Navigating NIH: Succeeding as an Independent Investigator

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Faculty Life at Harvard

- Build your research program
- Develop collaborations to expand your research in innovative areas
- Develop courses, teaching expertise
- Advise, mentor
What Does It Take to be an Independent Investigator?

• Ideas for a program of research in an important scientific area
• Pilot data
• Excellent writing and communication skills
• Good organizational and planning skills
• Tenacity

FUNDING!!
How to Design a Funding Stream: The World According to Karen

• Identify your very best developed idea
  • Apply for most ‘independent’ mechanism you can
  • Develop the strongest application

• In “down times”, begin developing next idea
  • Consider internal pilots, smaller mechanisms
  • When Idea #1 is submitted, write grant for Idea #2
  • When Idea #2 is submitted, conduct work that would address weaknesses in Idea #1 or set you up if funded

• Until you are fully funded, try to keep a couple of ideas in the “pipeline” simultaneously
Funding Sources

- NIH
- Corporate-Sponsored Research
- Foundations

Funding Types

- Research grants
- Pilot grants
- Gifts
NIH Funding 101
3 Funding Instruments for Extramural Research

- **Grant**: Investigator decides the research to be designed or developed and the approach
  - ~ 84-88% of extramural awards

- **Contract**: Government decides the research to fill their perceived need and establishes detailed requirements
  - ~ 8-10%

- **Cooperative Agreement**: Similar to grants, but awarding Institute/Center (IC) and recipient have substantial involvement in carrying out the project’s activities
  - ~ 4-6%
Mechanisms for NIH To Get Research Proposals

• **Investigator-Initiated Research**
  - Program Announcements (PA)
  - Unsolicited, from general institute extramural budget
  - R01, R21, R03
  - ~ 80% of awards

• **Request for Applications (RFA)**
  - Solicited; set-aside of funds for a certain number of awards
  - One-time competition to stimulate research in a priority area
  - R01, R21, R03, P01, Cooperative Agreement
  - If an RFA submission is not successful, a subsequent application should be submitted as a new application, not a resubmission
  - ~ 10% of awards
Mechanisms for NIH To Get Research Proposals, continued

• **Program Announcement and Special Review (PAR/S)**
  - Solicited, but no set-aside of funds
  - Reviewed by special emphasis panel

• **Program Announcement (PA)**
  - Solicited, but no set-aside of funds
  - Reviewed by standing study section
Watch for Funding Opportunities

- Harvard Catalyst Grant Central  https://grants.catalyst.harvard.edu/grants/spring/home
- Proprietary Funding Opportunity Databases
  - Community of Science  http://pivot.cos.com/funding_main
NIH Investigator Status
Types of NIH Investigator Status

New Investigator

- A Principal Investigator (PI) who has not yet competed successfully for a substantial, competing NIH research grant (R01 or ‘higher’) is considered a New Investigator
  
  http://grants1.nih.gov/grants/new_investigators/resources.htm

Early Stage Investigator (ESI)

- An individual who is classified as a New Investigator and is within 10 years of completing his/her terminal research degree or is within 10 years of completing medical residency (or the equivalent)
What Affects NI/ESI Status?

• PI of an R03 or R21? No
• PI of an NIH contract? No
• PI of a grant with another Federal agency? No
• PI of an SBIR/STTR? No
• PI of a U01, specifically for a foreign investigator? Receipt of U01 removes NI status.
• Inheriting an R01 from a PI who moved away or died? No
Multiple PIs

• To facilitate multi-disciplinary, “team” science

• Think carefully before submitting MPI application:
  
  - Does multiple PI approach fit the science?
    - Each PI must play key role and/or contribute critical intellectual input into project

  - How will multiple PI application affect your NIH funding strategies?
    - For new investigators, inclusion in MPI application may make it difficult to establish your own identity
    - New Investigators funded through MPI will lose new PI status
    - If MPI includes established PI, application will not qualify for NI payline

  - Must include a Leadership Plan describing roles, responsibilities, and working relationship of the PIs
    - How will you share leadership of the project?
Multiple PIs: Additional Considerations/ Cautions

- May be more complex to write MPI proposals
  - Must have clear Leadership Plan describing roles, responsibilities and working relationships of PIs
  - May be more difficult to ensure pieces of proposal are well integrated and coordinated

- MPI applications are more difficult to get funded

<table>
<thead>
<tr>
<th>Application Type</th>
<th>FY 2008 (in %)</th>
<th>FY 2009 (in %)</th>
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<tbody>
<tr>
<td>Multiple PI</td>
<td>12.6</td>
<td>16.2</td>
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<tr>
<td>Single PI</td>
<td>21.6</td>
<td>21.2</td>
</tr>
</tbody>
</table>
NIH Application and Funding Process
So How Does This All Work?

- You have an idea!
- You identify an appropriate NIH institute
- You find out about their priorities
- You talk with a Program Official
- You decide which of the eligible funding mechanisms are the best fit (e.g. R01)
- You watch the funding announcements and see an RFA, RFP, PAR, or PA that fits your research
- You identify best study section
- You write the grant!

Questions so far??
Reviewing Bodies

- Institutional Review Groups (IRG)
  - Study Section-- Review Group for CSR

- Members
  - Appointed for multi-year terms of service
  - A number of temporary ad hoc members are typically assigned to each meeting

- Special Emphasis Panels
  - Review groups formed on an ad hoc basis to review applications requiring special expertise (RFAs) or when a COI occurs
Reviewing Bodies continued

Review Group Descriptions
Web page

http://cms.csr.nih.gov/peerreviewmeetings/csirgdescriptionnew/
<table>
<thead>
<tr>
<th>IRGs</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>AARR</strong></td>
<td>AIDS and Related Research</td>
</tr>
<tr>
<td><strong>BBBP</strong></td>
<td>Biobehavioral and Behavioral Processes</td>
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<tr>
<td><strong>BCMB</strong></td>
<td>Biological Chemistry and Macromolecular Biophysics</td>
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<tr>
<td><strong>BDCN</strong></td>
<td>Brain Disorders and Clinical Neuroscience</td>
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<tr>
<td><strong>BST</strong></td>
<td>Bioengineering Sciences and Technologies</td>
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<tr>
<td><strong>CB</strong></td>
<td>Cell Biology</td>
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<tr>
<td><strong>CVRS</strong></td>
<td>Cardiovascular and Respiratory Sciences</td>
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<tr>
<td><strong>DKUS</strong></td>
<td>Digestive, Kidney and Urological Systems</td>
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<tr>
<td><strong>EMNR</strong></td>
<td>Endocrinology, Metabolism, Nutrition and Reproductive Sciences</td>
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<tr>
<td><strong>ETTN</strong></td>
<td>Emerging Technologies and Training in Neurosciences</td>
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<tr>
<td><strong>GGG</strong></td>
<td>Genes, Genomes and Genetics</td>
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<tr>
<td><strong>HDM</strong></td>
<td>Healthcare Delivery &amp; Methodologies</td>
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<tr>
<td><strong>IDM</strong></td>
<td>Infectious Diseases and Microbiology</td>
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<tr>
<td><strong>IFCN</strong></td>
<td>Integrative, Functional, and Cognitive Neuroscience</td>
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<tr>
<td><strong>IMM</strong></td>
<td>Immunology</td>
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<tr>
<td><strong>IMST</strong></td>
<td>Interdisciplinary Molecular Sciences and Training</td>
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<tr>
<td><strong>MDCN</strong></td>
<td>Molecular, Cellular, and Developmental Neuroscience</td>
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<tr>
<td><strong>MOSS</strong></td>
<td>Musculoskeletal, Oral and Skin Sciences</td>
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<tr>
<td><strong>OBT</strong></td>
<td>Oncology 1 – Basic Translational</td>
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<tr>
<td><strong>OTC</strong></td>
<td>Oncology 2 – Translational Clinical</td>
</tr>
<tr>
<td><strong>PSE</strong></td>
<td>Population Sciences and Epidemiology</td>
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<tr>
<td><strong>RPHB</strong></td>
<td>Risk, Prevention &amp; Health Behavior</td>
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<tr>
<td><strong>SBIB</strong></td>
<td>Surg Sciences, Biomedical Imaging, &amp; Bioengineering</td>
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<tr>
<td><strong>VH</strong></td>
<td>Vascular and Hematology</td>
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Cell Biology IRG [CB]

Research applications that focus broadly on the study of fundamental cell biological processes, including the functions, interactions and regulation of cells and cellular organelles. Reviews applications that involve a variety of disciplines including biochemistry, biophysics, chemistry, and genetics, and use a variety of techniques including microscopy, genomics, proteomics and computational techniques, with the primary goal of better understanding cell functions.

Topics to be covered include:

• cell growth, proliferation, and cell cycle control;
• nuclear architecture and transport;
• RNA trafficking and localization;
• post-translational modifications, protein processing, glycosylation and folding;
• membrane structure and function;
• lipid traffic and metabolism;
• cell asymmetry and polarity;
• ion transport and regulation, channels, transporters and junctions;
• organelle biogenesis, function, dynamics and protein translocation;
• the secretory pathway, endocytosis, exocytosis and phagocytosis; degradative processes;
• cell fusion; extracellular matrix and ECM receptors;
• signaling mechanisms and networks;
• integrative cell physiology including circadian clocks, stress and oxidative damage response;
• motors, filaments and cargoes; cell locomotion; mitosis and meiosis;
• programmed cell death and apoptosis
So How Does This All Work?

• You have an idea!
• You identify an appropriate NIH institute
• You find out about their priorities
• You talk with a Program Official

• You decide which of the eligible funding mechanisms are the best fit (e.g. R01)

What is the best mechanism for my project?
Common NIH Research Mechanisms
Common R Grants

R03
Small Research Grant

- Obtain preliminary data

R21
Exploratory Research Grant

- Explore a novel or high-risk research area
- Preliminary data may be included

R01
Investigator-Initiated Research Grant

- Hallmark of an established, independent investigator
- Often provides a steady “stream” of funding
- Must include preliminary data
Small Research Grant Program (R03)

- Discrete, well defined projects that realistically need **2 years** and **limited levels of funding** ($50K dc/year):
  - Pilot or feasibility studies, collection of preliminary data, secondary analysis, small, self-contained research projects, new technology development

- Evaluated on conceptual framework & general approach

- Justified through literature citations, data from other sources, or from investigator-generated data

- Preliminary data are not required, particularly in applications proposing pilot or feasibility studies

Small Research Grant Program (R03)—When to Apply

• Great “starter” mechanism
• If need to generate pilot data
• For proof of concept or methods development
• Can be useful while are doing R01, providing ‘bridge’ funding
Exploratory/Developmental Research Grant Program (R21)

- Investigation of novel scientific ideas, model systems, tools, or technologies with potential for significant impact on biomedical or biobehavioral research

- Combined (2 years) direct cost ≤ $275,000.

- Evaluated on the conceptual framework, level of innovation, potential to advance knowledge

- Justified through literature citations, data from other services, or, when available, from investigator-generated data

- Preliminary data are not required for R21 applications; include if available
Exploratory/Developmental Research Grant Program (R21)–When to Apply

- Novel, risky idea
- Larger scale methods development
- Can help to have a more established collaborator
- Scale of research must be appropriate for the mechanism
R01 NIH Investigator Initiated Research Project Grant Program

- Discrete, specified research project
- NIH’s most commonly used grant program
- Advance permission required for $500,000 or more (direct costs) in any year
- Budget reviewed separately from science, must “match”
- Generally awarded 3 to 5 years
- Utilized by all ICs
R01 Grant Program – When to Apply

- Have some evidence of ability to manage external funds
- Have evidence of publication productivity
- Have sufficient support for science proposed
- Have pilot data
- Typically hypothesis-generating or hypothesis-testing
- Aim to submit during NI/ESI eligibility
Writing an NIH Grant
So How Does This All Work?

- You have an idea!
- You identify an appropriate NIH institute
- You find out about their priorities
- You talk with a Program Official
- You decide which of the eligible funding mechanisms are the best fit (e.g. R01)
- You watch the funding announcements and see an RFA, RFP, PAR, or PA that fits your research
- You identify best study section
- **You write the grant!**
**“Research Plan”**

<table>
<thead>
<tr>
<th>1. <strong>Introduction to Application</strong>  (Resubs or Revisions Applications)</th>
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<td>2. <strong>Specific Aims</strong></td>
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| 3. **Research Strategy**  
  a. Significance  
  b. Innovation  
  c. Approach  
  ▪ Preliminary Studies for New Applications  
  ▪ Progress Report for Renewal/Revision Applications  
  ▪ Research Design and Methods |
Keys to Writing Your Best Possible Grant Application

- Plan Ahead
- Mentor Review
- External Review
- Editorial Review

Write the grant!
NIH Review Process
NIH Review Process

- **Scientific Review Officer**
  - Completeness of application
  - Assign reviewers

- **Peer Review**
  - Written critique & numerical scores for review criterion
  - Score/No Score; percentile
  - Summary Statement
  - Institute makes funding decisions
NIH Review Criteria

- **Overall Impact/priority score** – likelihood to exert sustained, powerful influence on field

- **Scored Criteria (1-9):**
  - Significance
  - Investigator(s)
  - Innovation
  - Approach
  - Environment
Confessions of a Reviewer

- Reviewers are busy, tired people; grant reviews are on top of their day job
- Impressions of the grant are formed early
- Of the 20-30 people on the study section
  - Likely only 1 or 2 are experts on your topic
  - Likely only 3 have read your grant
- Reviewers read many grants for each meeting; “stories” are easier to remember and to convey
- If you make the reviewer work harder (e.g. complex writing, minimal margins), they may be less generous in scoring
If Nothing Else, Remember There’s One Key to Success!

• You have to **sell your ideas to reviewers**

• You have to **inspire the Reviewer to be your advocate** in the Study Section
Grant is Submitted- Now what?!

Do the Happy Dance...

- Put on Your Armor!
- Start your next grant
- Watch for Score- Make Provisional Plans
- Watch for Summary Statements
- Ask Mentors/Colleagues to read
- Talk with Program Official
- Identify Fixable/Non-Fixable Issues
- Plan Resubmission – you get one shot!
Developing your Research Program & Funding Portfolio
How to Design a Funding Stream

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- Once funded, keep an eye on your/staff coverage levels
- Plan for next funding opportunity based on progress in your science AND funding levels
- Anticipate at least a 2-year process for getting an idea funded
How to develop a research program

• Your Resources:
  • Your ideas
    • Don’t panic
    • Expose yourself to opportunities to think, learn, and explore ideas
    • Carve time out to think and write
  • Your read on the gap areas in the literature
  • Your mentors
  • Harvard Catalyst, CRISP/NIH REPORTER
  • Pilot grant opportunities
Develop a Research Program

• Pilot grant opportunities
  • Write a 2-paragraph lay-ish brief of your interest areas to share with chair, mentor, development offices
  • Watch for relevant announcements
  • Use multiple submissions, but consider complementary projects
  • Look for “add-on” opportunities
How to become funded –

• And no, it’s not exactly the same as developing a research program!

• Idea

• Commitment

• Grant writing skills
Commitment

• Passion

• Attitude

  • I can’t
  → I can and I will
  • I don’t have time
  → I will reorder my priorities
  • There’s too much competition
  → I welcome the chance to compete
  • It’s good as it is now
  → It can always be better
  • I’ll submit now and “get in line”
  → I won’t submit until it’s the very best grant I can write

• Time
Planning & Strategy

• Plan for specific grant submission deadlines, and lay out specific timeline

• Then add 2-3+ months to timeline
Questions?