Request for Projects for Wake Forest Brain Tumor SPORE Application

This RFA is for three types of projects that will be taken into consideration for inclusion in the Wake Forest Brain Tumor Specialized Program of Research Excellence (SPORE) application. More information on the SPORE mechanism for translational cancer research support by the NCI is contained below under “Information about SPORE”. All submitted proposals will be reviewed internally and externally. The Executive Committee of Wake Forest Brain Tumor SPORE will decide about their inclusion in the application based on the reviews and programmatic priorities.

The largest focus of Wake Forest neuro-oncology is on research related to human gliomas. It is envisioned that these primary brain tumors will be researched in our SPORE application. However, we encourage submitting applications related to all neuro-oncology topics with an idea that such projects will benefit research on gliomas and vice versa. For example, radiation therapy is frequently used in the treatment of gliomas and also of brain metastases. Researching common denominators (like radiation sensitization) applicable to both clinical situations may represent a substrate for developing SPORE Projects.

The three types of projects include:

1. Research Projects
2. Developmental Research Program (DRP) Projects
3. Career Enhancement Program (CEP) Projects

Ad.1. RESEARCH PROJECTS

Research projects may be conducted solely through the Wake Forest University, or through collaborative associations that have been developed and/or are planned with other SPOREs and/or with other investigators in the biomedical research community.

The proposed project must meet the definition of translational research as described below. Investigators who are not certain about whether their projects fit this definition are advised to consult with Dr. Debinski (debinski@wakehealth.edu).

Projects containing basic research, e.g., employing animal models or cell lines qualify as translational only if a human application is included in the specific aims.

The proposal for Research Project must include:

a) Title of the project and names of research and clinical/translational co-leaders and category of the project
b) Summary of the project (limit 30 lines)
c) Specific Aims (one page)
d) Research Strategy including following sections (12 pages):
   i) Significance
   ii) Innovation
   iii) Approach; which human endpoint to be achieved, as defined by SPORE criteria, needs to be clearly specified

e) References cited
Ad.2. DEVELOPMENTAL RESEARCH PROGRAM (DRP) PROJECTS

The DRP Projects may be collaborative among scientists within one or more SPOREs, or with scientists outside the SPORE community including the international scientific community. **High risk/high payoff pilot projects are especially encouraged.** These pilot projects do not need to reach a human endpoint during the project period as do full projects. DRP studies may become full projects as part of the flexibility option as long as they have translational research potential within the SPORE.

The proposal for DRP Project must include:
   a) Title of the project and names of research and clinical/translational co-leaders category of the project
   b) Summary of the project (limit 30 lines)
   c) Specific Aims (one page)
   d) Research Strategy including following sections (4 pages):
      i) Significance
      ii) Innovation
      iii) Approach; which human endpoint is targeted, as defined by SPORE criteria, needs to be clearly specified
   e) References cited

Ad.3. CAREER ENHANCEMENT PROGRAM (CEP) PROJECTS

Funds from this program may be used to support junior faculty or established investigators who wish to enhance or refocus their careers on translational research. **This program is not a training program and does not support pre- or post-doctoral fellows, either pre-clinical or clinical.** However, advanced post-doctoral or clinical fellows who provide a letter from an institution stating that the candidate will be joining its faculty within the year are eligible for this program. Investigators supported by NCI career development awards (K series) may also be eligible for support through this program.

The proposal for CEP Project must include:
   a) Title of the project and names of research and clinical/translational co-leaders and category of the project
   b) Summary of the proposal (limit 30 lines)
   c) Specific Aims (one page)
   d) Research Strategy including following sections (4 pages):
      i) Significance
      ii) Innovation
      iii) Approach; which human endpoint is targeted, as defined by SPORE criteria, needs to be specified
      iv) Explanation how the CEP will help in applicant’s career in neuro-oncology field
   e) References cited

**WOMEN AND MINORITIES ARE STRONGLY ENCOURAGED TO APPLY.**
For all types of projects please be mindful of new Rigor and Transparency stipulations by the NIH (NOT-OD-16-011 and NOT-OD-16-012).

**Proposed projects format:** The projects should be written in a traditional format of NIH R01/R21 applications (0.5” margins, no more than 6 lines per inch). Please include NIH biosketch (new 5-page format) for all Key Personnel. Typical budget for Research Projects is 200-250K/year for 5 years (may vary). The budgets for DRP and CEP are at least 50K/year, usually for a maximum of two years. These numbers are given as examples only and should be kept in mind when deciding about the scope of the projects.

**The deadline for submitting proposals is September 9, 2016.** The proposals should be submitted as a single PDF document to sraiford@wakehealth.edu. The proposals not received by the deadline and not conforming to the above-listed formats will not be reviewed.

Any questions should be addressed to Waldemar Debinski ([debinski@wakehealth.edu](mailto:debinski@wakehealth.edu)) or Glenn Lesser ([glesser@wakehealth.edu](mailto:glesser@wakehealth.edu))
INFORMATION ABOUT SPORE

What is SPORE and what overall purpose does it serve? Specialized Program of Research Excellence (SPORE) application is a P50 Research Center Grant (PAR-14-353). The program funds P50 SPORE grants to support state-of-the-art investigator-initiated translational research that will contribute to improved prevention, early detection, diagnosis, and treatment of an organ-specific cancer (or a related group of cancers). For the purpose of this program, cancers derived from the same organ system (i.e., group of organs that perform common function) are considered related. Examples of such organ systems include gastro-intestinal, endocrine, circulatory, and other biological systems. Other programatically appropriate groups of cancers may include those centered around a common biological mechanism critical for promoting tumorigenesis and/or cancer progression in organ sites that belong to different organ systems. For example, a SPORE may focus on cancers caused by the same infectious agent, or sustained and promoted by dysregulation of a common signaling pathway. SPOREs are expected not only to conduct a wide spectrum of research activities, but also to contribute significantly to the development of specialized shared resources core facilities, improved research model systems, and collaborative research projects with other institutions. The research supported through this program must be translational in nature and must always be focused upon knowledge of human biology stemming from research using cellular, molecular, structural, biochemical, and/or genetic experimental approaches with the goal of a translational human endpoint within the project period of the grant.

SPORE applications are expected from institutions with demonstrated ability to conduct translational research in the prevention, early detection, diagnosis, and/or treatment of human cancer. Applications may address cancer in any organ site, but each application must be organ site specific or address cancers that are related. Traditionally, these have included leukemias, lymphomas, myelomas, sarcomas, and cancers of brain, breast, gastrointestinal (GI) system, bladder, kidney, cervix, endometrium, head & neck, lung, ovary, pancreas, prostate, skin, oral cavity & pharynx, eye & orbit, and endocrine system. In recent years, applications have been also encouraged when they focus on pathway-driven or other novel cross-cutting themes that have potential for innovation and high scientific impact.

What is translational research? Translational research uses knowledge of human biology to develop and test the feasibility of cancer-relevant interventions in humans and/or determines the biological basis for observations made in individuals with cancer or in populations at risk for cancer."

The term "interventions" is used in its broadest sense to include molecular assays, imaging techniques, drugs, biological agents, and/or other methodologies applicable to the prevention, early detection, diagnosis, prognosis, and/or treatment of cancer. SPORE translational research projects may involve the use of any cellular, molecular, structural, biochemical, and/or genetic experimental approaches.

By this definition, SPORE projects are permitted to move not only in the forward direction, toward clinical trials and studies in areas of prevention, early detection, treatment, development of biomarkers, and population science, but also in the reverse direction, using human biospecimens, often from clinical trials, to study new phenomena, to optimize previous findings, or to develop new hypotheses based on results from human studies.
All proposed SPORE projects must be translational. In every SPORE project, the development of new cancer-relevant interventions should include both a laboratory component and a human application that must be performed at some time during the 5-year term of the grant. When human biospecimens are the starting point for SPORE projects, these biospecimens must be used to study the biological basis of observations made in humans. For the purpose of these Guidelines, such human applications are defined as the human endpoints.

**What are human endpoints?** At least one of the following types of human endpoints should be proposed in each SPORE research project:

- Early phase clinical trials of new investigational drugs and biologics, experimental procedures, medical devices, or combinations thereof, or
- Early phase clinical trials of new combinations or new uses of the FDA-approved agents and devices, or
- Discovery and development of biomarkers, only when measurements are made in human specimens, or directly in human subjects, or
- IND-directed toxicology studies* conducted following a pre-IND meeting with the FDA in which the plan proposed by the investigators is acceptable to the FDA, or
- Population, behavioral, or psychosocial studies, when these studies address mechanistic aspects of the biology of the disease, or
- Clinical studies that lead to laboratory studies, which address new clinical hypotheses.

Experiments using cell lines, xenografts, or tumor grafts (using primary human tumors) may be important to the translational studies proposed and are encouraged, but are not sufficient to meet the human endpoint requirement.

Although IND-directed toxicology studies do not involve human beings, but as these studies are the last steps before clinical trials begin, they are considered programmatically appropriate as a human endpoint for SPORE translational projects.

**What are unique features of SPORE?** The SPORE program fosters highly interactive translational research based on a unique approach with the following characteristics:

- Focuses solely on translational research, using a team science approach, with at least four scientific projects, containing at least one specific aim that reaches a human endpoint within 5 years.
- In addition to translational research that involves basic research discoveries being applied in the clinic, the SPORE program encourages translational research projects that start with a clinical observation and return to the laboratory to explore the underlying biological mechanisms.
- Encourages projects on early detection, prevention or population science (defined below).
• Requires collaborations among individual SPORE awardees (inter-SPORE collaborations) and/or collaborations between individual SPOREs and other research programs.
• Encourages early phase clinical trials and handing off later trials to other mechanisms including industry and other governmental and non-governmental mechanisms.
• Expects each individual SPORE awardee and the "network" of SPOREs to conduct research that will have the most immediate impact possible on reducing incidence and mortality of human cancer.

Inherent in this process is the interdependence between investigators conducting basic and applied research. Clinical and/or epidemiological research that does not include a laboratory component or capitalize upon a biological discovery relevant to human cancer is not considered translational for the SPORE.

**Updated information related to the NIH applications:**
NIH has announced changes to Policies, Forms, and Instructions for Grant Applications submitted in 2016 (see, NOT-OD-16-004).

These changes are:
- Rigor and Transparency (see NOT-OD-16-011 and NOT-OD-16-012)
- Vertebrate Animals (see NOT-OD-16-006)
- Inclusion of Children: Change in NIH Definition (see NOT-OD-16-010)
- Research Training (see NOT-OD-16-007)
- Font Requirements (see NOT-OD-16-009)
- Assignment Request Form (see NOT-OD-16-008)
- Appendices (Notice will be issued by spring 2016)
- Biosketch Clarification (NIH is clarifying instructions)
- Data Safety Monitoring (NIH is adding a new attachment involving Clinical Trials)