Successful proposal development: developing your concept and getting organized

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Financial disclosure

• I have received consulting fees (less than $1000 lifetime) from the Gerson-Lehman Group not even slightly related to information presented today
Personal disclosure

- I have actually done everything I am going to talk about today and the system totally worked for me.

- My first three grants were an internal Wash U. grant, a societal grant, and a K08.

- I have turned that into 2R01s and am co-investigator on an R01, a grant from the CDC and a grant from the McDonnell Foundation.

- This is thanks to fantastic:
  - Mentors (Tim Buchman, Richard Hotchkiss on faculty, Jeff Gordon when I was a post-doc)
  - Lab members who actually do the work
  - Chairman support (Tim Eberlein)
  - University support and collaborators
  - Luck
The glass is half empty…

- Average age at which first R01 is obtained: 42 for PhDs and 44 for MDs & MD/PhDs
First-Time Awardees Have Remained at about 6 Percent of all Research Investigators During the Doubling of the NIH Budget

**NIH Traditional Research Project Awards (R01, R23, and R29)**

- First Time Awardees
- New Awards Made to experienced Investigators
- Competing Continuations or Supplements
- Noncompeting
The glass is half full

- The NIH WANTS you to succeed if you are a new investigator
- “New investigators are the innovators of the future - they bring fresh ideas and technologies to existing biomedical research problems, and they pioneer new areas of investigation. Entry of new investigators into the ranks of independent, NIH-funded researchers is essential to the health of this country's biomedical research enterprise. NIH’s interest in the training and research funding of new investigators is understandably deep and longstanding.”
New Investigators Program

NIH is Committed to Providing a Pathway to
Research Independence for New Investigators

New investigators are the innovators of the future - they bring fresh ideas and technologies to existing biomedical research problems, and they open new areas of investigation. Entry of new investigators into the ranks of independent, NIH-funded researchers is essential to the health of the country's biomedical research enterprise. NIH's interest in the training and research funding of new investigators is understandably deep and longstanding.

The NIH Pathways to Independence Program employs multiple strategies to facilitate receiving an R01 award earlier in an investigator's research career. These involve:

- Pathway to Independence Award
- NIH Director's New Innovator Award
- NRSA Individual and Institutional Training Awards
- Career Development Awards - K Kiosk
- Research Project Grant Program - (R01)
- NIH Institute and Center Practices
- Resources for New Investigators
Prior support through career (K) awards, R03, R21 confers some advantage in future funding

Funding Rates for R01-R29 Applications

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>Funding Rate</th>
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<tbody>
<tr>
<td>1993</td>
<td>10%</td>
</tr>
<tr>
<td>1995</td>
<td>12%</td>
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<td>1997</td>
<td>15%</td>
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</tr>
<tr>
<td>2001</td>
<td>20%</td>
</tr>
<tr>
<td>2003</td>
<td>22%</td>
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Mentored Career Awardee Applications
R03 Awardee Applications
R21 Awardee Applications
Applications from Those With No Prior RCP, R03, or R21 Support

NIH.gov
The bottom line

• Even in the best of times, getting grants is hard
• Really hard
• Really, REALLY hard
• IT TAKES MORE THAN A GOOD IDEA TO GET FUNDED
• Grantsmanship 101…
Who in this room will never have a good idea in their life?
Who in this room is an absolutely brilliant scientist, thinker, writer, communicator?
What percentage of your grant’s chances for success are based upon your ideas?
What percentage of your grant’s chances for success are based upon your ideas?

50 Percent
You’re an expert on your science but…

• Being a great graduate student/post-doc/resident/clinician does NOT mean you are a great (or even adequate) PI or grant writer or financial manager. They are different skill sets.

• Just because you can write a great paper doesn’t mean you can write a great grant.
TIMELINE

- 6 MONTHS in advance – Idea
- 3 MONTHS in advance – First page written
- 2 MONTHS in advance – Grant (science) written
- 2 MONTHS in advance – Grant (training plan) written
- 1 MONTH in advance – Critiques received
- FINAL MONTH – Rewrite proposal
Peer Review

• People don’t run for president without polling numbers to tell them how well they’re doing

• Coaches don’t come into professional sporting events without scouting to know each side’s strengths and weaknesses

• Professors don’t get jobs in academic medicine without someone making behind the scenes phone calls to find out if the applicant is worth hiring

• And yet you want to ask the NIH for hundreds of thousands of dollars without anyone telling you in advance if your idea is any good?
TIMELINE (FOR THE SCIENCE)

- 6 MONTHS in advance – Idea
- 3 MONTHS in advance – First page written

PEER REVIEW NUMBER ONE
- 2 MONTHS in advance – Grant (science) written
- 2 MONTHS in advance – Grant (training plan) written

PEER REVIEW NUMBER TWO
- 1 MONTH in advance – Critiques received
- FINAL MONTH – Rewrite proposal
Peer Review 1

• Your first page should be done three months in advance.

• It should then go out to at least three (preferably more) people in and out of your department and/or institution to review. Some of these people should have sat on study section.

• If your theme or your hypothesis or your specific aims don’t work, there is no point in writing the rest of your grant!!!
Peer Review 2

• Your “finished” grant should be done two months in advance
• It should then go out to at least three (preferably more) people in and out of your department and/or institution to review. Some of these people should have sat on study section.
• One cannot read a 10-25 page grant in 1 day. If you ask for a review to be back in 1 day, you run the high risk of getting no response or a worthless response.
• Expect a 2-4 week delay to get your “study section” review BEFORE you go to study section.
Peer Review 2b

• Your “finished” grant has two parts
  – Science
  – Everything else

• Most people spend countless hours on the science

• Most people spend countless minutes on
  – Training and career goals
  – Activities planned under this award
  – Training Site
  – Biosketch
  – Previous Research Experience
  – Respective Contributions
  – Selection of Sponsor and Institution
  – Responsible Conduct of Research
Peer Review 2c

- Your “finished” grant has two parts
  - Science
  - Everything else
- Everyone gets that if the science is insanely bad, you are not likely to get funded
- Many people do not understand that if everything else is subpar, you are also likely not to get funded.
- Although it seems self-evident, please understand that a training grant is evaluated heavily on the training plan and how you plan to transition into an independent investigator. Science alone is not enough!!!!!!
Mentorship

• Identifies the people to send your grant to for pre-review
• Knows what the study section “likes” and what they see as a “fishing expedition”
• Tells you how to direct your grant to the study section you want as opposed to a random assignment
• Tells you how to handle the fact that you do not have documented expertise in every technique you are proposing?
• Tells you whether your alternative plans make sense (and tells you to have an alternative plan, and to discuss statistics, etc). Remember, having a good idea and no self insight into the problems is nearly a guaranteed rejection.
• Tells you if your budget makes sense
Budget

• Being good at research does not mean you are good with money
• If you ask for too little, you will almost always be stuck with too little
• If you ask for too much, the NIH will cut your budget
• If you ask for way too much, you are likely to get triaged (if you are clueless about your budget, it is likely not the only thing you are clueless about)
Remember, there are a lot of non-scientific things involved with getting funded

• Doing them correctly doesn’t help get funded.
• Doing them incorrectly guarantees you won’t be funded.
• There is nothing fun about filling out the human studies/animal studies/assurances/etc paperwork.
• Having said that, you are asking the taxpayers of the United States to give you a million dollars. You have to make sure you have dotted every “i” and crossed every “t”.

Remember, there are a lot of non-scientific things involved with getting funded.

- Doing everything correctly REQUIRES that you utilize your partners within Washington University
- Remember: your Wash U. partners have submitted hundreds or thousands of grants – you have not
- Remember: your grant is the most important thing in the world to you – your grants partner will be submitting MANY grants on the same day so work with them early and often
- Remember the grant is awarded to Wash U. -- not to you
Your final proposal

• Specific aims (1 page)
• Most important page
  – Overarching theme
  – Hypothesis
  – 2-4 specific aims
• You can get triaged based upon this page alone
Your final proposal

• Background and significance (2-3 pages)
  – Remember not every reviewer will be familiar with your area of interest
  – Focused review based on your hypothesis
  – You are telling a story
  – Next to last paragraph summarizes what is known
  – This leads to…
  – Final paragraph, which summarizes what is unknown
Your final proposal

• Preliminary studies (6-8 pages)
  – Show what you’ve done
  – Don’t show too little so the reviewer can question whether you can do anything
  – Don’t show too much of what you’re proposing
  – Organized. Again you are telling a story.
  – Quantity of data does not equal quality
Your final proposal

• Research designs and methods (13-16 pages)
  – Most appropriate central experiment
  – Most appropriate controls
  – Anticipates a result and shows statistics to assure the result can be interpreted
  – Alternative approach if the preferred method does not work
  – Alternative direction if the method works but the result is contrary to prediction
  – Timeline
Your final proposal NRSA

- Scale everything down
- Specific aims (1 page)
- Background and significance (2 pages more or less)
- Preliminary studies (2 pages more or less)
- Research designs and methods (5 pages)
Cover Letters

Find out:
• Research interests of NIH institutes
• Study section members
• This is available online before you are reviewed
  – http://cms.csr.nih.gov/
  – Did you know that your grants are reviewed in a different institute than the one that funds your science?

Include in letter:
• Title
• At least 1 institute + 1-2 relevant study sections
• Reviewer(s) with possible conflicts of interest
And now you’re ready to...

Do science
And now you’re ready to...

Not So Fast...
Addendum?

• Aren’t you done when you submit your application?
• A little over 2 months later, it may be beneficial to submit a 2-3 page addendum (not mandatory)
• This tells the reviewers that you have started work on your research proposal and you have exciting new results, proving your idea was great and needs funding
• Study section must see this before they start reviewing your grant
• Please note addendums are risky
  – Upside – tells the reviewers you have been working and have exciting new results
  – Downside – reviewers are not obligated to read your addendum
And now you’re ready to…

Do science
And now you’re ready to…

Not So Fast…
It’s more likely than not that you didn’t get funded

• You’ll likely go through grief, rage, acceptance, etc.
• However, realistically, most grants don’t get funded the first go around.
• What next?
• RESUBMIT
Perseverance is key

- Having said that, your next version needs to be improved over your previous version.
- How do you make that happen?
- You will receive electronic comments on E-commons from your three reviewers (people will call these “pink sheets” although they are not pink and they are not sheets)
- You need to respond to EVERY comment on your pink sheets
  - It doesn’t matter if you think the comments are stupid, wrong, inane, brainless, moronic, insipid, idiotic
Resubmission

• You will be given 3 pages to respond explaining how you changed the grant.
• Respond to EVERY point. Not some of them. Not most of them. ALL of them.
• Your response cannot be “we respectfully disagree with the reviewer” and have left things as is.
• Nothing is more frustrating to a reviewer than to be ignored when recommending changes. You can rest assured this frustration will make it into your score.
And that’s all there is...

Unless they change the rules in midstream
E-mail received from the NIH on 3/3

- On February 28, 2008, the Final Draft of the NIH 2007-2008 Peer Review Self-Study was submitted to Dr. Elias Zerhouni, Director of NIH, marking the end of the diagnostic phase of the peer review enhancement effort.

- To obtain the PDF file of Final Draft Report: Final Draft Report (PDF, 1.69MB) - please go to the Peer Review Website: http://enhancing-peer-review.nih.gov/

- (Persons with disabilities experiencing problems accessing portions of the above PDF file should contact Kerry Brink (301) 435-2641).

- This Final Draft Report identifies the most significant challenges facing the NIH peer review system and proposes recommended actions. If you wish to comment on the Final Draft, please send your comments no later than Monday, March 17, 2008, via:

- Electronically: PeerReviewRFI@mail.nih.gov
So what’s the same?

- Your grant still has to be great
- Funding lines are not getting markedly better
What might be different?

- **Goal:** Reduce the number of applications that need to be submitted by helping applicants make faster, more informed decisions whether to refine an existing application or develop a new idea

- **Recommended Actions**
  - Provide unambiguous feedback to all applicants
  - Establish an NRR (not recommended for resubmission) decision option
  - Provide ratings for all applications

http://enhancing-peer-review.nih.gov/meetings/EnhancingPeerReviewACD2-21-08.pdf
What might be different?

- **Challenge:** Increasingly, three submission rounds are necessary before an application is funded
  - Support for meritorious science may be delayed when initial submissions are often placed at the end of the queue
  - Reviewers may favor “last chance” applications which may lead to support of less meritorious science

- **Goal:** Focus on the merit of the science as presented in the application and not the potential improvements that may be realized following additional rounds of review

- **Recommended Action**
  - Eliminate the “special status” of amended applications - consider all applications as being NEW

http://enhancing-peer-review.nih.gov/meetings/EnhancingPeerReviewACD2-21-08.pdf
To reiterate

- Eliminate the “special status” of amended applications - consider all applications as being NEW
- Translation:
  - You no longer get to respond to the “pink sheets” in a special section of the revised grant
  - Your reviewer no longer sees the “pink sheets”
  - Advantage – Every application is truly new
  - Disadvantage – Constantly moving target (answer every criticism and get bombed with a whole new set the next time)
What else might be different?

• Goal: To focus and elevate the level of discourse at the study section, rate multiple explicit criteria individually
• Recommended Actions
  – Modify the rating system for all RPGs (Scores + Rank)

• Impact
• Investigator(s)
• Innovation
• Plan
• Environment (including information on institutional support for the applicant)

http://enhancing-peer-review.nih.gov/meetings/EnhancingPeerReviewACD2-21-08.pdf
Is there some good news?

- **Challenge:** There are lower success rates for New Investigators at every stage of type 1 R01 application
- **Goal:** Continue to enhance support for new investigators
- **Recommended Actions**
  - Continue to fund more R01’s for early career investigators
  - Consider the merits of reviewing early career investigators separately, by generalists, to enhance innovation and risk-taking by applicants
  - Consider the merits of ranking early career investigators against each other
  - “Environment” criterion should take into account institutional commitment

http://enhancing-peer-review.nih.gov/meetings/EnhancingPeerReviewACD2-21-08.pdf
Regardless of what the review process looks like a year from now, submitting a logical, readable grant will continue to be key. May you have a long, productive, satisfying career.
The ones who actually do the work present and past
Acknowledgments

Coopersmith Laboratory

Present:
Drew Clark
Jessica Clark
Amy Wolf Fox
Erin Perrone

Past:
Kevin McConnell
Paul Stromberg
Keary Husain
Saju Rajan

Charles Robertson
Cheryl Woolsey
Dinesh Vyas
Pardis Javadi
Dan Amiot II

Tim Buchman
Richard Hotchkiss
Jeff Gordon
Tim Eberlein

NIGMS (GM072808, GM66202, GM00709)