A. OVERVIEW

The Southwest Oncology Group (SWOG) is among the largest NCI funded cancer cooperative groups in the world. With more than 5,000 investigators at over 400 sites, SWOG has 120 clinical trials available to its membership at any given time. Rich in both treatment and prevention/control trials, major recent undertakings in the prevention of prostate cancer included the Selenium and Vitamin E Cancer Prevention Trial (SELECT) and the Prostate Cancer Prevention Trial (PCPT). Together these trials randomized more than 53,000 men at risk for prostate cancer to intervention or placebo, generating substantial clinical data related to risk of development of prostate cancer and corresponding biorepositories for molecular epidemiologic and other studies.

The purpose of this RFA is to facilitate the conduct of high-quality, hypotheses-driven research in an efficient, coordinated, and equitable manner and to standardize procedures for the utilization of the SELECT and PCPT biorepositories and data elements to assure fair access and maximal utilization of these precious resources in the next stages of research stemming from the observations and findings of SELECT and PCPT.

SELECT is a Phase III, double-blind, placebo-controlled 4 arm study of selenium, vitamin E, selenium and Vitamin E, and placebo. Planned accrual was of 32,400 healthy men ages 55 or more (or 50 or more years for African Americans). Planned study duration was 12 years, with a five-year uniform accrual period and a minimum of 7 years of treatment. The primary objective of SELECT was to assess the effect of selenium and vitamin E alone and in combination on prostate cancer incidence as determined by routine clinical management. Secondary objectives included the effect of these agents on a) lung, colorectal and all cancer incidence b) prostate cancer-free, lung cancer-free and colorectal –free and cancer-free survival c) overall survival and d) serious cardiovascular events.

SELECT, the largest cancer prevention trial ever performed, recently reported that neither selenium nor vitamin E had any beneficial effect on prostate cancer incidence. SELECT demonstrates in a robust and generalizable fashion that in a generally healthy population of men at average risk for prostate cancer neither 200 µg of selenomethionine nor 400 IU of synthetic DL ά-tocopherol, given orally alone or combined had significant effects on the primary or secondary endpoints. The primary results of the study were published in the Journal of the American Medical Association (Lippman SM, Klein EA, Goodman PG, et al.: JAMA 2009;301:39-51). Actual accrual exceeded the goal and 34,888 men were included in the analyses.

A summary of the participant characteristics, the prostate cancers diagnosed, cumulative incidence of prostate, lung, colorectal and all cancers combined, other cancers detected, adverse events and deaths are available at the following portal: swog.org/select

PCPT: In 1993, the Prostate Cancer Prevention Trial (PCPT) was initiated as a randomized placebo-controlled clinical trial to determine whether finasteride could reduce the 7-year period prevalence of histologically proven prostate cancer. Men who

were at least 55 years old with a normal digital rectal exam (DRE) and a serum prostate specific antigen (PSA) $\leq$ 3 ng/ml were randomly assigned to receive either finasteride 5mg per day or placebo and followed for up to 7 years.

A total of 18,882 men gave informed consent for trial participation and use of biospecimens for research purposes. Following randomization, participants underwent DRE and PSA determinations annually. The PSA determinations were done centrally and extra serum was stored. If the DRE was abnormal or the serum PSA was elevated, then a transrectal ultrasound and prostate biopsy were recommended.

After 7 years, all participants not previously diagnosed with prostate cancer, irrespective of their DRE and PSA status, were to undergo a transrectal ultrasound and prostate biopsy. Approximately 60% of the men randomized underwent either an end-of-study biopsy or had an interim prostate cancer diagnosis. This aspect of the PCPT, the characterization of participants' biopsy-determined presence or absence of prostate cancer, makes the PCPT data and biorepository uniquely valuable for studies of prostate cancer etiology and prevention. The primary results of the study were published in The New England Journal of Medicine (Thompson IM, Goodman PJ, Tangen CM, et al. N Engl J Med. 2003 Jul 17:349(3):215-24).

The study design, study outcomes, tissue collection procedures, and sample availability are described at swog.org/pcpt

B. OBJECTIVES

This initiative is intended to provide a mechanism to encourage the development of novel translational research via utilization of the SELECT and PCPT biorepositories and associated data elements.

C. KEY DATES

Release date: October 28, 2010

Letter of Intent required: Due Date November 29, 2010 at close of business day 5pm (EST).

Applications are due by close of business day on Monday, January 10, 2011 5pm (EST). Reviews will occur in January/February 2011 and successful applicants notified by April, 2011. If sufficient initial interest is evident another call may be issued in June of 2011. This RFA will be repeated at least annually for 5 years.

D. ELIGIBLE APPLIANTS

All interested NIH-eligible researchers are encouraged to submit to this program. Awardees will be expected to present their work at the semiannual SWOG group meetings and to adhere to Group policies and procedures as applicable to the project. Specimens will not be released until proof of funding and appropriate IRB review has been provided. Applicants will have to reapply after one year from approval date if proof of funding and IRB approval have not been provided.

The repositories and clinical data are the intellectual property of the Southwest Oncology Group. The Principal Investigator of the Southwest Oncology Group CCOP Research Base grant is responsible for final decisions regarding the use of these biorepositories. Neither the PCPT, SELECT, nor the Southwest Oncology Group provides funding to support applicants' projects. Investigators are required to find funding to support their research projects as well as any additional costs for selecting, processing and shipping samples.

E. APPLICATIONS

1. Letter of Intent (LOI) (mandatory) – must include name(s) and institution(s) of PI and all investigators who would benefit/be involved, Title of Project, and Specific Aims. The LOI will not be made available to reviewers and is being requested to avoid potential conflict of interest in selection of reviewers. Please email your LOI to either select@swog.org or pcpt@swog.org, as appropriate.

2. Proposal
    a. A cover letter from the PI must accompany the application. It should be a PDF file not to exceed 5 pages and should include an abstract of less than 100 words.
        - Include PI contact (email and fax)
        - Provide a brief description of the required resources
        - Be descriptive of any unique resources available to the proposal
        - Summarize the tissue and/or other SWOG resources required to complete the project.
        - An NIH bio sketch for proposed PI and key personnel is required. Please combine all NIH bio sketches into a single PDF, separate from the cover letter.

    Applications will be scored by a review panel composed of internal and external experts as well as SWOG leadership on the following criteria:

    Significance: The potential significance of the research proposed.
    Approach: Adequacy of methods to address question. The amount and types of specimens should be precisely specified.
    Innovation: Originality and novelty of the experimental design, in particular why use of the SELECT and/or PCPT biorepositories is needed or advantageous.
    Plausibility: Likelihood of accomplishing project goals.
    Impact: Likelihood that completion of research will have a clinical impact.

    b. Applications including the cover letter PDF and the combined bio sketch PDF should be submitted via the online form at swog.org/SELECT or swog.org/PCPT.
    c. Samples committed for successful applicants will be embargoed from other usages for up to 3 years.

    All applicants will receive reviewer comments.

    Applications directed toward four major areas of research will be considered. Applications in all categories are welcome.

1. Prostate Cancer
2. Ancillary Studies to SELECT and PCPT (swog.org/select or swog.org/pcpt)
3. Non-prostate Cancers
4. Other Health Outcomes

e. The application should reflect a concise plan of the research to be performed during the proposed project period. A grant application involving humans or animals may be approved, but funds will not be committed until appropriate IRB approval is received. Final decisions are at the discretion of SWOG leadership.
f. Information about biorepositories and data elements is available at swog.org/select or swog.org/pcpt and includes the following features:

SELECT:
Documents/links:

1. Summary of SELECT and Centralized Follow up
2. Summary of ancillary studies and sub-studies based on SELECT
3. Specimens
    - Description of adherence cohort and other sample collections
    - Table of samples collected and analyzed to date (blood and toenail clippings)
    - Blood sample acquisition protocol
    - Tissue acquisition protocol
    - Table of tissues collected and stored
4. Case-cohort
    - Description of design, samples analyzed/DNA extracted
    - Power calculation
5. Additional SELECT documents
    - SELECT study protocol
    - SELECT informed consent
    - *JAMA* paper on SELECT results
    - Forms for SELECT (S0000) and Centralized Follow-up (S00002)
6. SELECT Data
    - Baseline characteristics – from *JAMA* plus additional, collapsed over arms
    - Data from *JAMA* paper plus additional detail
        - Cardiovascular events
        - Cardiovascular procedures
        - Deaths
        - Other cancers
    - Selenium and alpha- and gamma-tocopherol – distributions and summary statistics
        - Plasma levels
        - Toenail clipping levels

PCPT:
Documents/links:

1. Summary of PCPT trial and results
2. Summary of P01 grant and other approved or funded projects based on PCPT
3. Specimens
    - Blood sample and tissue acquisition protocols
    - Table of available specimens
        - Table of PO1 serum samples verified – with volumes
        - Table of non-verified serum samples – unknown volumes
        - Table of DNA orWBC available
        - Table of tissues collected and stored
4. Additional PCPT documents
    - Study protocol
    - List of published papers
    - Relevant study forms
5. PCPT data (all collapsed over arms)
    - Baseline characteristics
    - Endpoints
        - Prostate cancers
        - Other cancers
        - Deaths

F. INQUIRIES AND OTHER QUESTIONS REGARDING THIS RFA MAY BE DIRECTED TO:

Administrative Inquiries:
select@swog.org or pcpt@swog.org. You will receive a response to your questions via email.

Scientific Inquiries:

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