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TITLE: Epidermal Growth Factor (EGF) Receptor Intron 1 CA Repeat Polymorphisms in African-American and Caucasian Males: Influence on Prostate Cancer Risk or Disease Progression and Interaction with Androgen Receptor CAG Repeat Polymorphisms

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Epidermal Growth Factor (EGF) Receptor Intron 1 CA Repeat Polymorphisms in African-American and Caucasian Males: Influence on Prostate Cancer Risk or Disease Progression and Interaction with Androgen Receptor CAG Repeat Polymorphisms

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We are investigating the effect of a polymorphic epidermal growth factor receptor (EGFR) gene intron 1 CA repeat on prostate cancer (CaP) development, alone or in combination with a known androgen receptor gene CAG repeat polymorphism. We will characterize these repeats in DNA from African-American and Caucasian men with CaP. The data will be analyzed for any correlation using both parameters with clinical outcome (age of onset, rapid progression, or metastasis). The Human Subjects Protocol was approved by the US Army Medical Research and Materiel Command Human Subjects Research Review Board (USAMRMC HSRRB) on 24 November of 2003. However, the resignation of the individual who was to recruit subjects at the Cooper Hospital/University Medical Center this year and the failure of my clinical collaborator to train a new coordinator in a timely manner has resulted in additional delays in initiating subject recruitment. Fortunately, new clinical collaborators affiliated with a major research institution have agreed to participate in the study. Since no subjects have entered the study, there is no data to report. A new Human Subjects Protocol has been submitted to the IRB and DOD HSRRB to indicate the new clinical personnel, and we anticipate initiating subject recruitment shortly.
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INTRODUCTION: African-Americans are at increased risk of developing prostate cancer (CaP) relative to whites, and the lengths of two polymorphic repeats in the first exon of the androgen receptor (AR) gene contribute to that risk (Ries et al., 1990; Parker et al., 1996). The CAG repeat length is best correlated with prostate cancer risk, shorter repeats being associated with higher risk, and the prevalence of the shorter CAG alleles is greatest in African-American men, intermediate in Caucasian, and least in Asian-American men (Faber et al., 1989; Irvine et al., 1995; Kantoff et al., 1998; Pettaway, 1999). However, a multigenic etiology for CaP is likely. A polymorphic CA repeat has been described in intron 1 of the epidermal growth factor receptor (EGFR) gene, and the length of the repeat inversely correlated with transcriptional activity in vitro (Chi et al., 1992; Gebhardt et al., 1999). Preliminary evidence suggests that the CA repeat status affects EGFR content in breast cancer, and that shorter repeats might be a predisposing factor for breast cancer (Buerger et al., 2000). The EGFR is also important in regulation of prostatic epithelial and CaP cell growth, and androgen may affect that by increasing the levels of EGFR and its' ligands in CaP cells (Schuurmans et al., 1991; Liu et al., 1993). Shorter CA repeats in intron 1 of the EGFR gene, by resulting in transcriptional enhancement of EGF receptor expression, and potentially also by affecting alternative splicing of the EGFR transcript, could synergize with shorter CAG androgen receptor AR repeats to increase the risk of early onset prostate cancer and promote the development of androgen-independent, metastatic prostate cancer. In collaboration with The Prostate Cancer Risk Assessment Program at Cooper Hospital/University Medical Center, we will isolate DNA from blood samples from 300 African-American and Caucasian American men with (and some without) prostate cancer. We will determine the length of these two repeats, to determine whether the EGFR CA repeat, alone or in combination with the AR CAG repeat, affects CaP risk. Lymphoblastoid cell lines will be established for a representative subset of these samples, and will be made available to other researchers at the end of this study. The data will be analyzed for any correlation using both parameters with clinical outcome (age of onset, rapid progression, or metastasis).

BODY: Based on USAMRMC recommendation, a biostatistician, Dr. Constantine Daskalakis, was recruited to the study and a statistical analysis plan was developed. Note that the Cooper Hospital/University Medical Center IRB considers the present study (funded by award number DAMD17-01-1-0080) to be a sub-study of the Regional Prostate Cancer Registry and Risk Assessment Program at Cooper Hospital/University Medical Center. Previous delays in granting of approval to commence research were caused by turnover of HSRRB reviewers working with the DOD (six different reviewers) and the implementation of the new HIPAA regulations by the Cooper Hospital/University Medical Center Institutional Review. Approval to initiate my research was finally received from the US Army Medical Research and Materiel Command Human Subjects Research Review Board (USAMRMC HSRRB) in a letter dated 24 November 2003 (Modification No. P00001 to DAMD17-01-1-0080). Taking the long delay in obtaining HSRRB approval into account, the grant performance period was extended to 30 September 2005.

Unfortunately, shortly after receiving approval to initiate subject recruitment, the individual in Dr. Marmar's office who was to carry out the recruitment and specimen collection, Juliette May, resigned her position. This occurred in January of 2004. Being assured by Dr. Marmar that a new person would be hired soon, I acquired control cell lines and initiated laboratory work with these lines (see below). Evette Ortolaza was hired as Dr. Marmar's office manager, and was to begin subject recruitment for my project (CHS RP#02-046) upon completion of training in research with...
human subjects. Since she is not trained in phlebotomy, Dr. Marmar informed me that Ms. Ortolaza would not do the blood draws; rather they would be done by personnel at the Cooper Clinical Laboratory adjacent to the Urology Clinic. However, several months passed without any indication that Ms. Ortolaza had received approval from the Cooper Health System IRB for participation in research involving human subjects, despite regular communications from me. These repeated delays by my clinical collaborator in the Cooper Healthy System have prevented enrollment of any study subjects, and if continued, could pose a problem for the successful completion of this research project. Therefore, this summer I began to explore other avenues for subject enrollment, although I have kept the IRB protocol for the study at Cooper active, inasmuch as 100 samples collected under a prior protocol are available through Cooper’s Regional Prostate Cancer Registry.

After investigating several avenues to recruit subjects, I am pleased to report that Drs. Raffaele Baffa and Leonard Gomella of the Department of Urology at Thomas Jefferson University in Philadelphia have agreed to participate in this research project. The Kimmel Cancer Center at Thomas Jefferson University is an NCI-Designated Cancer Center serving the greater Philadelphia area. Dr. Raffaele Baffa is Director of Urology Research, Department of Urology, and Co-Director of the Genito-Urinary Cancer Program at the Kimmel Cancer Center, and he thus works closely with Dr. Gomella. Dr. Baffa is a colleague I have known since 1993 when I was also at the Kimmel Cancer Center, and his interest in cancer genetics is longstanding (see appended curriculum vitae). Raffaele was instrumental in bringing Dr. Gomella on-board for the current research.

Dr. Gomella is Bernard W. Godwin, Jr., Professor of Prostate Cancer, Jefferson Medical College, Chairman of the Department of Urology, and Director of Urologic Oncology in the Kimmel Cancer Institute at Thomas Jefferson University. Dr. Gomella is expert in urologic oncology, with a long-standing interest in prostate cancer, as shown in his appended curriculum vitae. In addition to seeing patients and clinical work in support of basic research, he is principal investigator in a number of clinical trials. Of particular importance in the current context are his role in a longitudinal study to determine the utility of prostate-specific antigen (PSA) for early detection of prostate cancer, and in the placebo-controlled Selenium and Vitamin E Cancer Prevention Trial (SELECT A). He has been PI in these studies since 1989 and 2001, respectively. He is also principle investigator in two prostate cancer treatment trials initiated in 2003. Thus, his office has a large pool of individuals already enrolled in clinical CaP studies, both with and without cancer. Importantly, this pool includes individuals with both metastatic and non-metastatic CaP diagnosed several years ago as well as recently. Since the focus of my study is on the role of specific inherited genetic polymorphisms in CaP, prior treatment of subjects will not interfere with the results. In combination with the regular patient pool, it is anticipated that this large pool of individuals who have already demonstrated a willingness to participate in research studies will facilitate the rapid accrual of subjects for the current study, since their opportunity cost for this study is minimal.

The clinical research coordinator in the Department of Urology, Ms. Christine Hubert, will enroll subjects. Ms. Hubert has acquired extensive experience as a clinical research coordinator in a variety of studies since 1997. Christine has been at Thomas Jefferson University since 1999, exclusively as Clinical study coordinator. This experience is outlined in her appended curriculum vitae, and Ms. Hubert has already proven her reliability by quickly arranging all the materials needed for approval of the study by the Jefferson Clinical Cancer Research Review Board (CCRRC).

Since no new subjects have been enrolled, there is no data to report. The Human subjects documents and new curriculum vitae are appended.
**KEY RESEARCH ACCOMPLISHMENTS:** New clinical collaborators at an NCI-designated Cancer Center have agreed to participate in subject recruitment (Task 1a). This is key to enrolling sufficient subjects for successful completion of the study. Control cell lines have been acquired and grown, and DNA has been isolated from these lines. My technician has been trained in isolation of mononuclear cells from blood, and in DNA isolation (these activities are part of Task 2b). PCR analyses of control cell lines are underway. No other results are yet available, since we have not been able to recruit any subjects to date.

**REPORTABLE OUTCOMES:** None.

**CONCLUSIONS:** Despite tremendous progress in research into the origins of prostate cancer (CaP), there are still many important, unresolved questions about the etiology of this common cancer. Perhaps the most urgent problem facing prostate cancer researchers -- and those with the disease -- is to identify the subset of CaP sufferers whose cancer will progress rapidly. Despite extensive research, no single marker has arisen as a definitive marker of such cancers. Indeed, a multigenic etiology for CaP is extremely likely. Among the candidate genes are those encoding the androgen receptor and the epidermal growth factor receptor (EGFR). The EGFR is clearly important in the regulation of prostatic epithelial and CaP cell growth, and is frequently overexpressed in BPH and CaP cells, but no studies have convincingly demonstrated that it is of great use in predicting the course of a particular CaP case. However, a polymorphic CA repeat has been described in intron 1 of the epidermal growth factor receptor (EGFR) gene, and the length of the repeat has recently been inversely correlated with transcriptional activity in vitro (Chi et al., 1992; Gebhardt et al., 1999). Androgen may also influence the expression of the EGFR by increasing the levels of its’ ligands, and perhaps directly in CaP cells (Schaumans et al., 1991; Liu et al., 1993). However, the possible contribution of EGFR CA repeat polymorphisms on prostate cancer risk or progression has never been investigated. Shorter CA repeats in intron 1 of the EGFR gene, by resulting in transcriptional enhancement of EGF receptor expression, and potentially also by affecting alternative splicing of the EGFR transcript, could synergize with shorter CAG androgen receptor AR repeats to increase the risk of early onset prostate cancer and promote the development of androgen-independent, metastatic prostate cancer. No work addressing these issues with respect to CaP has been published to date, although Buerger et al recently reported (2004) new results associating the allelic length of the EGFR CA repeat with EGFR gene amplification in breast cancers. This proposal will address these possibilities, and will also provide resources for definitive future studies.

      Given that only the site for subject recruitment and personnel have changed (and improved), we anticipate ready approval of the revised human subjects research protocol and expeditious recruitment of the research subjects.

      It is important to emphasize that subject recruitment is the limiting factor in this research. The mononuclear cell isolation, DNA extraction, and polymerase chain reaction (PCR) analyses are standard techniques with which the investigators have extensive experience, and large numbers of samples can be analyzed in a short period of time.
BACKGROUND REFERENCES:


HSRRB Log No. A-10414/ PC001407 - "Epidermal Growth Factor (EGF) Receptor intron 1 CA repeat polymorphisms in African-American and Caucasian males: Influence on Prostate Cancer risk or disease progression and interaction with Androgen receptor CAG repeat polymorphisms."

Human Subjects Protocol

1. This grant will utilize specimens and information accrued through The Prostate Cancer Risk Assessment Program, a collaborative project of Cooper Hospital/ University Medical Center and The Coriell Institute for Medical Research. The overall study is entitled "Development of a regional prostate cancer registry & risk assessment program".

2. This protocol does NOT involve the testing of Investigational New Drugs or Devices.

3. Principal Investigator (PC001407):

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5. Time required to complete: Expected Start: 24 November, 2003
   Completion: 31 September, 2005

6. 9. Protocol

a.  Research Hypotheses/ Objectives: This study involves the development of a prostate cancer database that will collect data not currently available on prostate cancer patients and their family members. Personal information and blood samples will be collected from all participants, and tissue samples will be collected from participants that undergo medically indicated biopsies or surgeries. Regarding PC001407, I hypothesize that shorter CA repeats in intron 1 of the EGFR gene, by resulting in transcriptional enhancement of EGF receptor expression, will synergize with shorter CAG androgen receptor AR repeats to increase the risk of early onset prostate cancer and/or promote the development of androgen-independent, aggressive prostate cancer. The status of Epidermal Growth Factor (EGF) Receptor intron 1 CA repeat and androgen receptor CAG repeat polymorphisms in African-American and Caucasian males will be determined by PCR analysis of DNA isolated from blood samples. These data will be studied in conjunction with the personal and medical information to determine whether the status of the EGF receptor polymorphism, alone or in combination with the androgen receptor polymorphism, influences the age of onset or biological characteristics (e.g., hormone dependence, invasiveness, metastasis) of prostate cancer. Further details are described in the included abstract.
b. **Study Population:** The study population will be comprised of approximately 300 males recruited from individuals who come to the Department of Urology at Thomas Jefferson University for prostate cancer treatment or screening, and to Cooper Hospital for the treatment of prostate cancer and via the Prostate Cancer Risk Assessment Program at Cooper Hospital. Cooper Hospital serves primarily Camden County and western Burlington County, New Jersey, and ethnically diverse area with significant African-American, Caucasian, and Hispanic populations.

c. **Inclusion and Exclusion Criteria:** All subjects recruited will be males in the age range of 35-69 years. Carcinoma of the prostate (CaP) is rare among individuals under age 35, whereas prostatic intraepithelial neoplasia (PIN) the presumed precursor of CaP, is very common among men older than 70, so older individuals are less likely to be informative regarding hereditary predisposition. Because the frequency of the various EGF receptor intron 1 CA repeat lengths in African-American men is currently unknown, and since African-American men are at greater risk of prostate cancer than the general population, we will recruit a significant fraction of subjects from the African-American community. Subjects accrued to date under the previously approved Prostate Cancer Risk Assessment Program protocol are ca. 50% African-American and 50% Caucasian.

d. **Informed Consent Process:** The Clinical Study Coordinator in the Department of Urology at Thomas Jefferson University or Clinical nursing staff at Cooper Hospital/University Medical Center will explain the Prostate Cancer Risk Assessment Program in lay terms to prospective subjects who come to the weekly screening clinic ("self-recruitment"). The Prostate Cancer Risk Assessment Program is open to men between the ages of 35 and 69 who are African-American, or of any race with a family history of prostate cancer. Prostate cancer patients of Dr. Joel Marmar will also be offered the opportunity to enroll in the study. Individuals uncertain about participation may discuss the study with friends and family members and return at a later time. Interested individuals will then be talked through the informed consent form (appended), with particular attention being focussed on the clauses regarding (a) the choice to be informed of any clinical implications of their results in the context of this or other relevant prostate cancer studies, (b) the risks of participation in the study, and (c) sample donation. Witnesses may be other clinic personnel or any other individual the subjects choose. As the document is discussed, the subjects and their witnesses will be asked to initial each page to indicate that it has been explained to them, as well as to sign the last page of the document to indicate their agreement to participate in the study. Two copies of the consent form will be completed so that the subjects can keep an original copy.

e. **Sample Size:** A target of 300 individuals will be sought over the course of 3 years. (The overall target for the Regional Prostate Cancer Registry and Risk Assessment Program is 400 subjects, but the time and funds for PC001407 will allow for analysis of 300.) By recommendation of peer review, a biostatistician has been consulted regarding sample size (appended), and will be consulted for subsequent data analyses. EGFR intron 1 CA repeat allele frequencies in the general populations of African-American and Caucasian American men will be determined by analysis of DNA samples from apparently normal individuals in existing Coriell Cell Repository panels.

f. **Protocol Design:** Male subjects (300) will be recruited from individuals who come for screening or treatment of prostate cancer and via the Prostate Cancer Risk Assessment Program at Cooper Hospital as described in b - d above. Notices will be published as in the appended Cooper Health system newsletter. After informed consent is obtained as described in (d), subjects will be asked to complete a Health History Questionnaire (appended), and to donate 3 (~10 ml each) tubes of blood. One tube will be used by the hospital for medical diagnosis (e.g., Prostate Specific Antigen
level), while the other tubes will be used at the Coriell Institute for Medical Research for (a) extraction of DNA and (b) isolation and cryopreservation of lymphocytes. Blood will be collected no more than once per year for the purposes of this study. The lengths of the EGFR intron 1 CA repeat and the AR CAG repeat will be determined by PCR analysis of the DNA (of the samples accrued to date on a previous protocol, the AR repeat has already been analyzed in several dozen). Epstein-Barr virus-immortalized lymphoblastoid cell lines will be established for individuals representing the possible combinations of these two polymorphisms. These cell lines will be deposited in the National Institute of Aging Repository in the Coriell Cell Repositories, and will be available to other researchers at the end of this study. We will also utilize prostate biopsies, when obtained as part of the subjects' medical care, to examine EGFR and AR expression and initiate prostate cell lines. The specimens, health histories, and clinical information will be encoded as PS### (e.g., PS100, PS101, etc.) by the Cooper Hospital clinical staff, such that all specimens and information received by The Coriell Institute for Medical Research will be separated from subject names. Coriell will receive only coded summaries of the Health History Questionnaires. Any cell lines accepted by the Coriell Cell Repositories for distribution to other researchers will be given new code numbers (e.g., AG00000) to ensure confidentiality. For PS### cell lines to be submitted to the Coriell Cell Repositories, Dr. Joel Marmar's clinical staff will assign new numbers from a list of the next available AG numbers; the list indicating the PS #s corresponding to the new AG numbers will be kept by his office for 4 years after completion of the study.

\[g\] \textbf{Risks to Subjects:} As this is not an interventional protocol, this project poses no greater than minimal risk to participants. Risks noted in the consent form include the risk of discovering a genetic predisposition to cancer, which may cause concern. Subjects may also have concerns even if they are not in the future told that they have a gene alteration that has been linked to an increased risk of prostate cancer. Subjects do not have to agree to have this information revealed to them or their family members. The risks and discomfort associated with giving blood include the possibility of bleeding and bruising. This rarely causes a significant problem.

\[h\] \textbf{Benefits to Subjects:} As noted in the consent form, subjects will not receive any immediate benefits as a result of participation in this study. It is possible that the study will reveal known or novel genetic polymorphisms that would indicate a statistically greater or lesser prostate cancer risk than the general population. This might prompt an individual to have regular screening for prostate cancer, which could affect their prognosis should cancer be discovered. However, such information is more likely to be of use in the future, rather than to subjects recruited in the current study.

\[i\] \textbf{Roles and Responsibilities of Study Personnel:} Local review boards have not found the protocol to be of greater than minimal risk, so no medical monitor has been assigned.

David K. Moscatello, Ph.D. Role: Principal Investigator (PC001407), 40%. Lymphocyte and DNA isolation, analysis of EGFR intron 1 CA repeats, analysis of Androgen receptor CAG repeats, preparation of DNA, RNA, and protein lysates from prostate specimens, immunohistochemistry and western blotting, reverse transcription-polymerase chain reaction (RT-PCR), Southern and Northern blotting, cryopreservation of viable prostate biopsies, and data analysis.
Bender, Patrick K., Ph.D. (Associate Professor and Supervisor, Division of Molecular Biology, Coriell Institute for Medical Research, 5%. Role: Analysis of Androgen Receptor CAG repeats.

Leonard Gomella, M.D., (Professor of Urology, Director, Urologic Oncology & Chairman, Dept. of Urology, Kimmel Cancer Center, Thomas Jefferson University. Role: subject recruitment.

Raffaele Baffa, M.D. (Associate Professor, Director of Urology Research and Co-Director Genito-Urinary Cancer Program, Department of Urology, Kimmel Cancer Center, Thomas Jefferson University). Role: subject recruitment.

Christine Hubert, B.A. (Clinical Study Coordinator, Department of Urology, Thomas Jefferson University). Role: subject recruitment, interviews, data entry and encoding.

Grana, Generosa, M.D., Assistant Professor of Hematology/Oncology and Medical Director, The Cancer Risk Evaluation Center, Cooper Hospital/University Medical Center, 5%. Role: Medical Director, The Cancer Risk Evaluation Center.

Marmar, Joel, M.D., Professor of Urology and Head, Division of Urology, Cooper Hospital/University Medical Center, 5%. Role: Procurement of benign and malignant prostate specimens.

Milagro Concepcion, B.A., Technician, Coriell Institute for Medical Research, 50%. Role: Lymphocyte isolation and cryopreservation, DNA isolation, and PCR.

Constantine Daskalakis, Sc.D., Biostatistics section of the Department of Medicine, Thomas Jefferson University, Philadelphia, PA, 5%. Role: Consultant for study design and data analyses.

10. Reporting of serious and unexpected adverse events. This is not an IND or IDE protocol. No medical interventions are proposed. However, there is a remote possibility of a severe adverse event such as excessive bleeding or infection as a result of blood collection. Should such an event occur, Adverse experiences that are both serious and unexpected will be immediately reported by telephone to the USAMRMC Deputy for Regulatory Compliance and Quality (301-619-2165) and send information by facsimile to 301-619-7803). A written report will follow the initial telephone call within 3 working days.

11. Description of Protocol Drug(s) or Device(s): Not applicable.

12. Disposition of data: All health history and clinical records will be maintained at Thomas Jefferson University Hospital or Cooper Hospital/University Medical Center according to their standard procedures. No disposal is contemplated, except for individuals who are withdrawn from the study (either voluntarily or otherwise), in which case the health questionnaires held at Cooper, and samples and associated data held at Coriell will be destroyed. Otherwise, encoded/tabulated data without personal identifiers of just the subset of samples that will be submitted to the NIA Cell Repository will be maintained in the secure files of The Coriell Institute for Medical Research indefinitely.

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13. **Modification of the protocol:** As this is not an IND/IDE protocol, no modifications are anticipated, with the possible exception of the recruitment of additional subjects. This might be necessary to achieve statistical validity of possible correlations between the genetic polymorphisms and clinical data. The use of additional methods to recruit subjects might be considered if targets are not met. If this becomes necessary, the revisions, including any proposed new recruiting methods, will be submitted to the Institutional Review Boards of both local institutions, and subsequently to the OTSG HSRRB for approval.

14. **Departure from the Protocol:** Any departures from the proposed protocol with respect to the consents, questionnaires, or specimens will be submitted to the Institutional Review Boards of both local institutions, and subsequently to the OTSG HSRRB.

15. **Roles and Responsibilities of Study Personnel:** See (i) above.

16. **USAMRMC Volunteer Registry Database:** Project judged not greater than minimal risk by local review boards, therefore not applicable.

Signature of Principal Investigator: __________________________

David K. Moscatello, Ph.D.

Date: ________________
STATISTICAL ANALYSIS PLAN

Our analyses will be based on samples obtained from 300 prostate cancer patients (prospectively collected) and from approximately 200 controls (from existing panels). The study's aims are to evaluate
(1) the association between EGFR intron 1 CA repeats and prostate cancer;
(2) the association between AR CAG repeats and prostate cancer; and
(3) the combined (synergistic) effect of EGFR and AR on prostate cancer.

The first two aims pertain to the main effect of each gene, while the third aim focuses on their possible interaction. Preliminary analyses will be based on two-by-two cross-classification tables of each gene with prostate cancer status (case/control). We will estimate and test the (crude) unadjusted odds ratio separately for each gene, using Fisher's exact test and Mantel-Haenszel stratification analysis. We will then model the outcome (prostate cancer case or control status) as a function of both genes via logistic regression. In this multivariable analysis, we will also control for age, race, and other potential confounders.

Finally, we will test the hypotheses of "no multiplicative interaction" and "no additive interaction" between the two genes. Using the long-EGFR/long-AR combination as the referent group, the hypothesis of no multiplicative interaction implies that the joint odds ratio for the short-EGFR/short-AR combination is equal to the product of the two main effects odds ratio (i.e., short-EGFR/long-AR and long-EGFR/short-AR). The test of this hypothesis involves testing the product interaction term; likelihood ratio and Wald tests are straightforward to compute in all statistical packages. The hypothesis of no additive interaction, on the other hand, implies that the joint odds ratio is the sum of the two main effects odds ratios minus one. Although preprogrammed software capabilities do not allow testing of this hypothesis in logistic regression, we have a SAS macro that will allow us to perform the corresponding likelihood ratio and Wald tests.

We have also planned secondary analyses to assess:
1. the effects of the two genes among Caucasian and African-American subjects (i.e., gene-by-race interactions); and
2. the association between the length of the repeats for each gene and cancer recurrence and/or survival (among the prostate cancer cases only).

SAMPLE SIZE AND POWER

Based on previous data, EGFR intron 1 CA repeats show a distribution with 3 peaks in the general population, at 20, 18 and 16 repeats. A smaller number of repeats (<17, approximately 45% in the general population) are hypothesized to be associated with higher risk of prostate cancer. With 300 cases and 200 controls, using a two-tailed Fisher's exact test with alpha of 0.05, we have 84% power to detect an odds ratio of about 1.75 (i.e., short allele in 45% of the controls vs. 59% of the cases).

Similarly, based on previous data, AR CAG short repeats (<20) seem to be present in about 30% of the general population. With 300 cases and 200 controls, using a two-tailed Fisher's exact test with alpha of 0.05, we have 82% power to detect an odds ratio of 1.75 (i.e., short allele in 30% of the controls vs. 43% of the cases).
In terms of the interaction between the two genes, we have good power to detect moderate interactions on both the additive and the multiplicative scale. All power calculations were performed via Monte-Carlo simulation, using the appropriate likelihood ratio tests in logistic regression, with alpha of 0.05.

Assuming main effect odds ratios for each gene of about 1.75, under the "no additive interaction hypothesis", we expect a joint odds ratio of 2.5 (i.e., 1.75+1.75-1) for the comparison of the short-EGFR/short-AR combination with the referent long-EGFR/long-AR combination. In our study, we have power to detect departures from additivity when the synergy factor is 3 or higher (i.e., an odds ratio for the joint effect of 5.5 or higher):

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<tr>
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<td>2.50*</td>
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<td>81%</td>
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(*) Additivity of effect (i.e., no additive interaction)

With the same assumptions of main effect odds ratios for each gene of about 1.75, under the "no multiplicative interaction hypothesis", we expect an odds ratio of 3.06 (i.e., 1.75x1.75) for the comparison of the short-EGFR/short-AR combination with the referent long-EGFR/long-AR combination. In our study, we have power to detect a multiplicative interaction factor of about 3 or higher (i.e., an odds ratio for the joint effect of 9 or higher):

<table>
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<tr>
<th>Allele EGFR AR</th>
<th>Effect type</th>
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<th>OR Power</th>
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<td></td>
</tr>
<tr>
<td>short short</td>
<td>joint</td>
<td>3.06*</td>
<td>9.2</td>
<td>75%</td>
<td>10.7</td>
</tr>
</tbody>
</table>

(*) Multiplicativity of effect (i.e., no multiplicative interaction)

**Constantine Daskalakis, ScD**
Assistant Professor,
Biostatistics Section, Thomas Jefferson University,
125 S. 9th St. #402, Philadelphia, PA 19107
Tel: 215-955-5695
Fax: 215-503-3804
Email: constantine.daskalakis@mail.tju.edu
**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2. Follow this format for each person. DO NOT EXCEED FOUR PAGES.

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moscatello, David Keith</td>
<td>Assistant Professor, Coriell Institute for Medical Research</td>
</tr>
</tbody>
</table>

**EDUCATION/TRAINING** (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pennsylvania State University, University Park,</td>
<td>B.S.</td>
<td>1971-1975</td>
<td>Microbiology</td>
</tr>
<tr>
<td>Purdue University, West Lafayette, IN</td>
<td>Ph.D.</td>
<td>1975-1984</td>
<td>Biology</td>
</tr>
</tbody>
</table>

**A. Positions and Honors**

**Positions and Employment**

- 1984-1987 Visiting Instructor of Microbiology, Dept. of Biological Sciences, Purdue University, West Lafayette, Indiana
- 1987-1992 Assistant Professor of Biology, Division of Natural and Mathematical Sciences, Richard Stockton College of New Jersey, Pomona, New Jersey
- 1992-1997 Postdoctoral Research Fellow in the laboratory of Albert J. Wong, M.D., Department of Microbiology and Immunology, Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, PA
- 1997-1999 Research Instructor, Department of Microbiology and Immunology, Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, PA
- 1999-Present Assistant Professor and Supervisor, Differentiated Cell Laboratory, Coriell Institute for Medical Research, Camden, NJ

**Other Experience And Professional Memberships:**

- 1981-1984 Graduate Instructor of Microbiology, Dept. of Biological Sciences, Purdue University
- 1987-present Member, American Association for the Advancement of Science
- 1990-1997 Board member, Atlantic County Unit, American Cancer Society
- 1998-present Member, American Association for Cancer Research
- 2001-present Member, American Association for Cell Biology
- 2003-2004 Member, Coriell Institute for Medical Research Board of Trustees

**Honors:**

- 1980-1981 David Ross Graduate Fellowship
- 1990 Stockton State College Distinguished Faculty Fellowship
- 1995-1997 National Institutes of Health Postdoctoral Research Fellowship
B. Selected peer-reviewed publications (in chronological order).


C. Research Support

**Ongoing Research Support**

BCS-0421304 Hanner (PI) 8/1/04-7/31/07

NSF Major Research Instrumentation Program:

Role: Application development

DAMD17-01-1-0080 Moscatello (PI) 9/01/03-8/31/05

DOD/USAMRMC

Epidermal growth factor (EGF) receptor intron 1 repeat polymorphisms in African-American and Caucasian males: Influence on prostate cancer risk or disease progression and interaction with androgen receptor CAG repeat polymorphisms.

Role: PI

NO1-GM-9-2102 Coppock (PI) 9/17/99 - 9/16/04

NIGMS

Title: Human Genetic Cell Repository

Role: Supervisor, Differentiated Cell Laboratory (Isolation and characterization of differentiated cells)

NO1-AG-1-2101 Coppock (PI) 1/31/00-12/31/09

NIH/NIA
Selection, Production, Characterization, and Distribution of Genetically Marked Cells for Aging Research, National Institute on Aging. The Coriell Institute produces, characterizes, and distributes cell cultures worldwide for aging-related research under this contract.
Role: Supervisor Differentiated Cell Laboratory (Isolation and characterization of differentiated cells)

**Completed Research Support**

(No grant number)  
Moscatello (PI)  
Ronald McDonald House of Southern New Jersey  
Optimization of Culture Conditions for Pancreatic Islets and Expansion and Differentiation of Pancreatic Islet Stem Cells  
Role: PI

(No grant number)  
Moscatello (PI)  
Lawrence C. Fuller, Jr., Memorial Diabetic Fund  
Equipment for Optimization of Culture Conditions for Pancreatic Islets and Expansion and Differentiation of Pancreatic Islet Stem Cells  
Role: PI

(No grant number)  
Moscatello (PI)  
American Society for Dermatologic Surgery (ASDS)  
Novel Methods for the Isolation, Culture, and Cryopreservation of Human Adipocytes and Adipose Stromal Cells from Tumescent Liposuction Procedures. Methods for manipulating and preserving human adipocytes (fat cells) for clinical and research uses were established.  
Role: PI

(No grant number)  
Moscatello (PI)  
Lawrence C. Fuller, Jr., Memorial Diabetic Fund  
Establishment of a Novel Hybrid Thymic Organ Culture System for Diabetes Research  
A thymic epithelial-stromal co-culture system for studies of T-cell development *in vitro* was established.  
Role: PI

**D. Patent Applications:**


Biographical Sketches

Provide the following information for the key personnel listed on page 1 of the Detailed Cost Estimate form for the initial budget period.

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>JOEL LESLIE MARMAR, M.D.</td>
<td>Professor of Urology and Head, Division of Urology, Department of Surgery</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (IF APPLICABLE)</th>
<th>YEAR(S)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Franklin and Marshall College, Lancaster, PA</td>
<td>B.S.</td>
<td>1960</td>
<td>Biology</td>
</tr>
<tr>
<td>University of Pennsylvania School of Medicine Philadelphia, PA</td>
<td>M.D.</td>
<td>1964</td>
<td>Medicine</td>
</tr>
</tbody>
</table>

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds two pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

1964-65 INTERNSHIP, Rotating, Albert Einstein Medical Center, Philadelphia, PA
1965-66 RESIDENCY: General Surgery, Jeanes Hospital, Fox Chase, Pennsylvania
1966-69 RESIDENCY: Urology, Temple University Hospital, Philadelphia, PA
1969-71 Major/Medical Corps, U.S. Army, Chief of Urology, 24th Evacuation Hospital, Vietnam
1984 - Present Professor of Urology, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson School of Medicine at Camden
1993 - Present Medical Director, Fertility Testing Laboratory, Philadelphia, PA

CERTIFICATION:
Urology, 1973 - American Board of Urology
Fellow, 1974 - American College of Surgeons

OTHER TRAINING:
Urologic Microsurgery Course. September 1980 University of Louisville, Louisville, Kentucky

Urologic Laser Surgery Course, September 1983, Temple University Hospital, Philadelphia, PA

Lithotripter Training, November 4-9, 1985, EDAP Instrument, Hospital Pont de Choisy, Paris, France
Dornier HM3, Hospital Necker, Paris, France
David K. Moscatello, Ph.D.

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

OTHER TRAINING (Cont'd.):

- Additional Lithotripter Training, November 13-20, 1988
  Direx Instrument,
  University de Liege au Bart Tilman, Liege, Belgium
  University Hospital, Maastrik, Holland
  Jeanne d'Arc Polyclinic, Lyon, France

- Laparoscopy Training, Worldwide Veterinary Services
  Parsippany, NJ March 1991

- Laser Prostatectomy Training, May 1992

- Prostate Cryosurgery Training, January 28 - February 1, 1994
  Widdington Hospital (Graham Watson, M.D.), London, England

- Prostate Surgery with TUNA (transurethral needle ablation)
  Philadelphia, PA June 1, 1997

HONORS AND AWARDS:

- Phi Beta Kappa, 1960
- Student Research Award, 1964
- Undergraduate Medical Society
  University of Pennsylvania School of Medicine

- Certificate of Appreciation (Vietnam Service) 1970
- Armed Forces of the United States

- Recognition Award, 1983, Leadership in the Field of Andrology
  Cooper Hospital/University Medical Medical Center

LICENSURE:

- State of New Jersey - MA24609
- State of Pennsylvania - MD008116E
- State of Florida - ME0015259

MILITARY SERVICE:

- Major/Medical Corps
- United States Army, 1969-71
- Chief of Urology, 24th Evacuation Hospital, Vietnam
Biographical Sketch

NAME
Constantine Daskalakis

POSITION TITLE
Assistant Professor

EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR CONFERRED</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Athens (Greece)</td>
<td>B.S.</td>
<td>1989</td>
<td>Biology</td>
</tr>
<tr>
<td>University of Massachusetts (Amherst, MA)</td>
<td>M.S.</td>
<td>1992</td>
<td>Epidemiology</td>
</tr>
<tr>
<td>Harvard University (Boston, MA)</td>
<td>Sc.D.</td>
<td>1997</td>
<td>Biostatistics &amp; Epidemiology</td>
</tr>
</tbody>
</table>

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

Professional Experience:
2000 - Present  Assistant Professor, Department of Medicine, Thomas Jefferson University
1997 - 2000  Research Fellow, Department of Biostatistics, Harvard University
1993 - 1996  Teaching Fellow, Department of Biostatistics, Harvard University
1992 - 1996  Research Assistant, Department of Epidemiology, Harvard University
1987 - 1991  Research Assistant, Department of Biostatistics & Epidemiology, University of Massachusetts

Honors and Awards:
1995  Teaching Assistant of the Year Award, Harvard School of Public Health
1994  Robert B. Reed Prize of Biostatistics, Department of Biostatistics, Harvard School of Public Health

Publications:


Daskalakis C, Lipsitz SR. Assessing additive interactions in logistic regression. *Biometrics* (submitted)
Biographical sketch

Provide the following information for the key personnel in the order listed on Form Page 2. Photocopy this page or follow this format for each person.

<table>
<thead>
<tr>
<th>NAME</th>
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</tr>
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<tbody>
<tr>
<td>GOMELLA, Leonard G., MD</td>
<td>Professor</td>
</tr>
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EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Queens College, SUNY, New York</td>
<td>BA</td>
<td>1976</td>
<td>Biology</td>
</tr>
<tr>
<td>University of Kentucky, Lexington, KY</td>
<td>MD</td>
<td>1980</td>
<td>MD</td>
</tr>
<tr>
<td>University of Kentucky, Lexington, KY</td>
<td>Internship</td>
<td>1982</td>
<td>General Surgery</td>
</tr>
<tr>
<td>University of Kentucky, Lexington, KY</td>
<td>Residency</td>
<td>1986</td>
<td>Urology</td>
</tr>
</tbody>
</table>

PROFESSIONAL EXPERIENCE:
1986-1988 Fellow, Urologic Oncology, Surgery Branch, NCI, NIH Bethesda, MD
1988-1993 Assistant Professor, Department of Urology, Jefferson Medical College
1993-2002 Associate Professor, Department of Urology, Jefferson Medical College
1996-Present Director, Urologic Oncology, Kimmel Cancer Center, Thomas Jefferson University
2002-Present Chairman, Urology Department, Jefferson Medical College, Thomas Jefferson University

HONORS AND AWARDS:
1994-2002, Bernard W. Godwin Jr. Associate Professor of Prostate Cancer, Jefferson Medical College
2002-Present Bernard W. Godwin, Jr., Professor of Prostate Cancer, Jefferson Medical College

SCIENTIFIC PUBLICATIONS: (Selected from 160 Articles and Chapters)
14. Valicenti RK, Chen CT, DeRose T, Lu JD, Mulholland SG, Hirsch IH, Gomella LG Sildenafil Citrate Effectively Reverses Sexual Dysfunction Induced By 3D Conformal Radiation Therapy, Urology 2001 Apr;

RESEARCH SUPPORT.

Urology Chair
American College of Radiology
RTOG Core Grant

Principal Investigator Period: 07/01/99-present
Longitudinal Study to determine the utility of PSA as a test for the early detection of Prostate Cancer
The purpose of the study is to determine if prostate specific antigen (PSA) blood test has value as a test for the early detection of prostate cancer. Changes in PSA values over study participants over time will be assessed for effectiveness in the early detection of prostate cancer.

Principal Investigator Period: 09/1989 - present
Longitudinal Study to determine the utility of PSA as a test for the early detection of Prostate Cancer
The purpose of the study is to determine if prostate specific antigen (PSA) blood test has value as a test for the early detection of prostate cancer. Changes in PSA values over study participants over time will be assessed for effectiveness in the early detection of prostate cancer.
Principal Investigator
NCI through SWOG
Selenium and Vitamin E Cancer Prevention Trial (SELECT A)
This is a placebo-controlled trial for the prevention of prostate cancer using selenium or the combination of selenium and vitamin E.

Principal Investigator
Novartis
Period: 03/15/03-03/15/05
The Effect of Zometa Compared to Placebo on Bone Mineral Density in Patients Undergoing Androgen Deprivation Therapy
To compare the effect of intravenous Zometa (zoledronic acid) 4 mg and placebo administered every 3 months for one year, on bone loss associated with initial androgen deprivation (ADT) (LHRH agonist with or without another antiandrogen agent or orchietomy) in men with non-metastatic prostate carcinoma.

Principal Investigator
Antigenics
Period: 07/22/03 - present
A Multi-Center, Randomized Phase III Study of Adjuvant Oncaphage® versus Observation in Patients with High Risk of Recurrence After Surgical Treatment for Renal Cell Carcinoma.
HSPPC-96, Oncaphage®, is an active, specific immunotherapy that uses renal tumor cells isolated from the patient’s own tumor following surgical resection. Post-operative vaccination of the patient with Oncaphage® will provide a highly unique, individualized treatment option that may prevent or delay subsequent tumor progression. The purpose of this study is to determine if patients who are treated with Oncaphage® for surgically resected, locally advanced renal cell carcinoma have a statistically longer survival than those who do not receive the vaccination.

Principal Investigator
Dendreon
Period: 09/04/03 - present
A Randomized, Double Blind, Placebo Controlled Phase 3 Trial of Immunotherapy with Autologous Antigen Presenting Cells Loaded with PA2024 (Provenge®, APC8015) in Asymptomatic Subjects with Gleason Sum = 7, Metastatic, Androgen Independent Prostatic Adenocarcinomas
This trial evaluates a new approach to prostate cancer treatment using an autologous cell product consisting of antigen presenting cells (APCs) loaded with prostate antigen PA2024, a recombinant fusion protein composed of prostatic acid phosphatase (PAP) linked to granulocyte-macrophage colony stimulating factor (GM-CSF). Previous research has shown that benefit was primarily confined to subjects with Gleason Sum = 7 malignancies. In short, this study uses a subject’s own cells that are responsible for stimulating certain immune responses. These cells have attached to the proteins that may direct a person’s immune reaction towards prostate cancer cells.

COMPLETED
Principal Investigator
PhotoCure
Period: 3/02-10/03
An Open Comparative within Patient Controlled Phase III Multicenter Study of Hexvix® Fluorescence Cystoscopy and Standard Cystoscopy in the Detection of Carcinoma in Situ in Patients with Bladder Cancer
The aim of the study is to see if this new drug, Hexvix® used with blue light cystoscopy, helps doctors to improve the detection of bladder cancers, when compared to white light (standard) cystoscopy in patients with bladder cancer. The study will also aim to show that the new drug is safe. This study will also compare Hexvix® cystoscopy with standard cystoscopy in the detection of carcinoma in situ (CIS) in patients with bladder cancer.

Co-Investigator (PI: R. Myers, MD)
NIH
Increased Access to Clinical and Educational Studies
Period: 07/01-4/03
BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME
Raffaele Baffa, M.D.

POSITION TITLE
Associate Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION | DEGREE (if applicable) | YEAR(s) | FIELD OF STUDY
--- | --- | --- | ---
University of Padova, Italy | M.D. | 1987 | Medicine

Positions and Employment

10/87-12/91 Residency in Pathology, Department of Pathology, University of Trieste, Italy
7/88-12/88 Visiting Scientist, Department of Cytopathology, Dr. Zajdel Laboratory, Curie Institute, Paris
1/91-6/91 Visiting Scientist, Department of Pathology, Dr. Ming Laboratory, Temple University, Philadelphia, PA
6/90-6/93 Assistant Professor, Pathology Department, Citadella Hospital, University of Padova, Italy.
7/93-6/97 Research Fellow, Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, PA
7/97-6/02 Assistant Professor of Urology and Microbiology and Immunology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
7/02-pre. Associate Professor of Urology and Microbiology and Immunology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
6/98-pre. Co-Director Genito- Urinary Cancer Program, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
7/02-pre. Director of Urology Research, Department of Urology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Honors

2001 Kimmel Scholar, Sidney Kimmel Foundation for Cancer Research

Publications (1995 to present)


Completed Research Support:

"Analysis of TS12Q, A Novel Putative Tumor Suppressor Gene at Chromosome 12q24"
P.I. Raffaele Baffa
The main goal was to determine if the TS12Q gene, a novel gene that we have previously identified at chromosome 12q24.1, a region frequently deleted in several cancers, is a legitimate tumor suppressor gene.

Ongoing Research Support:

Project II Aerodigestive and Bladder Cancer- Commonwealth Universal Research Enhancement (C.U.R.E.) program, Raffaele Baffa Co.P.I. (2/01/02-12/31/05)
The main purpose of this project is to accomplish a molecular characterization of carcinoma of the urinary bladder in order to identify appropriate molecular markers for an early diagnosis and a better follow-up of this disease, and to characterize novel targets for multi-modality therapies.

COXIB Medical School Grants Program, Merck
P.I. Raffaele Baffa (12/10/03-12/09/05)
"Rofecoxib and inhibition on N-Butyl-N-(4-hydroxybutyl)-nitrosamine induced urinary bladder cancer in FHit negative mice"
The major goal of this project is to investigate the role of rofecoxib in the prevention and treatment of bladder cancer in fhit knock-out mice.
PRESENT TITLE: Clinical Study Coordinator  
Thomas Jefferson University  
Department of Urology  
Philadelphia, PA

HOME ADDRESS: 104 Lake Avenue  
Glendora, NJ 08029  
(609) 939-2646

OFFICE ADDRESS: Thomas Jefferson University  
Department of Urology  
Room 1100 College  
1025 Walnut Street  
Philadelphia, PA 19107  
(215) 955-4202

CITIZENSHIP: USA

UNDERGRADUATE EDUCATION: Rutgers University  
1990-94 B.A.

GRADUATE EDUCATION: Thomas Jefferson University, College of Graduate Studies  
January 2000 – present  
MS in Pharmacology/Research Scientist

PREVIOUS EMPLOYMENT: Research Associate  
Cooper Hospital  
Department of Gastroenterology  
Camden, NJ  
1994-99

ASSOCIATIONS: Association of Clinical Research Professionals, 1999 - present  
Jefferson Clinical Research Association, Member since 1999

PUBLICATIONS:  
Original Articles:  


Abstracts:  


GRANTS
Prospective, Randomized, Double-Blind, Comparison of Ciprofloxacin Extended-Release 1000 Mg Tablets Given as Two Different Prophylactic Dosing Regimens (Regimen I- Single-Dose Ciprofloxacin MR 1000 Mg or Regimen II- Multiple-Dose Ciprofloxacin MR 1000 Mg Once Daily for 3 Days) for the Prevention of Post-Operative Infectious Complications in Patients Undergoing Transrectal Needle Biopsy of the Prostate. Bayer Pharmaceuticals. Study Coordinator 2004 – present.

A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Dutasteride 0.5mg Administered Orally Once Daily for Four Years to Reduce the Risk of Biopsy-Detectable Prostate Cancer. GlaxoSmithKline. Study Coordinator 2004 – present.


A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of RTX Topical Solution in Patients with Interstitial Cystitis. ICOS, Inc. Study Coordinator 2003-present.

A Multi-Center, Randomized Phase III Study of Adjuvant Oncophage® versus Observation in Patients with High Risk Of Recurrence after Surgical Treatment for Renal Cell Carcinoma. Antigenics, Inc. Study Coordinator 2002-present.

A Multi-Center, Open-Label, Flexible Dose Escalation Study to Evaluate the Correlation Between Event Log Parameters, Self-Esteem/Overall Relationships (SEAR), and Efficacy of Viagra (Sildenafil Citrate) in Men with Erectile Dysfunction. Pfizer, Inc. Study Coordinator 2002-present.


An Open Comparative within Patient Controlled Phase III Multicenter Hexvix Fluorescence Cystoscopy and Standard Cystoscopy in the Detection of Carcinoma in Situ in Patients with Bladder Cancer PC B 302/01 PhotoCure, Inc Study Coordinator 2002-present


Urodynamic Response to Treatment with Ditropan XL in Patients with Detrusor Hyperreflexia.
Alza Corporation.

A Phase III, Multicenter, Open Label Continuation Study of the Longterm Safety, Toleration, compliance and Efficacy of Controlled Release Darifenacin in Subjects with Overactive Bladder. Pfizer, Inc.
Study Coordinator 2000-present.

A Patient Acceptability Study of Once-Daily Formulation of Tolterodine. A Phase IIIB Open-Label Single Arm Trial in Adult Patients with Overactive Bladder and Symptoms of Urinary Frequency, Urgency and/or Urge Incontinence.
Pharmacia & Upjohn.
Study Coordinator 2001.

A Phase III, Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Controlled-Release Darifenacin Versus Tolterodine in the Treatment of Subjects with Overactive Bladder.
Pfizer, Inc.

A Randomized, Parallel-Group, Double-Blind, Placebo-Controlled Study Comparing the Safety, Tolerance, and Efficacy of RTX (resiniferatoxin) Topical Solution in Patients with Detrusor Hyperreflexia.
Afferon Corporation.

Post Approval Sacral Nerve Stimulation Study for the Treatment of Urinary Voiding Dysfunction.
Medtronic, Inc.
Study Coordinator 1999 – present.

A Prospective Evaluation of the Urethral Drainage Stent (UDS) for patients with Urinary Retention Secondary to Prostate Obstruction.
Boston Scientific.

An Open Label Study to Evaluate Patient Acceptance and Safety of OROS Oxybutynin Chloride in Urge Urinary Incontinence.
Alza Corporation.

Dose Escalating Study with Tolterodine in Patients with Overactive Bladder. A single blind study in patients with symptoms or overactive bladder including urinary urgency and frequency with or without urge incontinence.
Pharmacia & Upjohn.
Study Coordinator 1999.

Intron A & Ribavirin for Treatment of Patients with Chronic Hepatitis C not Previously treated with Interferon.
Schering Corporation.

Combination Therapy with Interferon alpha 2b and Ribavirin for Chronic infection with Hepatitis C Virus.
Schering Corporation.