National Cancer Institute

Molecular and Cellular Characterization of Screen-Detected Lesions (U01)

RFA-CA-14-010

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Scope

The goal of this Funding Opportunity Announcement (FOA) is to solicit applications from independent, multi-disciplinary teams to undertake a comprehensive molecular and cellular characterization of tumor tissue, cell, and microenvironment components to distinguish screen-detected early lesions from interval and symptom-detected cancers. (breast, prostate, lung, melanoma, and pancreas).

Objectives

Establish Molecular Characterization Laboratories (MCLs) to:

- Conduct a comprehensive characterization of screen-detected lesions from one of the specified tumor types to understand the biological underpinnings for progression from pre-neoplastic to early neoplastic lesions to indolent and malignant invasive cancer

- Use innovative approaches and enabling technologies to determine both the molecular and cellular phenotypes of early lesions, assess the degree to which progression of these lesions is predictable or stochastic, and to allow a better prediction of the fate of early lesions

Examples That Would Help Meet This Objective

- Molecular comparison of recurrent and non-recurrent screen-detected lesions and interval cancers, to determine whether a subset of aggressive, screen-detected lesions shares features with interval cancers that indicate their rapidly progressing phenotypes

- Analysis of tumor heterogeneity to determine whether lesion phenotypes can be distinguished based on the extent of their heterogeneity

- Phenotyping of cellular components of lesions, including tumor cells and the microenvironment with the goal of generating molecular signatures to detect early malignant lesions associated with increased mortality

- Detection of secreted factors in tumor microenvironment and/or in blood that are specific to a subset of early lesions, which can relate molecular characteristics of a tumor to its surrounding microenvironment that are relevant to necrosis or patterns of tissue invasion

- Generation of a repository of screen-detected lesions/cancers and interval cancers from existing repositories and from new, prospective collections

Requirements

- Annual budget of applications must not exceed $500,000 in direct cost
- The project period is up to 5 years
- All page limitations described in the SF424 Application Guide apply
- Applications must include:
  - Letters from collaborators and consultants
  - Letters provided by biospecimen repositories or cohorts on specimens and associated information available for the purpose of the proposed studies
- Resource Sharing Plans (in addition to NIH required), including:
  - Biospecimens accrued through MCL support
  - Emphasis on precompetitive data sharing

Requirements

- All multiple PD/PI applications are required to include a Leadership Plan
- Investigators will be expected to devote a portion of their effort to participating in collaborative activities with other Consortium members
- Applicants must set aside 20 percent of their annual budget for collaborative studies

Key Points To Remember
Address them Clearly in the Application

- How relevant are the proposed studies to the clinical management of screen-detected versus symptom-detected cancers? (underlying theme – overdiagnosis)
- Good understanding **of** the molecular and cellular factors distinguishing indolent from aggressive lesions, or screen-detected from symptom-detected, interval cancers?
- Well-assembled team of investigators with the expertise and experience of the PD(s)/PI(s) and other researchers in the context of proposed research?
- Does the investigative team bring sufficient complementary, multi-disciplinary scientific expertise required for integrated and comprehensive approaches to key research problems proposed?
- Do the team members have a relevant record of collaborations within and outside the applicant institution? Is the commitment of the PD(s)/PI(s) and other senior investigators adequate?
- To what degree, does the applicant team take advantage of a collaborative and interactive model of research? Are the structure and activities planned for the MCL adequate for the needs of the proposed studies and the anticipated trans-Consortium activities?
- How adequate are plans for prospective collection and use of specimens within the context of screen-detected and interval cancers?
- Does the team have the resources and expertise to collect specimens, an important requirement of this FOA?

Frequently Asked Questions

Q1. Is there a goal for analyzing both cystic and solid pancreatic lesions? Is a signature being sought that differentiates varied PanIN levels (II versus III, for example, as the latter might be expected to progress to cancer while the former is not or less likely)?

A1. *Responsive to the intent of FOA. Study of progression from cystic lesions is desirable.*

Q2. U01s are multicenter projects, but the allowable budget would not support a project of this magnitude. Should a submission be a single center project with multiple labs and/or investigators using pre-existing biorepositories in order to work within the limits of the budget?

A2. *Agree with the budget issue. The current FOA is considered to be a Pilot Program and its success will determine the future directions to be taken. Pre-existing resources are expected to complement the budget provided by this FOA.*

FAQ, continued

Q3. How is the Steering Committee assembled?

A3. *Two Investigators from each awarded MCL along with NCI staff will form the SC.*

Q4. Will a budget for computing and data storage be allowed?

A.4 *Limited storage would be required initially on clinical and Epi data. Eventually we will work with the NCI facility to provide such resources.*

Q5. Do I need letters of support from my institution to do this?

A5. *Yes*

Q6. Since this is a new RFA, can we partner with biotech companies?

A6. *Highly encouraged, though not required.*

Q7. Can a foreign collaborator be included in the proposal? If the answer is yes then can I include any salary plus the material cost for carrying out the experiment/analysis?

A7. yes to both

FAQ, continued

Q8. Can I change (add or replace) a collaborator from that submitted in the LOI?

A8. *yes*

Q9. Given the specified format of Sub-sections A (overview), B (research strategy), and C (prospective collection of specimens), totaling up to 30 pages --- would Section B be analogous to the typical 12-page Research Strategy of an R01?

A9. *As long as it is within a 30-page limit.*

Q10. Is it correct that one of the specific aims would likely be based on developing a data/tissue, etc. infrastructure?

A10. *No.*

Q11. Is it expected that we would have 2-3 scientific aims?

A11. *No. As a P.I. you decide the scope of the work considering the budget limitation and time constraints.*

FAQ, continued

Q12. Can I make a cosmetic change in the title from that submitted in the LOI?

A12. *Yes*

Q13. Can I buy equipment?

A13. *It is expected that the P.I. is in possession of require infrastructure and equipment. Other than smaller equipment, this FOA does not encourage a capital investment.*

Q14. Should we contrast malignant vs benign from a cellular/molecular phenotype level, or are you suggesting we compare malignant screen-detected/removed lesions from malignant symptom/clinical /interval-detected/[removed] lesions?

A14. *Both. But the method of detection should be known*.

Q15. The term “symptom and interval detected” tumors implies they [symptomatic versus interval-detected] are similar, here meaning interval cancers are those picked up between the annual screening (CT) events. Is this correct?

FAQ, continued

Q16. Where will the U01 (lung) samples come from?

Q17. How should consortium-source (lung) samples be described on the U01 application, as their features/collection criteria/procedures are not yet clear?

Q18. Is a Multiple PI approach to grant/project management this permissible? If so would it be possible to have more than 2 Principal Investigators, e.g., three, with a designated contact PI?

Q19. We are considering a research strategy that would not necessarily involve an epidemiologist in the leadership team. Would this be considered a deficiency?

Q20. It is not completely clear whether a separate listing of the numbers and types of samples available for distribution to Consortium institutions should be included in the application?