NIH Common Fund: Protein Capture Reagents Initiatives

RFA-RM-10-017 and RFA-RM-10-018

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Teleconference Agenda

- Introduction - Protein Capture (PC) Reagents Program
- RFAs Overview and Key Dates
- Application Process
- Review Process and Criteria
- Q & A Session: *Questions are encouraged to be sent in advance of the call by email to Leslie Adams* ***(adamslb@mail.nih.gov).*** *Questions received by email either in advance or during the call will be addressed first.*

FAQs are posted on the PC website:
http://nihroadmap.nih.gov/proteincapture/faq.asp

These slides will be posted at a later date

Protein Capture Initiative

Ultimate goal: Community resource of renewable high-quality protein capture reagents for all human proteins.

- Long history of discussion at NIH (more than 5 years)
- Most significant questions in five years of discussion: It is feasible scientifically, and practically?
- Much community input, and many claims. Wide range from: "Only classical monoclonals are ready" to: "Better approach is ready now".

Protein Capture Initiative

Conclusion before was— "classical approach too expensive to start a comprehensive effort. Wait until a better/cheaper method clearly proves itself."

2009 decision: **Go forward with a pilot for an important sub-proteome (human TF's); encourage alternate approaches that may be ready soon through the pilot. CF approved late 2009.**

Virtues: get moving, drive development for scale (don't wait for it to happen); at least get resource for human TF's even if expensive

Risks: Uncertainty about alternatives and when they will be ready to scale

NIH Workshop – October 2010

Consensus from workshop participants:

"There exists at least one approach that can right now obtain reagents 'in production' for human TF's in five years"

"There exist alternate approaches that are capable of demonstrating scale and superior performance within a few years if funded to do so"

One purpose of this workshop was to understand *in detail* the extent to which this view is correct. There are many important details: cost and cost drivers, quality/validation, benchmarks, utility, etc.

Protein Capture Initiative

Conceived as three components:

1. Immunogens for TF's (3 years)---already funded

2. Production effort for TF's using "low risk, ready to scale" approach (5 years): RFA-10-RM-017

3. Technology Development effort for protein capture reagents: Improve and/or develop approaches (e.g. higher throughput, lower cost) for generating high quality protein capture reagents (3 years): RFA-RM-10-018

NOTE: Must have pilot then assess. Will need to make case for full effort in ~4 years. Must have reasonable set of TF reagents as well.

Receipt, Review, and Anticipated Start Dates

- Letter of Intent Receipt Date: January 4, 2011
- Application Receipt Date: February 4, 2011
- Peer Review Date: June-July 2011
- Council Review Date: August, 2011
- Earliest Anticipated Start Date: September 2011

RFA-RM-10-017 Overview

Production of Affinity Reagents for Human Transcription Factors

Areas of Emphasis:

- Focus on developing, optimizing and scaling high quality renewable affinity reagent s for a subset of the human proteome (TFs)
- Develop an affinity reagent resource of the broadest possible utility (highest priority is ChIP)
- Pipeline implementation, including viable distribution plan with minimal constraints on reagent use
- Proposed approaches must be **convincingly scalable** at the present time, in order to produce a community resource consisting of high quality affinity reagents to all human transcription factors by the end of the funding period

Production RFA 2011-2016

- Open RFA competition funded by Common Fund (CF) Protein Capture Initiative and administered by NHGRI
- Considered a **pilot** that will inform the long-term objective of developing a comprehensive set of human protein capture affinity reagents
- Up to 2 centers (U54 Cooperative Agreements) are expected to be funded
- Direct Costs up to $2.6M per year and up to 5 years
- Foreign Organizations are eligible for this FOA

Application and Process RM-10-017

Uses standard PHS 398 form for both RFAs, but has *additional requirements:*

- **Research Strategy** (30 pgs. Max):
  -Pipeline from acquisition through validation

- **Resource Distribution Plan** (6 pages):
  -Minimal cost, and without undue intellectual property constraint
  -Distribution of protein affinity reagents through commercial and/or non-profit

- **Management Plan** (6 pages):
  -Project leadership /key personnel responsibilities
  -Center structure
  -Coordination among components and Protein Capture Program
  -Budget for committees and coordination (incl. travel)

Review Criteria RM-10-017

Standard review criteria with key points to include:

- Is there a high likelihood that the proposed center can produce high-quality affinity reagents TFs, at levels of throughput, data quality, and cost within the scope and award period anticipated by this FOA?
- Is there a likelihood that the activities of the proposed center will provide useful information about how to pursue a larger-scale effort?
- Does the applicant have adequate plans for increasing throughput while lowering costs? Does the applicant have a successful record in this regard?
- Is there adequate description of acquisition and coordination of immunogens from the currently funded immunogen production effort? If alternatives are proposed, are they likely to be an advantage in the ultimate production of affinity reagents?
- Is there evidence that systems are in place to support resource distribution?

Technology Development RFA-RM-10-018 Overview

- Open RFA competition funded by CF Protein Capture Initiative and administered by NIDDK
- Part of the overall pilot that will inform the long-term objective of developing a comprehensive set of human protein capture affinity reagents
- 3 to 5 centers (U54 Cooperative Agreements) are expected to be funded
- Direct Cost (excluding F&A) up to $1M per year and up to 3 years
- Foreign Organizations are eligible for this FOA

Technology Development for New Affinity Reagents Against the Human Proteome RFA-RM-10-018

Areas of Emphasis:

- Development of better approaches (e.g. cheaper, higher throughput, higher quality) for producing high quality affinity reagents.
- Applications should describe an approach for improving and/or developing protein affinity reagent technologies that can be ready for proteome scale projects within three to five years.
- Technology development should be put in the context of a production process.
- Proposed improvements or developments can be across the entire process or focused on specific aspects of the process (including target selection, antigen production, reagent validation)

“High Quality” Reagents

- High Affinity (nanomolar-range preferable)
- High Specificity
- Broadest possible utility (e.g. immunohistochemistry, immunofluorescence, immunoprecipitation)
- At least one specific application in addition to above (not just WB)

Application Structure for RFA-RM-10-018

Follow the instructions in the PHS398 Application Guide

Additional Requirements to Standard Research Plan:

- **Research Strategy** (30 pgs. Max) should address:
  I. Choice of targets and antigens production
  II. Renewable protein affinity reagents
  III. Characterization and validation

- **Resource Distribution Plan**:
  Reagents to be distributed at minimal cost, and without undue intellectual property constraint
  Distribution of protein affinity reagents through commercial and/or non-profit

- **Management Plan:**
  Project leadership /key personnel responsibilities
  Center structure
  coordination among components and Protein Capture Program
  Budget for committees and coordination

6 Pgs. limit for RDP + MP

Review criteria for RFA-RM-10-018

Typical review criteria (i.e. Significance, Investigator(s), Innovation, Approach, Environment)

Key points include:

- Is there a high likelihood that the proposed center can develop an approach that would substantially improve the throughput or reduce the cost of the pipeline that is presently used for producing high quality and validated protein affinity reagents?
- Will the approach proposed be amenable to a proteome scale project in three to five years
- Are the milestones proposed for assessing progress adequate (midterm review in 2nd year)

Selection Process for both RFAs

The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by peer review
- Availability of funds
- Relevance of the proposed project to program priorities;"program balance"

Contact Information

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