NIH Grants 101: Funding Mechanisms, Peer Review and Strategies for Success

Dr. Sharon L. Milgram, Director NIH OITE
You will decrease your stress level and have more time to focus on science if you take the time to understand the grant writing process - from first idea to final outcome.
How Grants Are Evaluated (and Funded)

1. Applicant Initiates Research Idea
2. University Submits Application
3. Electronic Submission
4. National Institutes of Health
5. Assign to Institute and Study Section
6. Peer Review
7. Institute Director Takes Action
8. Advisory Council Recommend Action
9. Institute (24 with funding authority) Evaluate Relevance
10. Redistribution of Funds
11. Conducts Research

Leaders in the biological and medical sciences, education, health care, and public affairs.

1st NIH Study Section 1946
Main Types of NIH Grants

- Research Training & Fellowships (T & F series)
- Career Development Awards (K series)
- Research grants (R series)
- Program project/center grants (P series)
- Trans-NIH Programs (Diversity supplements, GWAS studies, Director’s Challenge, Loan Repayment Programs)
Training and Career Development Awards

GRADUATE & MEDICAL STUDENT
- Pre-doctoral Fellowships (NRSA -- F30, F31, T32)
- Post-doctoral Fellowships (NRSA -- F32, T32)

POST-DOCTORAL
- K99-R00 Pathway to Independence Award
- K22 Career Transition Award
- K01 Mentored Research Scientist Development Award
- K08 Mentored Clinical Scientist Development Award
- K23 Mentored Patient-Oriented K Award
- K25 Mentored Quantitative K Award

FACULTY
- K02 Independent Scientist Award
- K24 Mid-career Award in Patient-Oriented Research
NIH Career Transition Awards for Intramural Fellows

- **K22: Career Transition Awards**
  - Not used by many ICs
  - U.S. citizens and permanent residents only

- **K99/R00: Pathway to Independence Award**
  - Used by most ICs
  - U.S. citizens, permanent residents, and foreign nationals
Which K?

- Assess your eligibility using the NIH K KIOSK
- Follow up by contacting your IC Training Director AND the appropriate NIH IC Program Officer
Pathway to Independence Award (K99/R00)

- To help new researchers secure a tenure-track position and launch an independent research career

- Eligibility:
  - Basic or clinical doctoral degree (i.e., postdoc or equivalent)
  - Domestic extramural or intramural institutions
  - US citizens or non-citizens
  - No more than 5 years postdoctoral research
  - Cannot have held independent faculty-level position
K99/R00 Details

- **K99 mentored phase (1-2 years):**
  - Supports mentored postdoctoral research training
  - Provides salary, research expenses (varies by IC), and 8% indirect costs
  - Covered by your IC

- **R00 Phase (up to 3 years):**
  - Requires tenure track or equivalent faculty position
  - $249,000 total costs per year (direct costs + full indirect costs)
  - Start-up should not be decreased as a result
K99/R00 Details for IRP Fellows

- Phase 1 funding will come from your current IC; the R00 phase may be funded by a different IC
- Your postdoctoral supervisor writes the **Statement by Sponsor** and is expected to review the complete application
  - Provides the information requested about your research career and the sponsor
  - Should also be a strong endorsement of your abilities
- Your SD or Lab/Branch Chief will provide the Environment and Commitment statement
- Your SD (or designee) will sign the cover sheet as the Institutional Signing Official and must have approved the application
# Application & Funding Data for the IRP

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<thead>
<tr>
<th></th>
<th>FY2007</th>
<th>FY2008</th>
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<tbody>
<tr>
<td>*Applicants</td>
<td>41</td>
<td>46</td>
</tr>
<tr>
<td>+Awardees</td>
<td>6 (14.6%)</td>
<td>14 (30.4%)</td>
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* NCI, NHGRI, NHLBI, NIA, NIAID, NICHD, NIDCD, NIDCR, NIDDK, NIEHS, NIMH, NINDS

+ NCI, NHGRI, NHLBI, NIDCD, NIDCR, NIEHS, NIMH, NINDS
Some Lessons Learned

- Training plans need to focus on ALL aspects of science, professional, and career development
  - Pay careful attention to grant writing and the academic job search
  - Be clear about IRP resources and what you will find beyond the IRP
- Identifying a co-mentor in the extramural community can be helpful
- Let your PIs know that their letter is a critical part of your application
NIH R Grants

R01 Research Project Grant
R03 Small Research Grant Program
R13 Support for Conferences and Scientific Meetings
R15 Academic Research Enhancement Award
R21 Exploratory / Developmental Research Grant
R41 Small Business Technology Transfer Grant
R43 Small Business Innovations Research Grant
New and Early Stage Investigators

- **New Investigator**: An application who has not previously competed successfully as PI for a significant NIH independent research award (R01)
- **Early Stage Investigator**: An applicant within 10 years of completing terminal research degree or within 10 years of completing medical residency (or the equivalent)
- Applies only to R01 applications
- New Investigators/Early Stage Investigators are clustered together for review
Funding for New and Early Stage Career Investigators

- NIH policy is to fund R01s of New Investigators and ESIs at more favorable paylines.

- Paylines and relative advantage differ by NIH Institute; 3%-10% more generous.

- Advice for New and Early Stage Investigators:
  - Apply NOW!!!
  - Apply for R01!!!!!
Sources of Guidance

- [www.nih.gov](http://www.nih.gov) (follow links to “training” or “peer review”)
  - Office of Extramural Research (“OER” grant programs, forms)
  - Center for Scientific Review (“CSR” review policy, procedures)
  - Institute web sites

- Mentor (current and/or proposed) and IC Training Director

- Department Chair or Administrator

- University/School Sponsored Programs Office

- Other colleagues & faculty

- RePORTER database online to look at what is already funded

- NIH Program Staff (before applying and after review)
RePORT Expenditures and Results (RePORTER) system
projectreporter.nih.gov/reporter.cfm
Study Sections and Peer Review
How Grants Are Evaluated (and Funded)

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   - Conducts Research

2. University Submits Application
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3. National Institutes of Health
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       - 1st NIH Study Section 1946

4. Institute (24 with funding authority)
   - Allocation of Funds
     - Takes Action
     - Institute Director
       - Recommend Action
       - Advisory Council
         - Leaders in the biological and medical sciences, education, health care, and public affairs.
         - Evaluate Relevance
Who Will You Interact With?

- **Program Officer (PO)**
  - Institute Staff
  - An important resource for applicants
  - Manages a portfolio of awarded grants
  - Monitors scientific progress made on grant

- **Scientific Review Officer (SRO)**
  - CSR or Institute Staff
  - Organizes and manages study section
  - Liaison between applicant and reviewers
  - Prepares summary statements

- **Grants Management Officer**
Interaction With The Program Officer

- All Program Officers manage a portfolio of grants in a specific area of interest to the Institute
  - Research and/or Training
  - You can find listings of Program Officers at [www.grants.nih.gov](http://www.grants.nih.gov)

- You should contact the Institute Program Officer:
  - For advice about your science, funding opportunities, submission strategies, potential study sections, and the summary statement
  - To discuss scientific issues on your funded grant

- It is important to speak with your program officer early in the submission process, especially for new grant writers
The Center for Scientific Review (CSR)

- Central receipt point for all grant applications
- CSR assigns applications to NIH Institute/Center as potential funding component
- Also manages ~200 Scientific Review Groups ("Study Sections")
  - Some grants are reviewed by study sections organized by an NIH Institute
How Applications Are Assigned To Study Sections

- Based on input from you -- in a cover letter
- Based on past review history of the application (if any)
- Based on the research area
- Depending on the type of application (R01, F32, K series, etc.)
The Cover Letter

- Can request a specific study section, and can request a specific Institute (information for later)
  - It is useful to contact the SRO or PO in advance to see if they agree with your requested assignment
  - If they agree, include the names of your contacts in the cover letter
- Can suggest the types of expertise that would be needed to review your application
  - Requests for specific reviewers will be ignored
- Can request that one or two specific individuals not be used as reviewers
  - Be prepared to discuss your reasons with the SRO
Study Sections and Reviewers

- Study sections typically review 70-120 applications.
- Applications are assigned a primary and secondary reviewer; most are also assigned one or two readers.
- Reviewers are typically assigned 9 - 12 applications to review.
- Reviewers write critiques for the applications on which they have primary or secondary responsibility; readers may also provide critiques.
- You cannot contact reviewers, before or after review.
What Reviewers Evaluate

For Rs:
- Overall Impact
- “Core” Criteria
  - Significance
  - Investigators
  - Innovation
  - Approach
  - Environment
- Additional Issues (e.g. Human Subjects Protections)

For Ks:
- Overall Impact
- “Core” Criteria
  - Candidate
  - Career Development Plan
  - Research Plan
  - Mentor(s)
  - Environment & Institutional Commitment to Candidate
- Additional Issues (e.g. Human Subjects Protections)
Overall Impact

- Reflects the reviewer’s assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved
- Based on the five core review criteria
- An application does not need to be strong in all categories to be judged likely to have major scientific impact.
# The Scoring System

<table>
<thead>
<tr>
<th>“Old” System</th>
<th>“New” System</th>
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<tbody>
<tr>
<td>Priority Score Range: 100-500</td>
<td>Overall Impact Score Range: 10-90</td>
</tr>
<tr>
<td></td>
<td>(integers only)</td>
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<tr>
<td></td>
<td>Criterion Scores: 1-9 (integers only)</td>
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- 1 is still the best
- Overall impact score need not be mathematically related to criterion scores. Reviewers weight the criterion scores as they believe appropriate in assigning overall impact score.
# Scoring Guidance

<table>
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<tr>
<th>Score</th>
<th>Descriptor</th>
<th>Additional Guidance on Strengths/Weaknesses</th>
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<tbody>
<tr>
<td>1</td>
<td>Exceptional</td>
<td>Exceptionally strong; essentially no weaknesses</td>
</tr>
<tr>
<td>2</td>
<td>Outstanding</td>
<td>Extremely strong; negligible weaknesses</td>
</tr>
<tr>
<td>3</td>
<td>Excellent</td>
<td>Very strong; only some minor weaknesses</td>
</tr>
<tr>
<td>4</td>
<td>Very Good</td>
<td>Strong but numerous minor weaknesses</td>
</tr>
<tr>
<td>5</td>
<td>Good</td>
<td>Strong but at least one moderate weakness</td>
</tr>
<tr>
<td>6</td>
<td>Satisfactory</td>
<td>Some strengths; some moderate weaknesses</td>
</tr>
<tr>
<td>7</td>
<td>Fair</td>
<td>Some strengths but at least one major weakness</td>
</tr>
<tr>
<td>8</td>
<td>Marginal</td>
<td>A few strengths; a few major weaknesses</td>
</tr>
<tr>
<td>9</td>
<td>Poor</td>
<td>Very few strengths; numerous major weaknesses</td>
</tr>
</tbody>
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What the Summary Statement Will Look Like

- Reviewers use a structured template
- Reviewers provide bulleted comments for:
  - Overall strengths & weaknesses
  - Strengths & weaknesses of each core criterion
  - Comments on Other Review Considerations
- Additional comments (“advice” to applicant)
- Goal: increase transparency of review process and to improve feedback provided to applicants.
What about Not Discussed Applications?

- Applications that are not discussed by the review panel:
  - Are generally those in the lower half
  - Do not receive an overall impact score
  - Receive summary statements that include the written critiques and criterion scores from the assigned reviewers but do not include an overall impact score
The Review process is a 2 Level System

- 1st Level: Initial Scientific Peer Review
  - Independent, outside reviewers
  - Evaluates the scientific merit and significance
  - Does NOT make funding decisions
- 2nd Level: IC National Advisory Council or Board
  - Evaluates quality of initial peer review
  - Makes recommendations to Institute staff on funding
  - Evaluates program priorities and relevance
Strategies for Success
Getting Started: Administrative Issues

- Download newest forms and carefully read instructions.
- Register for government internet-based application and award systems, particularly the eRA Commons.
- Talk with lab/IC administrators about budgeting, required approvals, and routing procedures.
- Contact collaborators and arrange for letters as needed.
Getting Started: Science Issues

- Read the literature broadly - not deeply; save important papers for a deeper read later
- Engage your lab, mentors and collaborators in the brainstorming process
- Find outside experts to talk with - but go prepared
- Talk with the relevant NIH Program Officer(s)
- Begin early to define, organize and plan the content

NOTE: Early means 4 - 6 months before the deadline
Important Point

- It is your goal to get people excited about your research
  - Let your enthusiasm for your research be reflected in your proposal.
  - If you are not enthusiastic when writing your proposal, it is unlikely the reviewers will see anything different
Important Point

- Your grant application will likely have several types of assigned reviewers:
  - An expert in the field
  - Someone who is smart but knows little about your field
- Therefore, your application must appeal to both audiences
Restructured Research Plan

Introduction
Specific Aims
Background and Significance
Preliminary Studies/Progress Report
Research Design and Methods
Inclusion Enrollment Report
Progress Report Publication List
Human Subjects Sections
  protections, women/minorities, enrollment, children
Other Research Plan Sections
  animals, select agent, consortium, support, sharing
Appendix
Specific Aims

- Provides an overview of the details - tells what your proposal is about, and how you will get there
  - start with 1 - 2 paragraph general overview
  - then list AIMS, each clearly defined
  - end with a brief statement of what you will learn if successful

- The reader must finish this section convinced that the proposed research is significant and that you have a feasible approach

- The aims should be clearly and concisely stated; many also include sub-aims

- Typically 2 - 4 related aims. Later aims should NOT depend on the success of previous aims
The specific aims page is your hook
Make it as perfect as possible
Significance

- The place to clearly state the importance of the proposed research
  - A proposal with a strong research plan will generate little enthusiasm if the problem is not seen as significant
- Looks both backward and forward
  - How we got “here” and where we need to be
- Points out any controversies and discrepancies that your work will address
- Should be appropriately referenced with an honest and balanced discussion of others’ work
Significance

- The issue is not: ‘why this disease is important.’

- The issue is: ‘why this intervention is important for this disease’ or ‘what is important about this basic research.’

- For clinical research grants, you must explain how your study will make a difference to patients.
Changes in review were designed to place more focus on **impact** and less on details of approach.

**Impact** combines significance and feasibility.
Feasibility = Preliminary Data

- To show that you can do what you say you are going to do
- To generate excitement and enthusiasm for the proposed studies
- To show you are a careful scientist who understands the value of controls and does not over-interpret data
- Typically contains several figures with clear legends; figures should be large enough for reviewers to easily read
Research Approach

- Organized by specific aims, not by techniques
- Include an overview of approaches and the rationale for experiments
- Define controls (positive and negative) for all experimental approaches
- Show you have thought through issues of feasibility, sample size, data analysis, etc.
- Include a discussion of expected outcomes, data interpretation, potential problems, and alternate approaches
Strong Research Plans:

- Explicitly state the rationale for the proposed studies
- Never assume reviewers will intrinsically appreciate or understand what you intend
- Use flow diagrams for overview, and for complex experiments and protocols
- Include well-designed, easy to follow tables and figures
- Address priorities if patients, reagents or resources will be limited
- Include a discussion of how the data will be analyzed and interpreted
- Include realistic discussions of pitfalls and provide alternate approaches
What To Cover In A Training Plan

- Additional technical training, not incremental advances in what you already know
- Didactic training
  - Depends on your educational level and background
  - Traditional and non-traditional ways
- Professional training
  - In anything you will need to be successful as an independent scientist
  - Including communication, teaching, management, and leadership skills
- Job Search information
  - Who will help and when
  - Availability of institutional resources
Strong Training Plans:

- Goes beyond the “standard stuff”
  - Standard is lab meetings, journal clubs, attending the obvious National/International meeting
- Are based on your career goals and not a standard institutional template or IDP
- Demonstrate that there is a meaningful interaction between the mentor and the mentee
  - Meaningful letters and specifics help
- Involves a mentoring team when appropriate
  - New mentors
  - Work diverges from mentor’s expertise
  - Career goals are outside the mentor’s expertise
- Show some evidence that you mean what you say
Common Criticisms

- Rationale for hypothesis or methods not sound
- Models over-hyped as relevant to the human situation
- Diffuse, unfocused or superficial examination of the field
- Unexciting science - an incremental advance for the field
- Mediocre preliminary data that are over-interpreted
- Lack of experience in required methodologies
- Unrealistic amount of work
- Lack of sufficient experimental detail
- Too many irrelevant experimental details
- Insufficient discussion of pitfalls and alternate approaches
- Lack of knowledge of published work
- Lacks evidence that the fellow and mentor worked together
- Lack of detail in the training plan; letters from mentors lack depth
What Reviewers Really Say

- This is the first of three very long aims that could make its own proposal. The subaims just go on and on.
- An important question and an elegant approach; however there is no discussion of how many targets are expected, and most importantly, what criteria will be used to select which targets to pursue.
- The role of these senior scientists needs to be defined.
- This is a horizontal contribution to the field.
- The investigator does not pay sufficient attention to feasibility issues, including the enrollment of research subjects and careful attention to inclusion issues.
- Insufficient information is given to indicate how the CART analysis will be implemented, and no discussion of power analysis is given. These omissions are particularly unfortunate.
How to Approach a Negative Review

- Give yourself the time and space to feel sad and angry, but appreciate that your colleagues, students, lab members are watching
- Avoid calling or writing your program officer until you have calmed down
- Then read the reviewer's comments CAREFULLY
- You will need to decide whether or not the reviewers show any enthusiasm for your application.
- Talk with:
  - A senior scientist with experience reading critiques
  - Your program officer
Amended Applications

- Can submit one amended application
- Must respond to reviewers’ criticisms
  - Do not have to agree or make the suggested changes, but must respond to the comments
  - Do not attack the reviewers’ competence, abilities, etc. This will only hurt your cause.
- No guarantees that amended application will score better than previous submission
  - Different reviewers
  - Different panel of applications
Reviewer 1 accurately pointed out that we had not sufficiently discussed the detergents used to prepare cell lysates for our assays. We now expanded this discussion in AIM 3 of the revised application.

Reviewer 2 pointed out that we lacked a clear way to address the relevance of these protein interactions in an animal model. There are no universally accepted animal models for CF lung disease, but we now include studies in mouse tissues and/or well-differentiated human primary airway epithelial (WD-PAE) cell cultures to further explore the physiological relevance of the interactions we identify.
We wholeheartedly agree with Reviewer 2 that unfocused research can indeed lead to “a quagmire of proteins”. However, we have several strategies in place to ensure that we do not go down such a path. Specifically, …….. As proof of principle, our progress since June 2004 clearly indicates that we can rapidly identify important proteins for further analysis. Therefore we have retained the protein interactions screens described in AIM 3 of the original application.
The Psychology of Grant Review

■ Reviewers are:
  □ Over-committed, over-worked and tired
  □ Inherently skeptical and critical
  □ Often only peripherally interested in your work

■ Make their job easier with:
  □ Well-organized, clearly written prose
  □ Lots of section headings and breaks in the writing
  □ Repeat important points at several places in the application
  □ Well designed flow diagrams, charts, figures

■ And avoid irritating them by:
  □ Exceeding page limits, using small fonts and narrow margins
  □ Putting information in the wrong section
  □ Omitting or mislabeling references/figures
  □ Submitting an application that is sloppy or full of typographical errors
It’s About More Than The Science

- **Observation I:**
  - Strong writing cannot compensate for bad ideas, but weak writing easily ruins good ideas

- **Observation II:**
  - You can learn to write well; find outstanding resources as early as possible
Conclusion

- Only some of the deserving R01 applications can be funded, unfortunately
- Maximize your chances for success by
  - Planning ahead
  - Remembering your target audiences
  - Showing the reviewers that you’ve thought about your project
  - Preparing a reader-friendly application
  - Remaining optimistic, and letting your enthusiasm for your science come through
Helpful Web Resources

- NIH Home page http://www.nih.gov/
- NIH Grant Application Basics (Includes guides, tips, and tutorials) http://grants.nih.gov/grants/grant_basics.htm
- Information on Study Sections http://cms.csr.nih.gov/
- Science magazine GrantsNet http://sciencecareers.sciencemag.org/funding
Contact your INTRAMURAL Training Director for:
- Information on IC grant-writing workshops
- Information on IC-specific rules

Visit the OITE webpage, training.nih.gov) for:
- Links to useful resources
- Spring grant writing workshops
- Videocasts on electronic submission and grant writing
- Information on our month-long writing courses

Find EXTRAMURAL Program staff at www.grants.nih.gov