M.D. OR CO-PRINCIPAL INVESTIGATOR, STEVEN P. STRATTON, PH.D. OR AUTHORIZED REPRESENTATIVES OF THE ARIZONA CANCER CENTER. I DO NOT GIVE UP ANY LEGAL RIGHTS BY SIGNING THIS FORM. A COPY OF THIS SIGNED CONSENT FORM WILL BE GIVEN TO ME

 I allow genetic testing for study purposes only.

OR

☐ I do not allow genetic testing for study purposes only.

Subject's Signature Date _____ AM/PM
Time

Witness' Signature (If necessary) Date

INVESTIGATOR'S AFFIDAVIT

I have carefully explained to the subject the nature of the above project.

Signature of Presenter _____ Date _____ Time _____ AM/PM

PHASE III TRIAL OF SELENIUM FOR PROSTATE CANCER PREVENTION
(NEGATIVE BIOPSY TRIAL) HSC#: 99-11

I hereby certify that to the best of my knowledge the person who is signing this consent form understands clearly the nature, demands, benefits, and risks involved in his participation and his signature is legally valid. A medical problem or language or educational barrier has not precluded this understanding.

Signature of Investigator

Date

SUBJECT'S AUTHORIZATION FORM FOR USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH

Subject # _____

HSC #: 99-11 Phase III Trial of Selenium for Prostate Cancer Prevention (Negative Biopsy Trial)

The United States government has issued a new privacy rule to protect the privacy rights of individuals enrolled in research. The Privacy Rule is designed to protect the confidentiality of an individual's health information. This document hereafter known as an "Authorization for Use and Disclosure of Protected Health Information for Research" describes my rights and explains how my health information will be used and disclosed for this study.

PURPOSE

I am being invited to participate voluntarily in the above-titled research project studying the use of daily Selenium supplements in the prevention of prostate cancer. The purpose of this study is to determine if Selenium supplementation will decrease the risk of developing prostate cancer. Two different dosages of Selenium will be used to try to determine which one would be the most effective dose to use in the prevention of prostate cancer. This study does not use Selenium as a treatment option for the possible cure of prostate cancer. My full participation will involve the study staff obtaining, using, creating and disclosing certain pieces of health information that are protected by the Privacy Rule. Without access to this information, the data developed from my participation in this trial will not be useful for scientific analysis.

USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

If I agree to participate, the following information will be used or disclosed:

- My medical history: This is necessary to determine if I am eligible for the study;
- My blood lab tests: These are necessary to determine if I am eligible for the study and to monitor my safety during the study;
- Pathology reports and medical records throughout the duration of my participation in the study: These are necessary to monitor the status of my health on a continuing basis;
- Prostate tissue from all biopsies I had prior to entering the study and tissue from any subsequent biopsies I have during the study: This is necessary to examine levels of certain proteins of prostate cancer;
- Data about my health habits: This is necessary to assess my risk for developing cancer;
- Data about the kinds and amounts of food I eat: This is necessary to account for the estimated amount of Selenium I consume through my diet;
- Data about my urinary functions and sexual activity: This is necessary for monitoring my PSA.
- Data about my moods: This is necessary for monitoring my mental well-being.

All of my PHI will remain strictly confidential.

This information will be **used** for determining whether I am eligible for the study and to analyze the safety and effect of Selenium on the prevention of prostate cancer. The information is provided to the study staff by me and by the labs and doctors analyzing my blood and prostate tissue. My PHI will remain associated with my identity indefinitely. My PHI may be **disclosed** to investigators, study staff, representatives of regulatory agencies (including the University of Arizona Human Subjects Protection Program), the National Cancer Institute, and the federal Food and Drug Administration who may access my records to ensure quality of data and study conduct. I have the right to access my PHI that may be created during this study as it relates to my treatment or payment. My access to this information will become available **only after the study analyses are complete.**

CONTACTS

I can obtain further information from the principal investigators, Frederick R. Ahmann, M.D. or Steven P. Stratton, Ph.D. at 1-800-243-6519 extension 24. If I have questions concerning my rights as a research subject, I may call the Human Subjects Protection Program office at (520) 626-6721.

AUTHORIZATION

I hereby authorize the use or disclosure of my individually identifiable health information. I may withdraw this authorization at any time by notifying the Principal Investigator in writing. The address for the Principal Investigator is 2504 E. Elm Street, Tucson, AZ 85716. If I do withdraw my authorization, any information previously disclosed cannot be withdrawn and may continue to be used. Once information about me is disclosed in accordance with this authorization, the individual or organization that receives it may re-disclose it and my information may no longer be protected by Federal Privacy Regulations. I may refuse to sign this authorization form. If I choose not to sign this form, I cannot participate in the research study. *Refusing to sign will not affect my present or future medical care and will not cause any loss of benefits to which I am otherwise entitled.* This authorization will expire on the date the research study ends. I will be given a copy of this signed authorization form.

Subject's Signature

Date

Printed Name of Subject

Signature of Subject's Legal Representative (if necessary)

Date

Printed Name of Subject's Legal Representative

Relationship to the Subject