The NIH R03 and R21 Grant Mechanisms

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NIH Exploratory/Developmental Research Grant Award (R21)) (Funding Opportunity Number (FOA): PA-25-307)

Purpose: intended to encourage exploratory/developmental research by providing support for the early and conceptual stages of project development

Characteristics:

- High risk/high reward studies
- No risk is required but risk is tolerated
- No preliminary data is required, but
- Any preliminary data provided will be evaluated
- Rationale needs to be supported
- "fishing expedition" criticism is relatively muted

Investigators are strongly encouraged to consult with NIH Scientific/Research staff during the concept development stage of the application to determine if an R21 application is appropriate

NIH Exploratory/Developmental Research Grant Award (R21))
(Funding Opportunity Number (FOA): PA-25-307)

Project funded for up to two years

The combined budget for direct costs for the two-year project period may not exceed $275,000. Direct cost for a single year may not exceed $200,000

Typical requests are $125,000 one year and $150,000 for the other.

R21s can not be renewed

Step 1: Developing the idea

Example:
Developing a new stem cell-based infection model that enables studies of clinical samples of hepatitis C virus

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- No such model exists and studies of this virus from clinical samples are urgently needed for drug and vaccine development.
- Successful development of this model will also enable mechanistic studies of why clinical samples cannot infect the existing model. i.e. liver cells obtained from normal people, providing novel insights on the interplay between host and pathogen

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- The risk is that stem-cell derived cells cannot be infected, so no model in the end.
- Here some preliminary data on the ability to generate the cells, ready to be tested for permissiveness for infection would be useful.
- **Rationale for potential success:**
  - Current model are mature hepatocytes
  - Stem cell-derived hepatocytes have been shown to be immature
  - Immature cells have been shown to have immature antiviral response compared with their mature counterparts
  - The rationale and hypothesis here is that stem cell derived hepatocytes may be more susceptible to clinical virus

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- "Fishing expedition" is more tolerated in this mechanism. Looking for a new model, new drug/target, testing a new provocative idea etc.
- Successful of the project should lead to a more comprehensive mechanism-driven project such as a R01.
- **In this case:** if the model is developed, in addition to clinical applications, understanding the mechanism that underlies the success of the model is a R01.

Step 1: Developing the idea

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Step 2: Writing the Science part

The Science Sections

Project Summary/abstract (up to 1 page)

Introduction to application (if resubmission)

Specific Aims (1 page)

Research Strategy (up to 6 pages)

- **Background and Significance**
- **Innovation**
- **Preliminary data (if any)**
- **Approach**

Step 2: Assembling the proposal

Proposal SECTIONS

- **Project Summary/abstract**
- **Project Narrative (2-3 sentence description for public and Congress)**
- **Facilities, equipment, and Resources**
- **Biosketches** (form changes every few years, not sure why)
- **Budget and budget justification**
- **Introduction to application**
- **Specific aims**
- **Research Strategy**
- **Data management plan**
- **MPI plan**
- **Vertebrate Animals**
- **Human Subjects**
- **Resource Sharing**
- **Letters of Support**

SCORED REVIEW CRITERIA

- **Factor 1: Importance (Significance and Innovation) 1-9**
  - Why do this? Has this been done before?

- **Factor 2: Rigor and Feasibility (experimental approach) 1-9**
  - How would you do this? Will the approach work?

- **Factor 3: Expertise and Resources (Investigator and environment) pass/fail**
  - Are you capable? Is your school real?

NIH Small Research Grant Program (Parent R03) (Funding Opportunity Number (FOA): PA-25-302)

Purpose: The NIH R03 funding opportunity announcement (FOA) supports discrete, well-defined projects that realistically can be completed in two years and that require limited levels of funding, such as:

- Pilot or feasibility studies
- Secondary analysis of existing data
- Small, self-contained research projects
- Development of research methodology

The combined budget for direct costs for the two-year project period may not exceed $100,000. No more than $50,000 in direct costs may be requested in any single year. Cannot be renewed.

Tend to be institute specific in terms of targeted areas. Not all institutes have general R03 mechanisms. NIAID has this mechanism.

An example for a potential R03 project

To determine if cells in human testes can be infected by the monkeypox virus: **A pilot study** for investigating potential sexual transmission of monkeypox virus

The Science Sections

Project Summary/abstract (up to 1 page)

Introduction to application (if resubmission)

Specific Aims (1 page)

Research Strategy (up to 6 pages)

- **Background and Significance**
- **Innovation**
- **Preliminary data (not needed but can be provided)**
- **Approach**

Common Score-lowering Issues

- **Poor writing** (reviewers are humans with shorter and shorter attention spans these days)
- **Mediocre idea** (should be novel but supported)
- **Lack of feasibility** (don't propose experiments can only done on Mars)
- **Poor research design** (if experiments worked, they should answer your questions)
- **Flawed or missing interpretation of potential outcomes**
  - *A common flaw here is to only focus on potential technical challenges and ignore (head in the sand approach) the possibility that your whole hypothesis could be proven wrong by your own experiments.*
- **Lack of institutional commitment** (got to have a bench)
- **Poor or modest productivity** (pubs, recent pubs, and relevant pubs)

TIPS

- Start writing early. At least 2 MONTHS before deadline
- READ and FOLLOW INSTRUCTIONS.
- If you are struggling to write research strategy, it probably means that you do not have a well-developed idea.
- Work closely with your mentor/co-Is.
- Talk to your program officer (get on their radar screen).
- Write grant proposal using the style of the magazine *Scientific American*. In the old days, this is described as "your admin who makes copies for the proposal should understand your summary and specific aims page".
- Graphs and tables are excellent.
- Have others with experience read your grant. However, give them a finished draft and do so with ample time to modify your grant to address their criticisms. DO NOT use them as proof-readers or make them work on your schedule.