Developing NIH Grant Proposals

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Office of the Vice President for Research

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Course Objectives

- Understand federal R&D budget process
- Learn NIH organizational structure
- Identify NIH research priorities
- Understand NIH funding ("mechanisms")
- Navigate submission & review processes
- Develop grant writing skills
- Improve advocacy skills
US Federal Revenues & Expenditures 2000-2020
Source: CBO (data after 2009 are projections)
R&D as Percent of the Federal Budget:
FY 1962-2017, in outlays

Source: Budget of the U.S. Government FY 2017 Historical Tables. FY 2017 is the request. © 2016 AAAS
Composition of the Federal Budget
Outlays as share of total budget, 1962 - 2016

Source: Budget of the United States Government, FY 2016. "Investments" include outlays for R&D, education and training, direct nondefense infrastructure, and other grants, primarily for transportation. "Payments to Individuals" are primarily entitlement programs like Medicare, Medicaid, and Social Security, but also include many other public assistance programs. © 2015 AAAS
Figure 1: Composition of the FY 2018 Budget
Total Outlays = $4.1 trillion
outlays in billions of dollars

- Defense Discretionary: $586
- [Defense R&D]: $57
- Nondefense Discretionary: $540
- [Nondefense R&D]: $61
- Social Security: $1,005
- Medicare: $582
- Medicaid: $404
- Other Mandatory: $545
- Net Interest: $315

Source: Budget of the United States Government FY 2018. © 2017 AAAS
obligations in billions of constant FY 2016 dollars

"Other" includes research not classified (includes basic research and applied research; excludes development and R&D facilities). Life sciences are split into NIH support for biomedical research and all other agencies' support for life sciences.

Source: National Science Foundation, Federal Funds for Research and Development series. FY 2015 and 2016 data are preliminary. Constant-dollar conversions based on OMB's GDP deflators. © 2016 AAAS
NIH Organizational Structure

• Largest agency of Department of Health & Human Services (DHHS)
• Headquarters: Office of the Director
• NIH organized into 27 institutes & centers
  – One center conducts most NIH peer reviews
  – Two centers support intramural activities
  – 24 institutes provide extramural research support - each with specific research priorities
NIH Institutes & Centers

- NCI – Cancer
- NHLBI – Heart, Lung & Blood
- NIDDK – Diabetes & Digestive & Kidney Diseases
- NIDA – Drug Abuse
- NIAAA – Alcohol Abuse & Alcoholism
- NIBIB – Biomedical Imaging & Bioengineering
- NINR – Nursing Research

- NIA – Aging
- NICHD – Child Health & Human Development
- NIDCD – Deafness & Other Communication Disorders
- NIAID – Allergy & Infectious Diseases
- NEI – Eye Institute
- NHGRI – Human Genome Research
- NIMH – Mental Health
NIH Institutes & Centers

- NIAMS – Arthritis & Musculoskeletal & Skin Diseases
- NIDCR – Dental & Craniofacial Research
- NINDS – Neurological Disorders & Stroke
- NIEHS – Environmental Health Sciences
- NIGMS – General Medical Sciences
- FIC – Fogarty International Center
- NLM – National Library of Medicine
- NIMHD - National Institute on Minority Health & Health Disparities
- NCCAM – National Center for Complimentary & Alternative Medicine
- NCATS – National Center for Advancing Translational Sciences
- CSR – Center for Scientific Review
- CC – Clinical Center
- CIT – Center for Information Technology
- OD – Office of the Director
Research directions set by Director – not Congress or President

Tension between investigator-initiated and ‘big science’
Broad Scientific Areas of Interest to NIH

• Research of direct or strong indirect relevance to understanding and preventing disease

• Research on basic biological and psychological processes of potential interest *if* there is disease relevance
Challenge of Rising U.S. Health Expenditures

Biomedical Research Must Deliver

National Health Expenditures as a Percent of GDP

- Actual
- Projected

$4.1 trillion

Percent of U.S. GDP

8% 10% 12% 14% 16% 18% 20%

Years:
- 1980
- 1982
- 1985
- 1988
- 1991
- 1994
- 1997
- 2000
- 2003
- 2006
- 2009
- 2012
- 2015

GDP:
- 1980
- 2015

Actual:
- $4.1 trillion

Projected:
- $4.1 trillion
NIH FY18 R&D Budget

- Largest U.S. research spending increase in a decade
- 8.3% increase of $3 Billion
- $37 Billion budget
- Well above increases proposed by House or Senate
- Blunt rejection of 22% cut proposed by White House
Final FY18 Funding: NIH
(Selected Institutes)
% change from FY17 enacted
$ in () are the FY18 enacted amounts

-22% NIH Total ($37,084 M)
-21% Cancer ($5,965 M)*
-18% General Medical Sciences ($2,785 M)
-25% Eye ($772 M)
-25% Deafness and Other Communication Disorders ($460 M)
-21% Biomedical Imaging and Bioengineering ($378 M)

Trump Request Final

* Includes $300 million provided by the 21st Century Cures Act for the Cancer Moonshot Initiative.
NIH FY18 Budget Priorities

• Alzheimer disease research funding increases by $414 Million to $1.8 Billion

• Clinical & translational science funding increases by $27 Million to $543 Million
NIH FY18 Payline

- NCI: R01s - 9%tile. R21s - 7%tile. R03s/R15s - 25 priority score
- NIAID: R01s - 13/17%tile for established/ESI PIs. R21/R03 - 32 priority score
- NHLBI: R01s - 15/25%tile for established/ESI PIs. R21/R03 - 10-33 priority score
- NINDS: up to 15%tile for RPGs; 25%tile for ESI
- NIMH: 3/4 of applicants under 20%tile; ESI up to 25%tile
- NIAMS: 13/22%tile for established/new PIs. R21, 13%tile. Priority score of 22 for R03, 29 for K01/K08/K25
NIH BRAIN Initiative

• Launched with $100 M in FY14 budget - funded by NIH, DARPA, NSF

• Private Sector Partners
  - Allen Institute for Brain Science
  - Howard Hughes Medical Institute
  - Kavli Foundation
  - Salk Institute for Biological Studies

• Strong academic leadership from high-level working group: co-chairs, C. Bargmann & W. Newsome
  - Define detailed scientific goals
  - Develop multi-year scientific plan - timetables, milestones & cost estimates

• http://www.nih.gov/science/brain/
Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative®

- Expand efforts to address fundamental neuroscience questions
- Increase investment to support groundbreaking neuroscience research, neuroimaging, training
- Explore collaborations with industry to develop/test devices for mapping/tuning brain circuitry
FY 2017 NIH Budget
$33.1 Billion – Estimated Percent Total by Mechanism

- Research Centers: 7.8%
- Intramural Research: 10.9%
- Research & Development Contracts: 9.6%
- Research Training: 2.6%
- Research Management and Support: 5.2%
- Facilities Construction: 0.5%
- Other Research, Superfund, Office of the Director: 8.5%
- Research Project Grants: 54.9%
NIH Grants & Contracts
Solicited Applications

• Request For Applications (RFA)
  – Set-aside $$
  – Special review
  – Special deadline

• Program Announcements (PA)
  – Typically no set-aside
  – Typically regular receipt dates apply
  – Typically review is by standing committees
  – PAS: $$ for some grants above payline
  – PAR: specific review

• Cooperative Agreements (U’s)
  – “Significant government participation”
  – Clinical Trials, Translational grants

• Request for Proposals (RFP)
  – Contract solicitation
  – Acquisition; gov’t buys a product
NIH Grants and Contracts
Unsolicited Applications

• Traditional “bread & butter” NIH grant support
• Regular receipt deadlines
• Review by pre-existing (“standing”) review committees (typically CSR)
• Increased likelihood of success if fits in with Institute priorities
• NIH permission needed if budget exceeds $500K in any one year
# R01 Review and Award Cycles

<table>
<thead>
<tr>
<th></th>
<th>Cycle I</th>
<th>Cycle II</th>
<th>Cycle III</th>
</tr>
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<tbody>
<tr>
<td><strong>Receipt Date</strong></td>
<td>February 5</td>
<td>June 5</td>
<td>October 5</td>
</tr>
<tr>
<td><strong>Scientific Merit Review</strong></td>
<td>June - July</td>
<td>October - November</td>
<td>February - March</td>
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<tr>
<td><strong>Advisory Council Review</strong></td>
<td>September - October</td>
<td>January - February</td>
<td>May - June</td>
</tr>
<tr>
<td><strong>Earliest Project Start Date</strong></td>
<td>December</td>
<td>April</td>
<td>July</td>
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Submitting an Unsolicited Grant Application

- Assignment to Institute for funding consideration
- Assignment to particular review committee
Managing the Process

• Receipt and Referral
  - *All* NIH grant applications sent to CSR
  - CSR assigns them to Institutes and peer review committees
    - Based on “referral guidelines” &/or PI request in a *cover letter*
    &/or an ARA from Program staff

• You can request which Institute & program you want to be assigned for funding consideration
  - Letter to CSR; contact with Program official

• You can request which committee you want to conduct the peer review
  - Letter to CSR; contact with Program official
Popular Grant Mechanisms

- **Fellowship Programs**
  - F31: Predoctoral Individual National Research Service Award
  - F32: Postdoctoral Individual National Research Service Award

- **Research Career Programs**
  - K01/K02: Research Scientist Development Awards
  - K05: Research Scientist Award
  - K07: Academic/Teacher Award
  - K08: Clinical Investigator Award
  - K12: Physician Scientist Award
  - K18: Career Enhancement Award
  - K20/K21: Senior Development Awards
  - K22: Career Transition Award
  - K23: Mentored Patient-Oriented Research Career Development Award
  - K24: Midcareer Investigator Award in Patient-Oriented Research
NIH Career Development Awards

- Grant to do research on small scale and obtain training in scientific area
- Mentored v. nonmentored awards
- Basic v. clinical research
- Traditionally easier to get than traditional Research Project (R01) award BUT…

http://grants1.nih.gov/training/careerdevelopmentawards.htm
NIH Grant Mechanism Timetable

Approx. Stage of Research Training and Development

Graduate/Medical Student

Postdoctoral

Early

Mentored Research Scientist Development Award (K01)
Mentored Clinical Scientist Development Award (K08)
Mentored Patient-Oriented RCDA (K23)
Mentored Quantitative RCDA (K25)

Mentored Patient-Oriented Research (K24)

Senior Scientist Award (K05)

Senior Scientist Award (K05)

Small Grant (R03)
AREA Grant (R15)
Research Project Grant (R01)
Exploratory/Developmental Grant (R21)

MECHANISM OF SUPPORT

Predoctoral Institutional Training Grant (T32)
Predoctoral Individual NRSA (F31)
Predoctoral Individual MD/PhD NRSA (F30)
Postdoctoral Institutional Training Grant (T32)
Postdoctoral Individual NRSA (F32)

Predoctoral Individual NRSA (F31)
Predoctoral Individual MD/PhD NRSA (F30)
Postdoctoral Individual NRSA (F32)
Grant Mechanisms

- Research Program Projects & Centers
  - P01: Research Program Projects
  - P20: Exploratory Grants
  - P30: Center Core Grant
  - P50: Specialized Center

- Research Projects
  - R01: Research Project
  - R03: Small Research Grant
  - R21: Exploratory/Developmental Grants
  - R41/R42: Small Business Technology Transfer (STTR) Grants
  - R43/R44: Small Business Innovation Research Grants (SBIR)
NIH Research Projects

• R01 grants: Unsolicited (investigator-initiated) grants from one or more labs
  – Cornerstone of NIH funding
  – Reflect scientists’ interests, assessment of the field, and feasibility

• R03 grants: Small, self-contained research projects; feasibility

• R21 grants: High-risk / high-return
  – Time and dollar limits; Institutes differ
  – Less stringent need for preliminary data

• R41/R42, R43/R44 grants: Small businesses
  – SBIR: small business, commercialization
  – STTR: same, with a university component
  – Phases (1, 2, fast-track)
How Does an Application Get Funded?

• Application submitted to CSR
  - Regular receipt date (unsolicited apps)
  - "Special" receipt date (solicited apps)
• Application assigned to Institute for funding consideration
• Application assigned to peer review committee
• Multiple levels of review
• Grants Management Office of Institute collects necessary information
Multiple Levels of Evaluation

• **Peer review, scientific review committee**
  – Members drawn from extramural scientific community
  – Major effect on probability of being funded

• **Approval of review, Scientific Advisory Council**
  – Each institute has its own Council
  – Members drawn from extramural scientific community
  – Nonscientific members
  – Typically, minimal effect on probability of being funded

• **Program evaluation**
  – Evaluation for agreement with Institute priorities
  – Greatest effect on probability of being funded
Research Grant Application -> School or Other Research Center

Initiates Research Idea -> Submits Application

National Institutes of Health

Center for Scientific Review
- Assigns to IRG/Study Section & IC
  - Study Section
    - Evaluates for Scientific Merit
      - Institute
        - Evaluates for Program Relevance
          - Advisory Councils and Boards
            - Recommends Action
              - Institute Director
                - Takes final action for NIH Director

Conducts Research -> Allocates Funds
NIH Research Plan

✦ Specific Aims – 1 page
✦ Research Strategy - 12 pages
  – Significance
  – Innovation
  – Approach
  – Preliminary Studies (New Applications) or
  – Progress Report (Renewal/Revision Applications)
Specific NIH Review Criteria

• **Overall Impact** - After considering all of the review criteria, briefly summarize the significant strengths and weaknesses of the application and state the likelihood of the project to exert a sustained powerful influence on the field.

• **Significance** - Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

• **Investigators** - Are the PD/PIs, collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project.
Specific NIH Review Criteria

• Innovation - Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

• Approach - Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed?

• Environment - Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?
Other Review Considerations

• Protection for Human Subjects

• Inclusion of Women, Minorities & Children

• Vertebrate Animals

• Biohazards

• Budget & Period Support

• Resource Sharing Plans
Additional Considerations

- **New Investigator:** An NIH research grant Program Director/Principal Investigator (PD/PI) who has not yet competed successfully for a substantial, competing NIH research grant is considered a New Investigator. For example, a PD/PI who has previously received a competing NIH R01 research grant is no longer considered a New Investigator. However, a PD/PI who has received a Small Grant (R03) or an Exploratory/Developmental Research Grant Award (R21) retains his or her status as a New Investigator. A complete definition of a New Investigator along with a list of NIH grants that do not disqualify a PD/PI from being considered a New Investigator can be found at [http://grants1.nih.gov/grants/new_investigators/resources.htm](http://grants1.nih.gov/grants/new_investigators/resources.htm).

- **Early Stage Investigator (ESI):** An individual who is classified as a New or First-Time 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) is considered an Early Stage Investigator (ESI). The 10 year period after completion of the terminal degree or residency may be extended to accommodate special circumstances including various medical concerns, disability, pressing family care responsibilities, or active duty military service. If an extension has been approved, the SRO will bring this to the reviewers’ attention.
Ranking and Priority Scores

- 2-3 assigned reviewers discuss a grant, and may be the only ones who read it
  - The primary reviewer by far has the greatest impact on the score!
  - All reviewers (~30) vote on all grants, based on discussion at the meeting
  - If it’s not in the research strategy, they don’t have to read it (appendices, and last minute data)

- Grants are scored from 1 (exceptional) - 9 (poor) for the overall impact/priority score as well as the individual review criteria. Ratings are provided only in whole numbers, not decimals

- Applications judged unanimously by the peer reviewers as less competitive, based on preliminary impact/priority scores (roughly the bottom half of applications for that review meeting), will not be discussed and will not receive a final impact/priority score.
## NIH Grant Application Scoring System

<table>
<thead>
<tr>
<th>Impact</th>
<th>Score</th>
<th>Descriptor</th>
<th>Additional Guidance on Strengths/Weaknesses</th>
</tr>
</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
A Few Last Points on Review

• Program staff can attend reviews, but can’t influence reviewers

• You will be sent a score and percentile after review; SROs release summary statements in 4-6 wks
  – (They are \textbf{NOT} available to Program till then, either)
  – USE \url{https://commons.era.nih.gov/commons/} !!

• You can request (with good reason) that someone not review your grant, but can’t suggest reviewers
Percentage of NIH R01 Principal Investigators Age 36 and Younger and Age 66 and Older (Fiscal Years 1980 to 2010)
Average NIH Grant Size

Average Grant Size (Direct + Indirect X $1000)

- Research Project Grants (RPG)
- R01 Equivalent Grants
- Constant 1995 Dollars (Thousands)


- 1995: $252
- 1997: $218
- 1999: $265
- 2001: $293
- 2003: $341
- 2005: $378
- 2007: $431
- 2009: $473
- 2011: $261
- 2013: $238
Success Rates for New (Type 1) Applications
NIH Competing Awards

Line graph showing the trends of different types of NIH awards from 1995 to 2015. The categories include:
- RPG plus Supplemental Appropriation (ARRA) RPG
- Research Project Grants (RPG)
- R01 Equivalent Awards
- First-time R01 Equivalent Awards

The graph indicates a significant increase in awards in 2009, with the peak in 2010.
Advice: Writing the Proposal

- Abstract and Specific Aims: clearly state what you propose to do - why and how, *without* distracting detail
- State hypotheses clearly and design clear answers from your experiments
  - Address interesting and significant issues
  - Make the design win-win by assuming the worst
  - Develop alternative strategies for potential problems
- Preliminary Data: prove you can do the work, analyze the results, and draw sound conclusions
- **Avoid being overly ambitious**
Advice: Writing the Proposal

- Make it easy for the primary reviewer
  - S/he will present your case
  - Clear significance, fair literature review
  - Clear and sound hypotheses
  - Demonstrate productivity and feasibility
  - Logical experimental design
    - Avoid Aims that may make next step impossible
  - Don’t assume they know what you mean, *tell them*
  - Make it “sexy”
  - Present it in readable, attractive format
    - Spell check; avoid too many acronyms

- Spell check; avoid too many acronyms
Helpful Websites

• http://www.usc.edu/research/for_researchers/funding/federal/
• NIH - www.nih.gov
• NIH peer review
  - www.csr.nih.gov/review/peerrev.htm
  - www.csr.nih.gov/review/irgdesc.htm
• NIH Guide for Grants & Contracts
  - grants.nih.gov/grants/guide/index.html
More Helpful Websites

http://grants2.nih.gov/grants/grant_tips.htm
http://www.niaid.nih.gov/ncn/grants/
http://www.nigms.nih.gov/funding/tips.html
http://www.nigms.nih.gov/funding/moregrant_tips.html
http://deainfo.nci.nih.gov/EXTRA/EXTDOCS/gntapp.htm
http://12.46.245.173/cfda/cfda.html
http://cpmcnet.columbia.edu/research/writing.htm
Building Key Relationships

• Critical difference between program and review staff [firewall between them]
  - Program staff make funding decisions
    • Former scientists, specific areas of expertise
    • Based at individual Institutes
    • Take Institute priorities, review scores into account
    • Attend review meetings
  - Review staff: Scientific Review Administrators (SRAs)
    • Former scientists who coordinate study sections at CSR or within Institutes
    • Oversee standing review committees or special emphasis panels (SEPs)
    • Based at CSR or individual Institutes
Advocacy Tips

• Make sure there is close match between your research & institute priorities
• Work with Program Staff early
  - Find a ‘champion’
  - ‘Light touch’ - avoid at all costs pressure, manipulation, shameless self-promotion
  - Identify right person
  - Respect hierarchy
  - Get advice
  - Build enthusiasm – enlist him/her as your advocate
  - Send papers, data
Summary

• NIH is ‘crown jewel’ of fed R&D agencies
• Institute R&D priorities matter!
• NIH director has influence but institute priorities & programs persist for years
• Find homes for your research - both review & funding (‘champion’)
• Write best proposal you can – tightly focused, “sexy,” with “A-List” personnel
• Be patient and tenacious
DC Office for Research Advancement

Additional questions, advice:
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