Winning an NIH Grant: 
Tips and Strategies to Increase Your Chances of Success

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National Institutes of Health
Grants Process
At-A-Glance

Planning, Writing, and Submitting

Planning: Applicant should start early, collect preliminary data, and determine internal deadlines.

Writing: Applicant often begins writing application several months prior to application due date.

Submitting: Applicant organization submits most applications to NIH through the Federal portal, Grants.gov.

Receipt and Referral

Applications compliant with NIH policies are assigned for review by the Division of Receipt and Referral in the Center for Scientific Review (CSR).

CSR assigns application to an NIH Institute/Center (IC) and a Scientific Review Group (SRG).

Scientific Review Officer (SRO) assigns applications to reviewers and readers.

Peer Review

Initial Level of Review: SRG members review and evaluate applications for scientific merit.

Priority Score: Available to Principal Investigator in eRA Commons.

Summary Statement: Available to Principal Investigator in eRA Commons.

Second Level of Review: Advisory council/ board reviews applications.

Award

Pre-Award Process: IC grants management staff conducts final administrative review and negotiates award.

Notification of Award: Institute/ Center issues and sends Notice of Award (NoA) to applicant institution/organization.

Congratulations! Project period officially begins!

9 - 10 Months

Post-Award Management

Administrative and fiscal monitoring, reporting, and compliance


NIH Office of Extramural Research

National Institutes of Health
“Well, we got the grant.”
What I Will Cover Today

- Planning, Writing, and Submitting an NIH Grant Application
- Deciphering NIH Peer Review
- The Psychology of NIH Peer Review
- Helpful Online Resources
Planning, Writing, and Submitting
Planning Timeline

- months
  - prepare
  - internal deadline

- Due
  - 1
  - 2
  - 3
  - 4
  - 5
  - 6
  - 7

- up to 20
  - review
  - Council
  - funding
  - end-of-year funding

- hypothetical timing
  - 4 months before your institution's deadline
  - plan
  - get feedback from PO and colleagues
Writing Timeline
Submission Timeline
# Types of Funding Opportunity Announcements

<table>
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<tr>
<th>Type of FOA</th>
<th>Description</th>
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| Program Announcement (PA, PAR, PAS)               | • Highlights areas of focus  
• Usually open for 2-3 yrs.  
• Often uses the standard receipt dates |
| Request for Applications (RFA)                     | • Narrowly defined scope  
• Usually single receipt date  
• Has designated funds  
• Usually uses customized review panel |
| Parent Announcement                               | • For investigator-initiated/unsolicited research applications  
• Generally spans the breadth of NIH mission by grant type (R01, R03, etc.)  
• 80 percent of NIH budget |
Career Stages of Funding Programs

- Institutional Training Grant (T34)
- Institutional Training Grant (T32)
- Individual NRSA Fellowship (F31, F30)
- Institutional Training Grant (T32)
- Individual NRSA Fellowship (F32)
- Pathway to Independence Award (K99/R00)
- Mentored Research Scientist Development Award (K01)
- Mentored Clinical Scientist Development Award (K08)
- Mentored Patient-Oriented RCDA (K23)
- Mentored Quantitative RCDA (K25)
- Independent Scientist Award (K02)
- Midcareer Investigator Award in Patient-Oriented Research (K24)

Small Grant (R03)
Research Project Grant (R01)
Exploratory/Developmental Grant (R21)

Senior Scientist Award (K05)

Graphic represents a small sample of NIH funding mechanisms available.
Parts of an (R01) Application

- Abstract/Summary
- Research Plan
  - Specific Aims - 1p.
  - Significance
  - Innovation
  - Approach
- Budget and Justification
- Assurances
  - Human Subjects
  - Vertebrate Animals
- Resources and Environment
- Other (refs., bios, support letters, appendices)

As you write and review, make sure everything is in sync, i.e., the who, what, when, where, and how should agree!
The Research Plan \(\Rightarrow\) Specific Aims

1. Start with an overview:
   a) State the goal of your project
   b) State your hypothesis
   c) Summarize the rationale and significance of your project

2. List specific aims:
   a) Each one should be specific and focused.
   b) Each one should test the hypothesis.
   c) As a whole they should synergize (but shouldn’t be dependent on one another)

3. End with important information your project will uncover:
   a) 1-3 sentences
Specific Aims – Example 1

The goals of this proposal are to identify microRNAs (miRNAs) and elucidate gene networks that regulate limb regeneration. Elucidation of microRNA-dependent regulation during amphibian regeneration should enable identification of key molecular components and regulatory steps that could potentially permit the therapeutic activation of regenerative processes in mammals.

Our studies will -

1. Identify microRNAs expressed in intact, regenerating, and non-regenerating limbs.
2. Characterize miRNA-mRNA regulatory interactions
3. Conduct a functional analysis of selected miRNAs in limb regeneration
Reviewer Comments:

“…an unfocused screen for potential miRNAs that participate in limb regeneration…”

“The functional characterization is less focused and thus more uncertain in outcome. The potential unique assay offers a tantalizing opportunity, but it would be stronger if a more comprehensive analysis of all candidates were proposed.”

“The functional analysis is diffuse and overly ambitious. There is a major concern that the results will not lead forward to a more mechanistic understanding of limb regeneration.”
Specific Aims – Example 2

We will investigate the molecular mechanisms for Factor X-induced Receptor A trafficking. We will show that chronic drug exposure upregulates the expression of Factor X, which triggers and sustains the exocytotic trafficking and surface expression of functional Receptor A.

More specifically, our studies will -

1. Determine the signaling pathways mediating Factor X-induced Receptor A trafficking
2. Determine Factor X involvement in drug-induced Receptor A trafficking
3. Determine the synaptic sites of Receptor A trafficking and Receptor A-B interactions
4. Determine the behavioral significance of emergent Receptor A and behavioral Receptor A-B interactions
Reviewer Comments:

“Strengths...include novel and innovative hypotheses, sound experimental design...and a high likelihood of meaningful findings.”

“Strengths include the significance of the central hypothesis, the well-designed experimental plan...”

“...the rationale for the studies is clearly delineated...scope of the studies is appropriate...”
Microscopy has emerged as one of the most powerful and informative ways to analyze cell-based high-throughput screening (HTS) samples in experiments designed to uncover novel drugs and drug targets. However, many diseases and biological pathways can be better studied in whole animals—particularly diseases that involve organ systems and multicellular interactions, such as metabolism and infection. The worm Caenorhabditis elegans is a well-established and effective model organism that can be robotically prepared and imaged, but existing image-analysis methods are insufficient for most assays. We propose to develop algorithms for the analysis of high-throughput C. elegans images, validating them in three specific experiments to identify chemicals to cure human infections and genetic regulators of host response to pathogens and fat metabolism. Novel computational tools for automated image analysis of C. elegans assays will make whole-animal screening possible for a variety of biological questions not approachable by cell-based assays. Building on our expertise in developing image processing and machine learning algorithms for high-throughput screening, and on our established collaborations with leaders in C. elegans research, we will:

**Aim 1:** Develop algorithms for C. elegans viability assays to identify modulators of pathogen infection

**Challenge:** To identify individual worms in thousands of two-dimensional brightfield images of worm populations infected by Microsporidia, and measure viability based on worm body shape (live worms are curvy whereas dead worms are straight).

**Approach:** We will develop algorithms that use a probabilistic shape model of C. elegans learned from examples, enabling segmentation and body shape measurements even when worms touch or cross.

**Impact:** These algorithms will quantify a wide range of phenotypic descriptors detectable in individual worms, including body morphology as well as subtle variations in reporter signal levels.

**Aim 2:** Develop algorithms for C. elegans lipid assays to identify genes that regulate fat metabolism

**Challenge:** To detect worms versus background, despite artifacts from sample preparation, and detect subtle phenotypes of worm populations.

**Approach:** We will improve well edge detection, illumination correction, and detection of artifacts (e.g. bubbles and aggregates of bacteria) and enable image segmentation in highly variable image backgrounds using level-set segmentation. We will also design feature descriptors that can capture worm population phenotypes.

**Impact:** These algorithms will provide detection for a variety of phenotypes in worm populations. They will also improve data quality in other assays, such as those in Aims 1 and 3.

**Aim 3:** Develop algorithms for gene expression pattern assays to identify regulators of the response of the C. elegans host to Staphylococcus aureus infection

**Challenge:** To map each worm to a reference and quantify changes in fluorescence localization patterns.

**Approach:** We will develop worm mapping algorithms and combine them with anatomical maps to extract atlas-based measurements of staining patterns and localization. We will then use machine learning to distinguish morphological phenotypes of interest based on the extracted features.

**Impact:** These algorithms will enable addressing a variety of biological questions by measuring complex morphologies within individual worms.

In addition to discovering novel anti-infectives and genes involved in metabolism and pathogen resistance, this work will provide the C. elegans community with (a) a versatile, modular, open-source toolbox of algorithms readily usable by biologists to quantify a wide range of important high-throughput whole-organism assays, (b) a new framework for extracting morphological features from C. elegans populations for quantitative analysis of this organism, and (c) the capability to discover disease-related pathways, chemical libraries, and drug targets in high-throughput screens relevant to a variety of diseases.
The Research Plan \( \Rightarrow \textbf{Significance} \)

1. Summarize the pivotal work before yours.
   a. Strive for balance and completeness
   b. Include any controversies and discrepancies your project will address

2. State the key scientific questions that remain and why they need to be answered.

3. Summarize what you propose to do to answer one of these questions or fill an important gap in our understanding.

4. Explain how the research will improve scientific knowledge, technical capability, clinical practice, or health services.
Law of Gravity!

Oranges also follow the law of Gravity!

High Impact Paper

Low Impact Paper
The Research Plan \implies Innovation

Explain how your project is innovative and will add significantly to existing knowledge.

- Don’t assume that your reviewers will understand why your project is innovative.

But don’t overreach.

- You don’t have to propose something entirely new:
  - You can simply improve on - or propose a new application of - an existing concept, method, or clinical intervention
  - You can be innovative in any number of ways, e.g.: an innovative hypothesis, methodology, instrument, OR intervention
  - You probably shouldn’t be so far off the beaten track that you think you will shift a paradigm.
The Research Plan $\iff$ Innovation

Be on the edge without going over it.
The Research Plan ⇒ Approach

1. For each specific aim, describe your approach for your first set of experiments:
   a. Your methods (with an explanation for why you chose them)
   b. Your preliminary data (even when “not required”)
   c. A description of any samples (including size, inclusion/exclusion criteria, sampling approach, and proof you have access to them)
   d. Your measures (and any conceptual frameworks for them)
The Research Plan

Approach

e. Your data collection process (including a description of collection procedures and validation methods)

f. Your data management plan (including procedures for data entry, auditing, and quality control)

g. Your data analysis plan (including descriptions of approach, software used, validation methods, and theoretical underpinnings)

h. Study limitations (including potential sources and consequences of bias and strategies to minimize bias; also any confounding variables and strategies for addressing them)
The Research Plan ⇒ Approach

2. Then **outline** your next steps, e.g., “if I get result x, I will follow pathway x. If I get result y, I will follow pathway y.”
   a. If this gets complex, illustrate it with a flowchart.
   b. Another good practice is to estimate the number of experiments needed and put them on a timeline.

3. **Discuss expected results and their interpretation.**

4. **Discuss strategies for addressing potential problems.**
   a. For example: identify highest priority studies if patients, reagents or other resources could become limited.
Sidebar: Preliminary Data

Why provide it if even if it’s not required?

- Preliminary data helps answer these questions:
  - Is the hypothesis scientifically sound?
  - Does the investigator have the skills and experience to do the proposed experiments?

What if you don’t have any?

- Use your start-up funds or beg your department chair for funds.
- Collaborate
- Consider an NIH small research grant (R03) or exploratory/developmental research grant (R21).
The Budget

- Must match your project
  - Average amount for an R01 application in FY14 was ~$330K in first year direct costs

- Must be appropriate for your career level
  - 71 percent of new investigators, and 44 percent of established investigators, requested $250K or less in first year direct costs.

- Each item should be well justified - and also referenced in the research plan.

- Highlight efforts to keep costs down, e.g., sharing.
The Budget (cont.)

- **Personnel**
  - Poor justification: “Dr. Johnson will analyze all data associated with the investigation.”
  - Better justification: “Dr. Johnson (10% effort requested) will be responsible for statistical analyses of data collected in experiments 1-3, which are tied directly to specific aims 3 and 4.”
  - New investigators should include a level of effort of at least 25 percent

- **Equipment**
  - Request funds for major equipment only if the equipment is –
    - absolutely essential
    - unique to your project (i.e., JHSPH would not be expected to have it)
    - used at least half the time
The Cover Letter and PHS Assignment Request Form (New)

Use it to request a specific NIH study section or NIH institute or a specific kind of expertise

But do this first:

- Write your title, abstract, and specific aims with your preferred study section or institute in mind
- Contact the NIH program officer or scientific review officer to see if s/he agrees (and if s/he does, include his/her name in letter)

Keeping in mind that assignment is based primarily on the research topic and the application type
Deciphering NIH Peer Review
Standard Review Criteria

- **For Research Grant Applications:** Significance, Investigator(s), Innovation, Approach, Environment, Other Considerations*
  - Each is addressed by answering multiple questions (see handout)
  - All are considered together to determine overall Impact score (the chief factor determining funding)

- **For Training Grant Applications:** Candidate, Career Development Plan, Research Plan, Mentor(s) and Collaborator(s), Environment and Institutional Commitment, Other Considerations*

*human subjects, animal use, select agents, data and organism sharing plans
### Guide for Determining Overall Score

<table>
<thead>
<tr>
<th>Impact</th>
<th>Score</th>
<th>Descriptor</th>
<th>Additional Guidance on Strengths/Weaknesses</th>
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</thead>
<tbody>
<tr>
<td>High</td>
<td>1</td>
<td>Exceptional</td>
<td>Exceptionally strong with essentially no weaknesses</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Outstanding</td>
<td>Extremely strong with negligible weaknesses</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Excellent</td>
<td>Very strong with only some minor weaknesses</td>
</tr>
<tr>
<td>Medium</td>
<td>4</td>
<td>Very Good</td>
<td>Strong but with numerous minor weaknesses</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Good</td>
<td>Strong but with at least one moderate weakness</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Satisfactory</td>
<td>Some strengths but also some moderate weaknesses</td>
</tr>
<tr>
<td>Low</td>
<td>7</td>
<td>Fair</td>
<td>Some strengths but with at least one major weakness</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Marginal</td>
<td>A few strengths and a few major weaknesses</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Poor</td>
<td>Very few strengths and numerous major weaknesses</td>
</tr>
</tbody>
</table>

**Non-numeric score options:** NR = Not Recommended for Further Consideration, DF = Deferred, AB = Abstention, CF = Conflict, NP = Not Present, ND = Not Discussed

**Minor Weakness:** An easily addressable weakness that does not substantially lessen impact

**Moderate Weakness:** A weakness that lessens impact

**Major Weakness:** A weakness that severely limits impact
Non-Numeric Scores:

- **Not Discussed (ND)** -
  - Less competitive (lower half)
  - No overall score but summary statement includes reviewers’ written critiques and criterion scores

- **Not Recommended for Further Consideration (NRFC)** -
  - Lacks significant merit and/or presents serious ethical problems
  - Cannot be funded

- **Deferred (DF)** -
  - Lacks sufficient information or (occasionally) peer reviewers can’t reach agreement
Fatal Flaws (Unlikely to be Funded)

- Unclear or unfocused specific aims
- Lack of significance
- Lack of innovation
- Weak or missing hypothesis (or the approach does not test the hypothesis directly)
- Overly ambitious
- PI’s productivity has been low recently
- Insufficient expertise
- Insufficient institutional support
Fatal Flaws (cont.)

- Insufficient preliminary data
- Lack of necessary controls
- Weak statistical plan or no power (for quantitative research)
- Little or no discussion of how data will be interpreted
- Little or no discussion of next steps
- Little or no discussion of potential problems (or strategies for addressing them)
- Poorly written or poorly organized
Peer Review Meeting Simulation

- https://www.youtube.com/watch?v=fBDxI6l4dOA&feature=youtu.be
The Psychology of NIH Peer Review
"Agreed. We fund only those proposals we can understand."
Reviewers are -

- Overworked and overcommitted
- Sharp-eyed by nature
- Often only peripherally interested in the topic of the application
Make Their Job Easier By -

- Including lots of section headings and breaks in the text*
- Repeating important points in several places
- Including bold text and underlined text when they might be helpful
- Including flow charts, graphic figures, and charts when they might be helpful

*But not too many breaks - too much white space invites “not enough detail”
And Avoid Imitating Them By -

- Exceeding page limits
- Using a small font size (<11 pt.) or narrow margins (<0.6 in.)
- Placing information in the wrong section
- Mislabeled references or figures; leaving out legends
- Failing to correct misspellings and typos
- Misusing the appendix
Common Criticisms and What They Really Mean

“The project is an unfocused/superficial/descriptive examination of the problem.”

“ The project is a fishing expedition.”

- The project lacks a firm, focused hypothesis
- The specific aims are too broad
- The proposed experiments don’t follow a logical sequence (or don’t align with the hypothesis or specific aims)
- The applicant hasn’t gathered enough preliminary data to give the project direction (or the preliminary data doesn’t support the hypothesis).
Common Criticisms and What They Really Mean (cont.)

“The rationale for this hypothesis is not demonstrated adequately.”
- The application provides insufficient information about our current understanding of the field.
- The application lacks sufficient preliminary data.

“The application describes an overly ambitious project.”
- Each of these very long specific aims could be its own proposal!
- The applicant is unrealistic about what s/he can accomplish during the grant period.
- The budget (or amount of time or level of effort) is not sufficient.

“This project is weak. The results will not make an important enough contribution to the field.”
- The project is not exciting or significant.
- The specific aims are too narrow.
Common Criticisms and What They Really Mean (cont.)

“The preliminary data is over-interpreted.”
- The application lacks sufficient preliminary data to show feasibility or capability.

“The application is too dense.”
- The application is too difficult to read because the text and figures are too small, so I probably missed some important information.

“The role of the collaborators/senior scientists needs to be better defined.”
- The collaborators appear to be window dressing for this application.
- I’m not convinced that these senior scientists are committed to the training/career development of this applicant.
If Your Project Isn’t Funded -

- Talk to the program officer to gain further info about the project’s review
  - The critique/summary statement does not include all weaknesses in the application.
  - The program officer can assess a revised application’s prospects.
- Get mentoring
- Be persistent
- If/when you revise -
  - Be attentive and responsive to all reviewer comments
  - Use it as an opportunity to improve the rest of the application
Some Key Points:

- Start early
- Get institute success rates, paylines, and plans
- Talk to your program officer before submitting and resubmitting
- Explain the significance and innovation of your project in detail (but don’t overreach)
- Don’t forget to discuss next steps, data interpretation, and possible problems
- Make sure that all parts of the application are in sync
- Get feedback from colleagues
Helpful Online Resources

NIH Grant Application Basics -
http://grants.nih.gov/grants/grant_basics.htm

How to Apply (Including Forms and Deadlines) –

Writing an NIH Grant Application –
http://grants.nih.gov/grants/writing_application.htm

Sample Applications and Summary Statements –
Helpful Online Resources

NIH Funding Opportunities and Policy Notices –

Application Success Rates by Grant Type and Institute –

Study Section Rosters –
  [http://public.csr.nih.gov/StudySections/Pages/default.aspx](http://public.csr.nih.gov/StudySections/Pages/default.aspx)

NIH Grants Policy Statement (Terms and Conditions of Award) –
A Professor’s Prayer

Grant me the Patience to Endure the Students I cannot Change...
The Audacity to Publish the Things I can...
And the Wisdom to get Tenure so none of it makes a difference.
But mostly, just Grant Me.

WWW.PHDCOMICS.COM
Additional Slides
When is the best time to submit a new application?

- By Feb 5, June 5, or Oct 5 (for R01)\(^1\):
  - Feb 5: Longest waiting time for award but also longest time to resubmit in the same fiscal year
  - Jun 5: Moderate waiting time for award but also shorter (perhaps insufficient) time to resubmit in the same fiscal year
  - Oct 5: Shortest waiting time for award but also no time to resubmit in the same fiscal year

\(^1\) Standard due dates for R03 and R01 are Feb 16, Jun 16, and Oct 16. Due dates for renewals, resubmissions, and revisions are Mar 5, Jul 5, and Nov 5.
Use Matchmaker to Find the Right IC
Use Matchmaker to Find the Right IC (cont.)