Ten Things to Consider to be Competitive for NIH Funding

Craig R. Rush, PhD [Professor]
Department of Behavioral Science
University Research Professor
University of Kentucky

August 18, 2022

Disclaimer and Conflict

The views, opinions and recommendations expressed today are solely mine and do not necessarily represent those of the University of Kentucky.

I do not have any relevant conflicts of interest.

Disclaimer

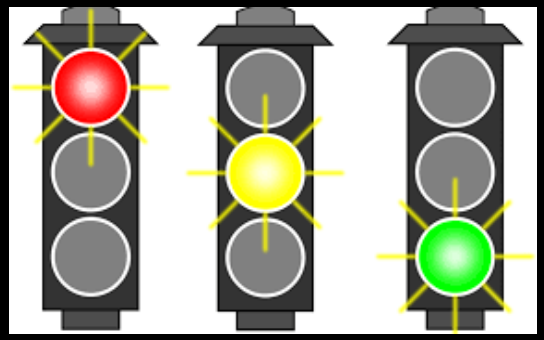
- I will present **A** way to approach writing an NIH grant.
- It is not necessarily **THE** way!

Number 1

- You must allow enough time to prepare the application.

Time Management

- Many investigators, established and junior, fail to commit adequate time to preparing a competitive application.
- Do you have the time to commit to preparing a competitive application?
- You must be able to commit at least 50% effort to preparing the proposal for several months (i.e., 3-6).
- Identify a place and time you can effectively read, think, and write.



- Today is August 18, 2022
- NIH Due Dates:
  - *October 5, 2022*
  - *February 5, 2023*
  - *June 5, 2023*
  - *October 5, 2023*
  - *February 5, 2024*

Why so much time?

Allows you to:

- Engage in critical “pre-writing” activities.
- Write the proposal and then re-write it several times before soliciting input (3-4 months).
- Have senior investigators read, digest and critique your proposal (i.e., ~1 month).
- Significantly modify your application based on the comments of senior investigators (i.e., ~1 month).

Pre-Writing Activities

- You need to be clear as to what the agency funds.
- This is easily accomplished today by searching NIH RePORTER (Research Portfolio Online Reporting Tool)
  - http://projectreporter.nih.gov/reporter.cfm
- You must search using multiple strategies or keywords.
- You must also subscribe to and read pertinent electronic newsletters.

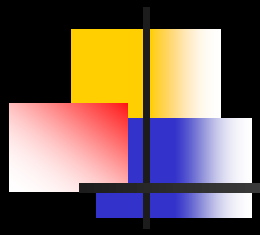
Pre-Writing Activities

- New proposals similar to currently funded projects are less appealing to a funding agency.
  - Funding agencies consider the breadth of their portfolio.

Number 2

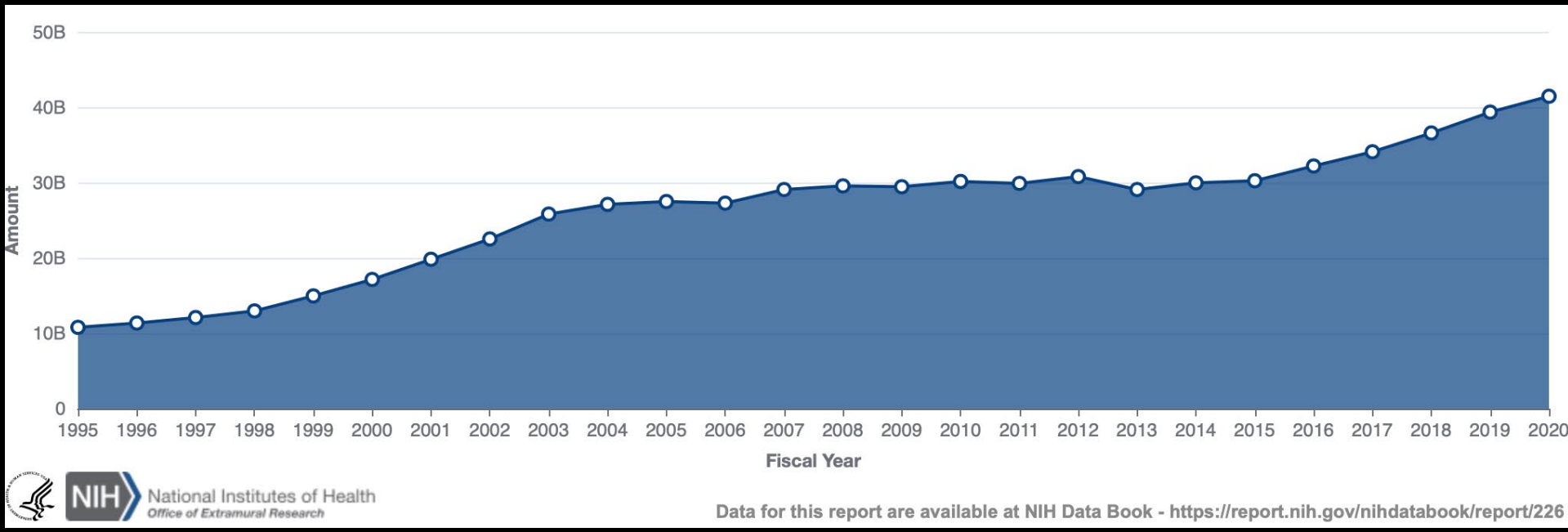
- You must be hard working, patient and persistent.

HARD
WORK
AHEAD

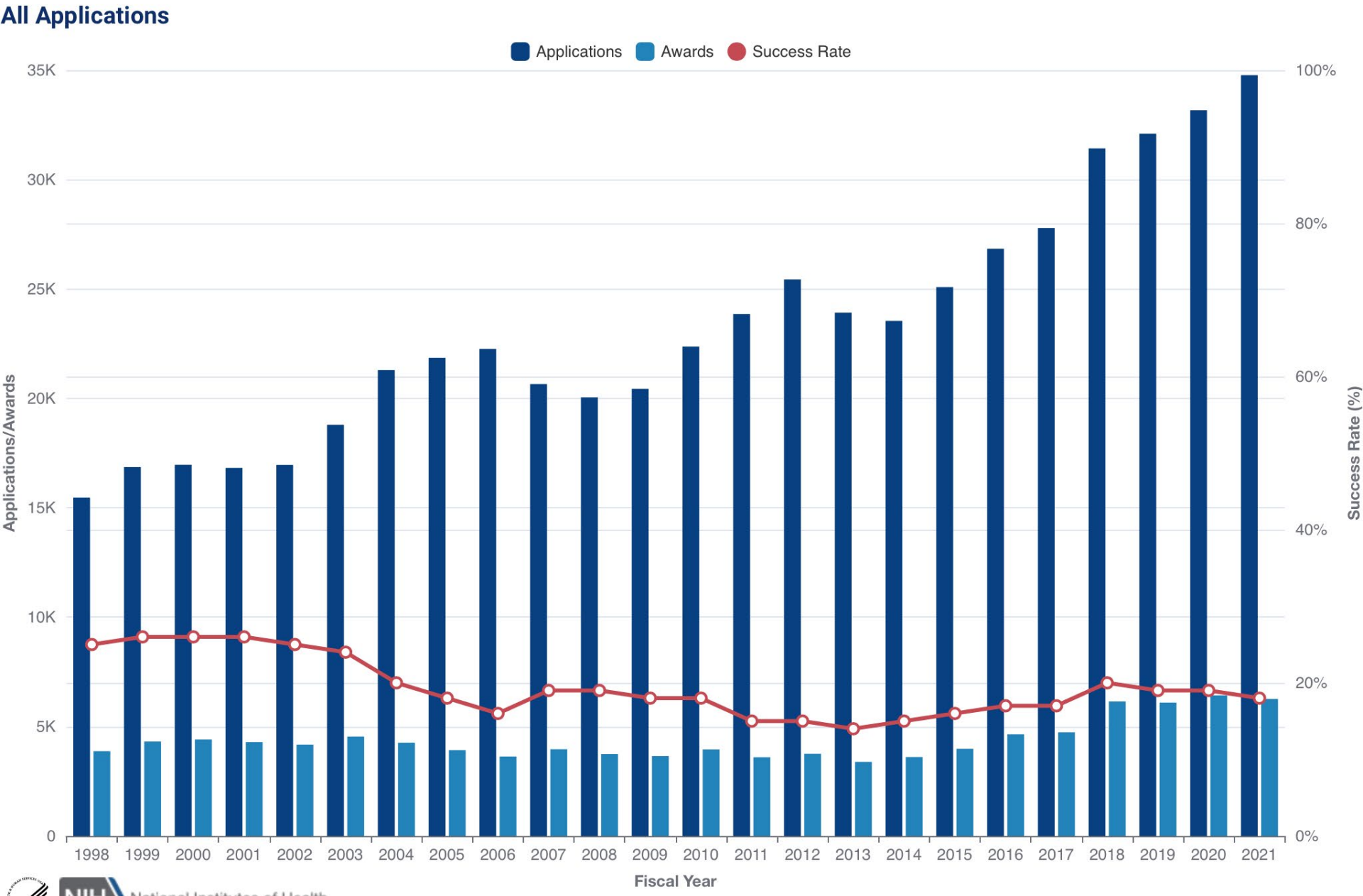


- You may need to write multiple grants to get one.
- Many workdays will be 12+ hours and 7-day work weeks.
- It could take 3-5 years to get funded.
- Average age of first R01:
  - MD = 45
  - PhD = 43

NIH Funding Trend



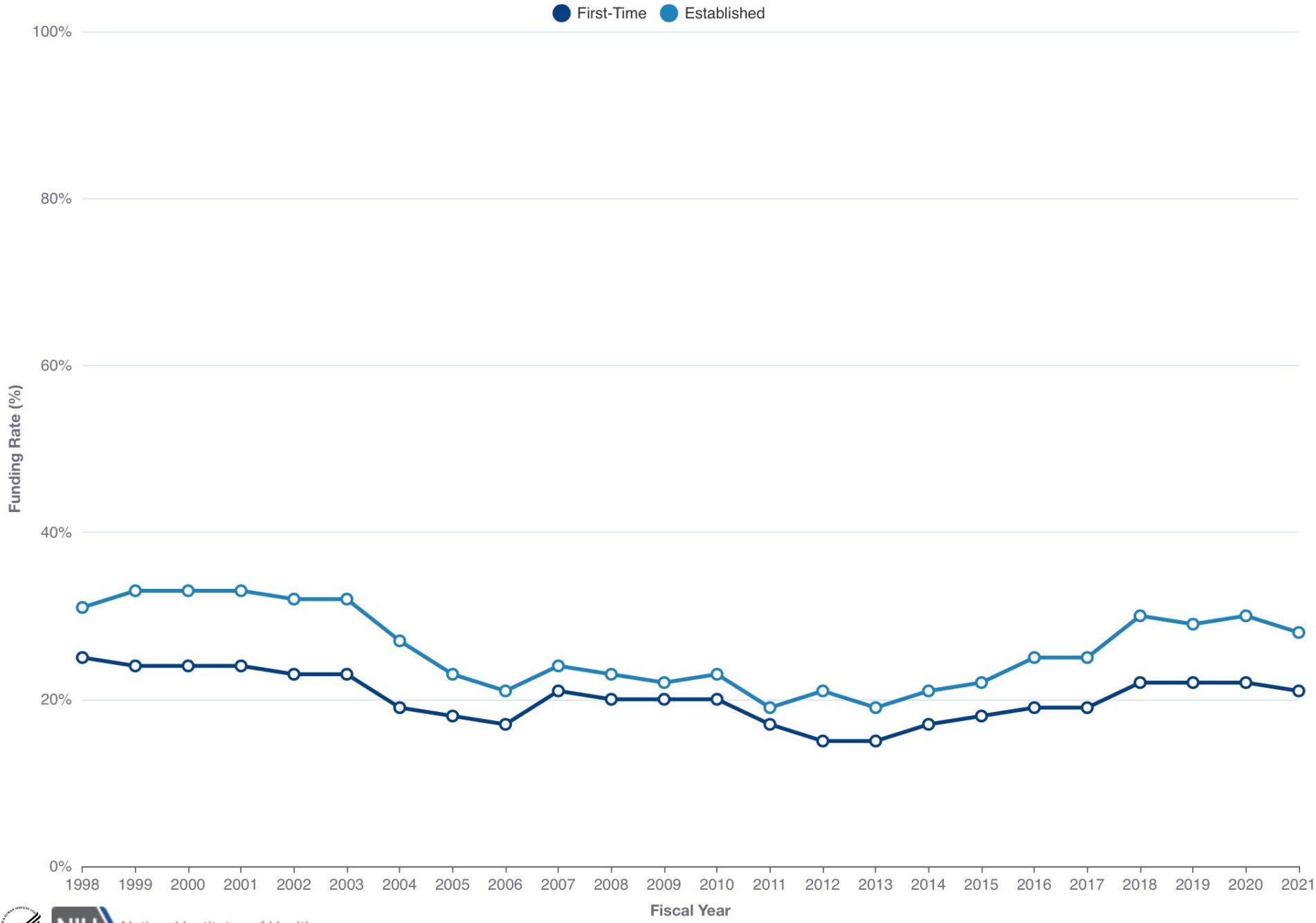
Applications, Number of Awards and Success Rates



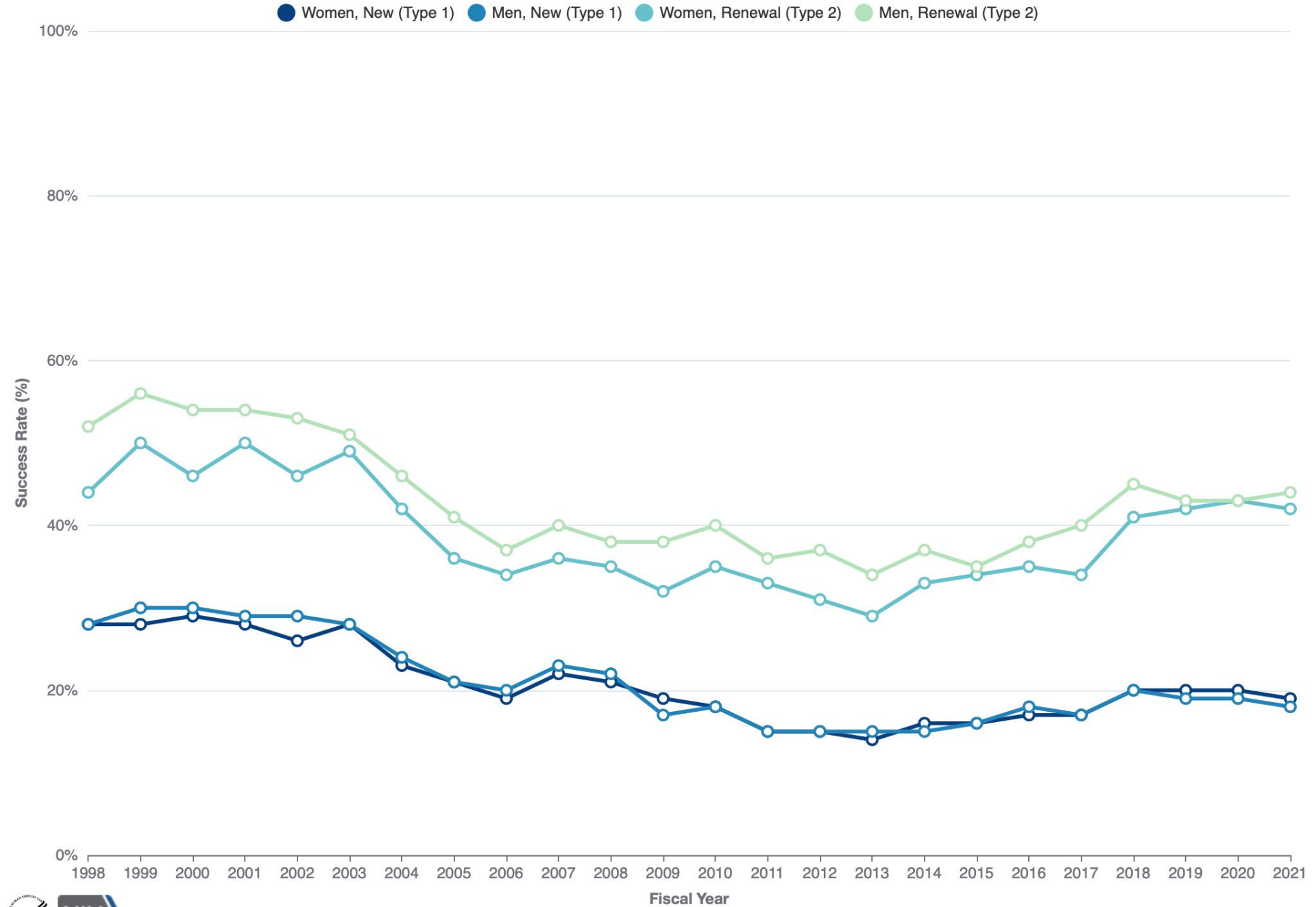
National Institutes of Health
Office of Extramural Research

Data for this report are available at NIH Data Book - https://report.nih.gov/nihdatabook/report/136

Funding Rates by Career Stage

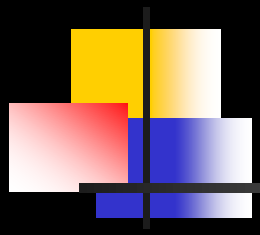


R01-Equivalent Grants: Success Rates, by Gender and Type of Application



NIH National Institutes of Health
Office of Extramural Research

Data for this report are available at NIH Data Book - https://report.nih.gov/nihdatabook/report/131



- The funding situation, while difficult, is not abysmal.
- It is equally difficult for everyone, and nobody seems to have a clear advantage.
- You need to explore all mechanisms of funding within an agency and consider alternative funding sources (e.g., private foundations).

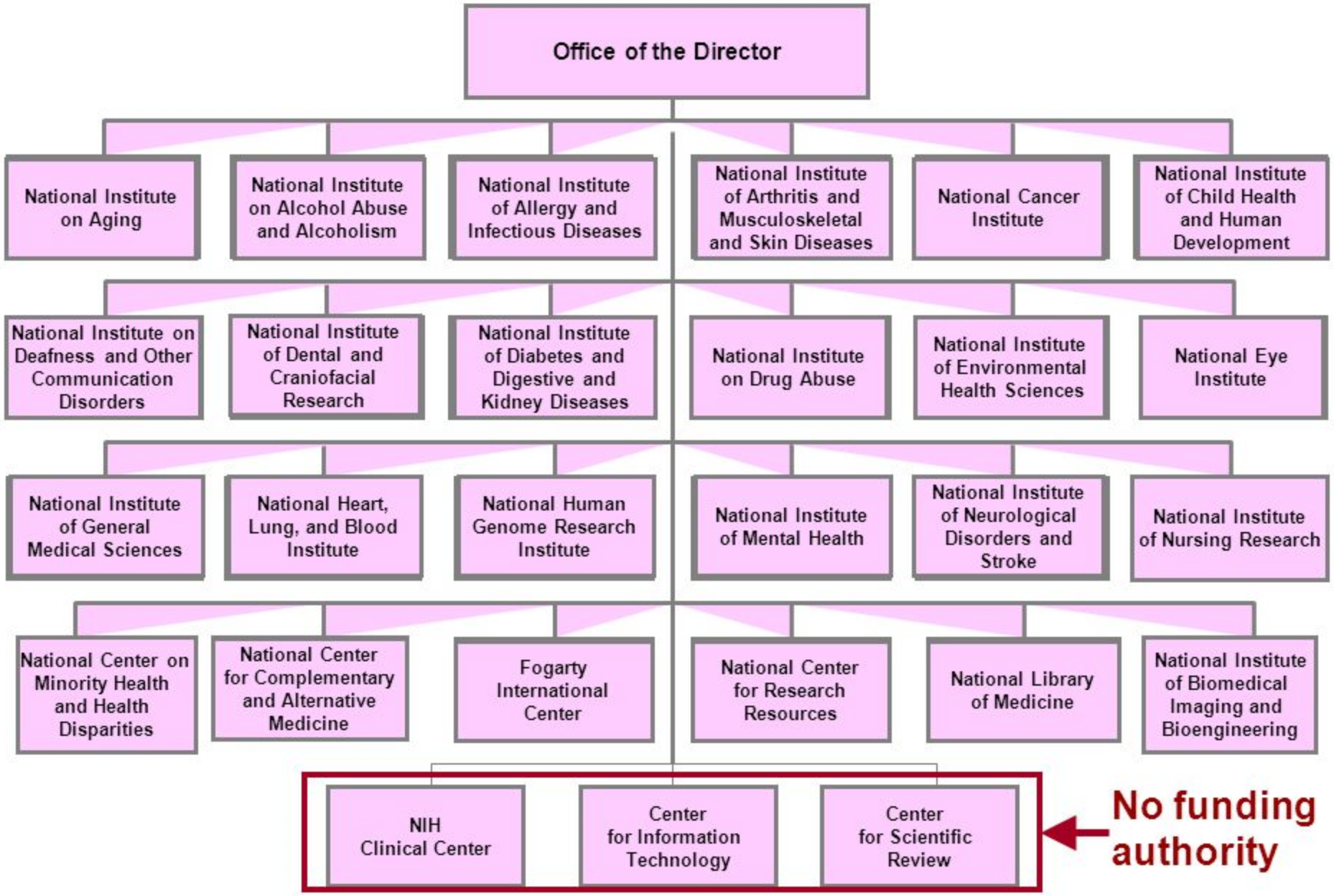
Friend and Colleague Said

- “Not only have you chosen a career you have picked a lifestyle”.

Number 3

- You must be familiar with the organizational structure of NIH and Center for Scientific Review (CSR).

NIH Organizational Structure



National Institute on Drug Abuse

Dec 202

HIV RESEARCH PROGRAM
Redonna Chandler, Ph.D.
Director
Vasundhara Varthakavi, DVM, Ph.D.
Associate Director

OFFICE OF THE DIRECTOR
Nora D. Volkow, M.D., Director
Wilson M. Compton, M.D., M.P.E., Deputy Director
Joellen Austin, MPAff, MSM, Deputy Director for Management

INTERNATIONAL PROGRAM
Steven Gust, Ph.D.
Director

OFFICE OF RESEARCH TRAINING, DIVERSITY AND DISPARITIES
Wilson M. Compton, M.D., M.P.E.,
Acting Director

Albert Avila, Ph.D.,
Deputy Director

OFFICE OF TRANSLATIONAL INITIATIVES & PROGRAM INNOVATIONS
Elena Koustova, Ph.D.
Director

OFFICE OF MANAGEMENT
Joellen Austin, MPAff, MSM
Director
Dave Daubert
Deputy

OFFICE OF SCIENCE POLICY AND COMMUNICATIONS
Jennifer Hobin, Ph.D..
Director

TBD
Deputy Director

ADMINISTRATIVE MANAGEMENT BRANCH
Amy Doster
Branch Chief

FINANCIAL MANAGEMENT BRANCH
Nathaniel Davis
Branch Chief

INFORMATION RESOURCE MANAGEMENT BRANCH
Gregg Friedman
Branch Chief

MANAGEMENT ANALYSIS BRANCH
Gloria Dabbondanza
Branch Chief

OFFICE OF ACQUISITIONS
Chris Belt
Director
Brian O'Laughlin
Deputy Director

CONTRACTS MANAGEMENT RED BRANCH
Ken Goodling
Branch Chief

CONTRACTS MANAGEMENT BLUE BRANCH
Scott Bredow
Branch Chief

CONTRACTS MANAGEMENT GREEN BRANCH
Brian O'Laughlin
Branch Chief

DIVISION OF EXTRAMURAL RESEARCH
Susan Weiss, Ph.D.
Director
Katia Howlett, Ph.D., MPP, MBA
Deputy

GRANTS MANAGEMENT BRANCH
Pamela Fleming
Branch Chief

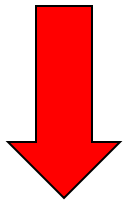
OFFICE OF EXTRAMURAL POLICY & REVIEW
Troy Zacone, Ph.D.
Director

SCIENTIFIC REVIEW BRANCH
Dharmendar Rathore, Ph.D.
Branch Chief

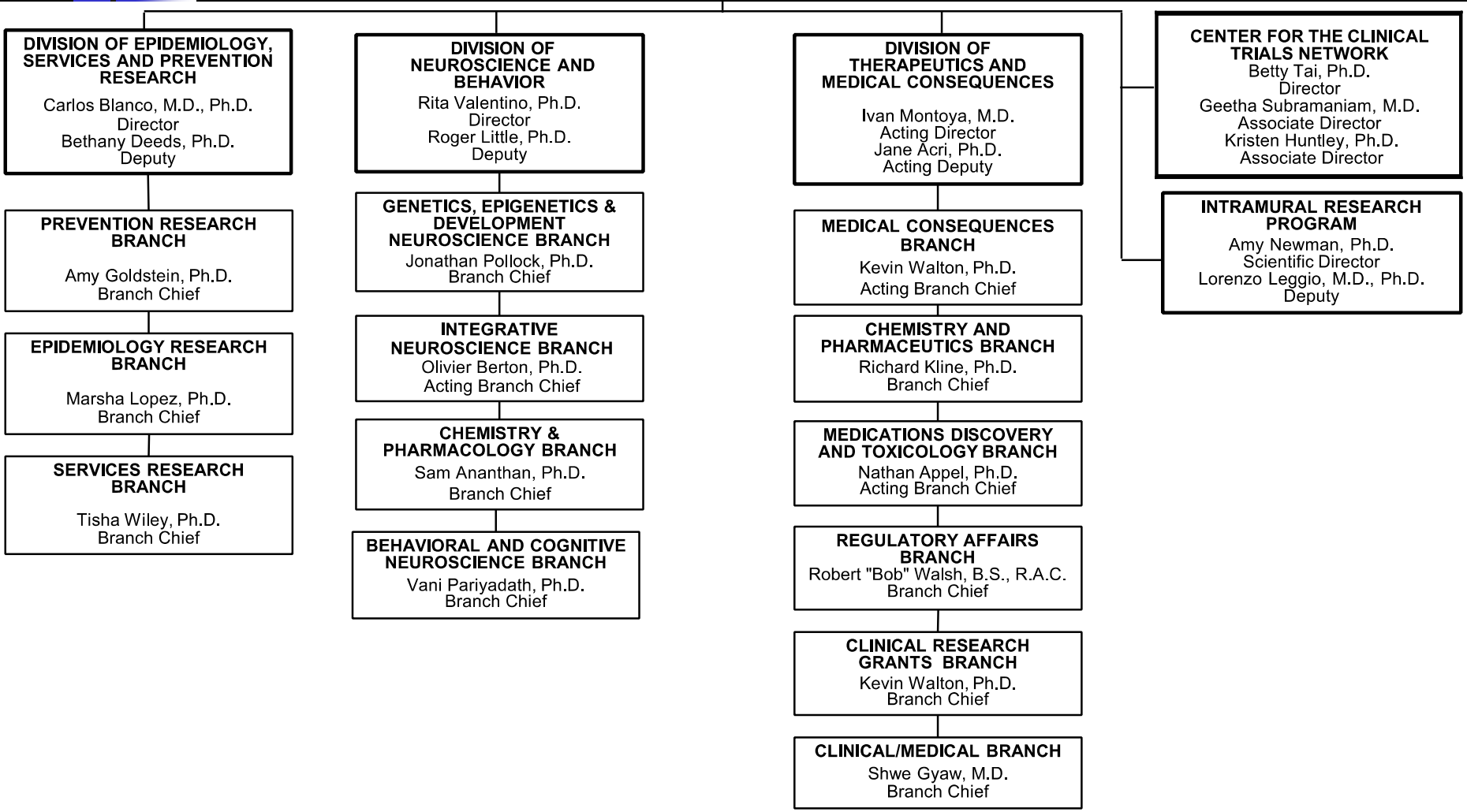
EXTRAMURAL ACTIVITIES & INITIATIVE DEVELOPMENT BRANCH
Troy Zacone, Ph.D.
Acting Branch Chief

COMMUNICATIONS BRANCH
Anne Rancourt, MPS
Branch Chief

SCIENCE POLICY BRANCH
Emily Einstein, Ph.D.
Branch Chief



National Institute on Drug Abuse (NIDA)

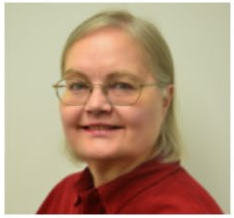


Center for Scientific Review: Organizational Structure

Office of the Director (OD)

Dr. Kristin Kramer
Director,
Office of Communications & Outreach

Dr. Noni Byrnes
Director



Dr. Christine Melchior
Senior Advisor to the Director

Dr. Gabriel Fosu
Associate Director,
Diversity and Workforce Development

Dr. Bruce Reed
Deputy Director

Dr. Amy Wernimont
Chief of Staff

Ms. MonaLisa Lynch
Director,
Deputy Ethics Counselor

Ms. Bonnie Ellis
Executive Officer

Dr. Miriam Mintzer
Director,
Office of Training & Development

Division of Management Services (DMS)

Ms. Bonnie Ellis
Director

ASB - Vacant
Ms. Blair Gosnell, Team Lead
Ms. Kelli Reid, Team Lead
CMB - Ms. Sharon Sealey
FMB - Vacant
SREA - Vacant

Division of Planning, Analysis, and Information Management (DPAIM)

Dr. Dipak Bhattacharyya
Director

Division of Receipt and Referral (DRR)

Dr. B. Duane Price
Acting Director
Deputy Director

Division of AIDS, Behavior and Population Sciences (DABP)

Dr. Valerie Durrant
Director

BP - Dr. Maribeth Champoux
HSS - Dr. Thomas Beres
EPH - Dr. Lisa Steele
CCHI - Dr. Jacinta Bronte-Tinkew
SCIL - Dr. Elia Ortenberg

Division of Basic and Integrative Biological Sciences (DBIB)

Dr. Raymond Jacobson
Director

MBBC - Dr. James Mack
BBBT - Dr. Vinod Charles
CDB - Dr. Maqsood Wani
MGG - Dr. Elena Smirnova
MCST - Dr. Mark Caprara
BTC - Dr. Amy Rubinstein

Division of Neuroscience, Development and Aging (DNDA)

Dr. Delia Olufokunbi Sam
Director

AN - Dr. Wei-Qin Zhao
CN - Dr. Samuel Edwards
NV - Dr. Joseph Rudolph
ICN - Dr. Alexei Kondratyev
BN - Dr. Gagan Pandya

Division of Physiological and Pathological Sciences (DPPS)

Dr. Ross Shonat
Director

DCAI - Dr. Emily Foley
KUDS - Dr. Jonathan Ivins
EMS - Dr. Elaine Sierra-Rivera
IIDA - Dr. Kumud Singh
IIDB - Dr. Audrey Lau

Division of Translational and Clinical Sciences (DTCS)

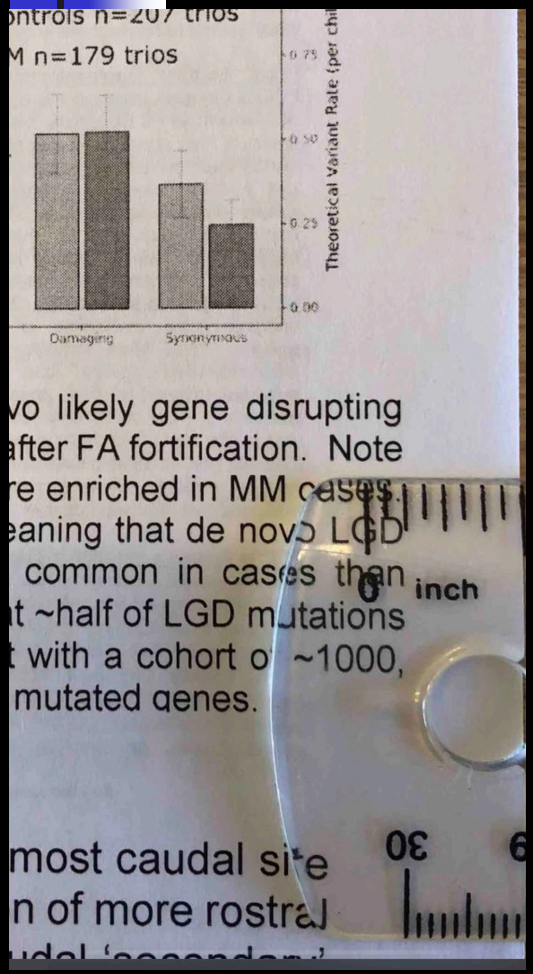
Dr. John Bowers
Director

RCCS - Dr. Eugene Carstea
MSDS - Dr. Chee Lim
CTH - Dr. Lambratu Rahman Sesay
CDPT - Dr. Syed Quadri
ISB - Dr. Yuanna Cheng
IVBH - Dr. Katherine Malinda

*tentative name

Number 4

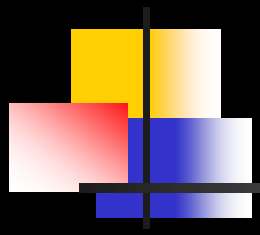
- You need to be intimate with the guidelines and carefully follow the instructions (e.g., margins, number of pages; font type and size; budget limitations).



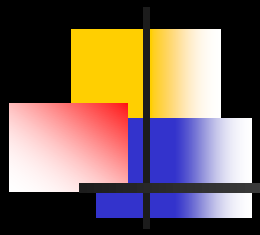
"I just had an NIH grant rejected by CSR prior to review because a figure legend creeped into the 0.5 in margin. I wish NIH had other things to focus on than page margins but be careful!"

Number 5

- You must know what the institute:
  1. is interested in funding;
  2. is currently funding; and
  3. has funded in the past.



- New proposals similar to currently funded projects are less appealing to a funding agency.
- Funding agencies consider the breadth of their portfolio.



Use relevant electronic databases:

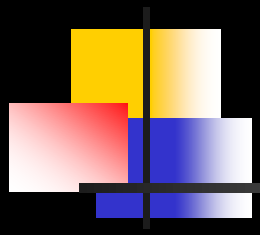
- Grants.gov: http://www.grants.gov
- NIH RePORTER: https://reporter.nih.gov
- You must search using multiple strategies or keywords.
- Subscribe to pertinent newsletters
- Take advantage of institutional resources: Program Development Office (PDO)

Contact a Program Officer

- Start with a pleasant e-Mail explaining your idea and its relevance to the institute. You do not need to provide every detail.
- Arrange to talk with a program officer on the phone.
- If this is your first time, consider having a more senior investigator on the phone/zoom so that he/she can interpret the comments of the program officer.

Number 6

- You must view your career and grant writing as a progression.



- NIH and reviewers respond favorably to young investigators progressing:

Internal Funding => F/K Award => R03/R21 => R01

Developmental Mechanisms

- R03
- R21
- R34
- K99/R00

R03

- Limited funding for a short period to conduct pilot or feasibility studies, secondary data analysis
- Up to $50,000/year in direct costs
- 2 years
- 1 page aims, 6-page plan
- More than half of Institutes and Centers

R21

- New, exploratory and developmental research, including pilots
- Up to $275,000 total in direct costs
- 2 years
- 1 page aims, 6-page plan
- Most Institutes and Centers

R34

- Clinical trial planning grant
- Development of proposed trial, including essential elements (e.g., surveys, interventions, etc.)
- Depending upon the announcement, $100,000-$450,000 total in direct costs
- 1-3 years
- 1 page aims, 12-page plan
- Only select Institutes and Centers

K99/R00

Completed	Document	Page Limits
☐	Project Summary/Abstract	30 lines of text
☐	Project Narrative	3 sentences
☐	Introduction to Resubmission/Revision	1 page (only necessary for resubmissions)
☐	Candidate Information and Goals for Career Development and Research Strategy	12 pages total
☐	Bibliography and References Cited	No limit
☐	Specific Aims	1 page
☐	Training in the Responsible Conduct of Research	1 page
☐	**Plans and Statements from Mentor and Co-Mentor*	*6 pages*
	**Mentor and Co-Mentor Current and Pending Support (PHS 398/2590)*	
☐	**Letters of Support from Collaborators, Contributors, and Consultants*	*6 pages total*
☐	Description of the Institutional Environment	1 page
☐	**Institutional Commitment to the Candidate's Research Career Development*	*1 page*
☐	Personal Biographical Sketch (NIH Biosketch)	5 pages
	**Mentor and Co-Mentor Biosketch*	*5 pages/biosketch*
☐	Vertebrate Animals	No limit
☐	Human Subjects and Clinical Trail Information	No limit
☐	Facilities and Other Resources	No limit
☐	Equipment	No limit
☐	Select Agent Research	No limit
☐	Resource Sharing	No limit
☐	Authentication of Key Biological and Chemical Resources	No limit
☐	**Budget Justification*	*No limit*
☐	**Reference Letters*	*3-5 letters*

Number 7

- You must clearly state the public health implications of the proposed work.

- “People living with HIV/AIDS (PLWHA) smoke at nearly three times the rate of the general population. The proposed trial will demonstrate the efficacy, safety and tolerability of theta burst stimulation (TBS), a form of non-invasive brain stimulation, in conjunction with varenicline for smoking cessation in PLWHA”.

Number 8

You must carefully prepare each element of the application reviewers will score.

- Significance
- Investigator(s)
- Innovation
- Approach
- Environment

R01

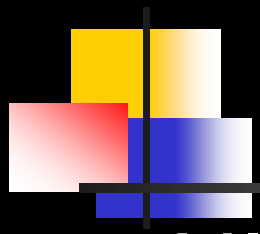
- Most commonly-used grant program
- Supports a discrete, specific, circumscribed research project
- Up to $500,000/year in direct costs
- 3-5 years
- 1 page aims, 12-page plan
- All Institutes and Centers

Significance (3 pages)

- The Background and Significance section must provide an authoritative review of the extant literature.

The Background and Significance section must:

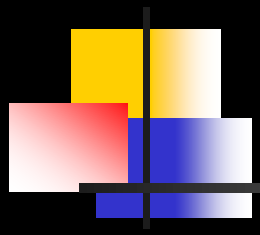
- Identify gaps in the current knowledge base and clearly indicate how the proposed research with help fill this void.
- Clearly indicate your proposed research is consistent with the agenda or mission of the funding agency.
- Provide the justification for funding.



- NIH is not particularly interested in “incremental” advances.
- NIH is interested in research that may produce a significant and sustained impact on the field.
- Different ≠ Significant
- Highly innovative proposals must include appropriate preliminary data.

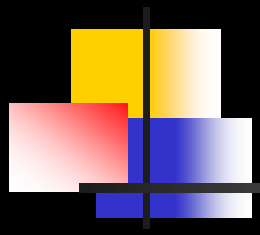
Specific Aims (1 page)

- This is the most important part of any grant application.
- This section should provide an enthusiastic overview of the proposal including everything that is significant and innovative.
- The aims serve as the road map for the remainder of your application.
- Write, rewrite and perfect this section before moving on.



- “Once you have written the specific aims, the rest of the application is just filling in blanks”

George E. Bigelow, PhD, Johns Hopkins School of Medicine.



- A fatal mistake is subsequent aims depend on successfully accomplishing a preceding aim.
- Specific Aim 1: The first aim is to demonstrate maintenance on bupropion-naltrexone combinations are well tolerated and attenuate the behavioral effects of cocaine under controlled medical conditions.
- Specific Aim 2: The second aim is to demonstrate maintenance on bupropion-naltrexone combinations reduce cocaine use in a clinical trial.

Investigators

- You must assemble an appropriate team of investigators.
- Include collaborators with skills that complement yours (i.e., translational science, statistician).
- Include senior/successful researchers (i.e., solicit and incorporate their comments; name recognition).
- Respect the expertise of your collaborators.

Innovation

- New proposals similar to currently funded projects are less appealing to a funding agency.
- Highly innovative proposals must include appropriate preliminary data.
- Different ≠ Innovative

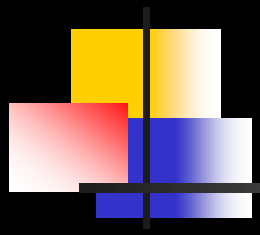
C. INNOVATION AND IMPACT

There are several innovative features of the proposed work. **First**, we will use a multipronged approach to determine the role of glucocorticoid receptor antagonism in the behavioral and neuroendocrinological responses to experimentally induced stress, the pharmacodynamic effects of ALC, and ALC use, craving and stress in the natural ecology in participants with AUD. Second, the proposed study will use a novel chemical entity, PT150, for selectively targeting glucocorticoid receptors. Until recently, studies with humans relied on mifepristone, a non-selective glucocorticoid receptor antagonist, to show efficacy in treating psychiatric disorders or AUD [16, 90, 121]. **Third**, a novel stress-induction procedure will be used which includes a physical (bilateral foot Cold Pressor Test) and social/cognitive (Paced Auditory Serial Addition Task) stressor [38, 39]. Laboratory stress-induction procedures have previously been shown to produce behavioral and neuroendocrine responses [38, 122, 123]. The “double-stressor” produces robust behavioral and neuroendocrinological responses [38, 39, 124]. **Fourth**, the proposed study could provide the impetus for clinical research to develop PT150 as an adjunct therapy for AUD. **Fifth**, because HPA dysregulation and altered cortisol levels may be transdiagnostic, this project could spur interest in targeting the HPA axis with selective glucocorticoid receptor antagonists in cocaine, methamphetamine, opioid, and tobacco use disorders.

Approach (8 pages)

- This is where you explain how you are going to do the “science”.
- You need to provide sufficient details to demonstrate you understand the relevant issues.
- When you choose between two approaches, methodological or statistical, you must justify your decision (i.e., decision tree).

- You must carefully describe how the data will be handled (i.e., cleaned, transformed, analyzed).
- Should include a biostatistician.
- If possible, to save space, refer to previous publications that describe the methods in detail.
- Cite review papers if available.
- You do not need to provide every painstaking detail.

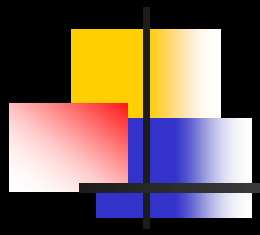


- Include appropriate preliminary data.
- You must be tastefully self-promoting!
- Use to demonstrate your expertise and productivity.
- Use to demonstrate your collaborative relationships.
- Use to demonstrate your proposed methods are sensitive and valid.
- The more novel (innovative) your approach, the more preliminary data you will need.

- A picture is worth a 1,000 words, use figures!
- When using a figure, make sure it is:
  - Large enough to easily read
  - Accompanied by an appropriate legend that is also easy to read
  - As close as possible to the point to which it is referred.

Environment

- You must demonstrate the institution has the necessary resources and infrastructure (i.e., equipment, personnel, technology, targeted samples) for the successful completion of the project.
- If your institution does not have the necessary equipment (e.g., mass spectrometer), you must make the necessary arrangements.



- Will the institution provide adequate “release” or “protected” time for the investigators to conduct the research (especially important if you have teaching or clinical responsibilities).
- Include letters of institutional support.

Number 9

- You must carefully prepare the supporting documents.

Title

- This part of your application will be read the most and the importance cannot be overemphasized.
- It should capture the essence of the proposal.
- It must convey enthusiasm and be eye-catching.
- It will, in part, determine the individuals who review your application.

Abstract/Summary

- You usually have a well-defined limitation (e.g., 30 lines).
- The abstract of your proposal should be very much like one you would write for a manuscript you are trying to publish.
- The abstract must capture all aspects of the proposal while staying within the limits:
  - Significance
  - Investigators
  - Methods
  - Innovation
  - Environment

Biograhical Sketches

- Every funding agency, public and private, seriously considers the qualifications of the investigators.
- The biographical sketch is essentially your CV reduced to 5 pages.
- The biographical sketch should be tailored to each application (i.e., personal statement; relevant publications).

Budget/Justification

- Propose a reasonable number of investigators and effort for each.
- Be aware of budget limitations (i.e., 500,000/year direct costs).
- Not all items can be purchased with grant funds.
- You must justify all expenses in the Budget Justification.

Common budget mistakes include:

- Exceeds limit of funding mechanism
- Too little or too much effort by the PI
- Too many co-investigators
- Too much effort for a co-investigator
- Too much travel
- Budgets right on the limit raise suspicions and scrutiny:
  - Year 1: $499,995
  - Year 2: $499,990
  - Year 3: $499,999

Timeline

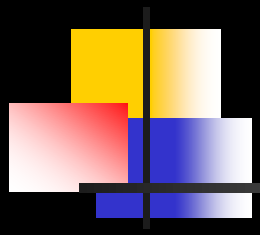
- Propose a reasonable timeline.
- Provide a precise description of the timeline.
- Allow time for unforeseen difficulties.
- The typical R01 is funded for 3-5 years
- DO NOT attempt to get additional years of funding when the project can be reasonably accomplished in a shorter period (e.g., request funding for 4-5 years when project can be completed in 3 years).

Clinical Trial Documents

- Availability Of Investigational New Drug (IND)/Investigational Device Exemption (IDE) Status
- Data Safety Monitoring Plan
- Dissemination Plan
- Inclusion of Individuals Across the Lifespan
- Inclusion Women and Minorities
- Protection Human Subjects
- Recruitment and Retention Plan
- Statistical Design and Power
- Study Timeline
- Overall Structure of the Study Team

Number 10

- You need to recognize you will probably need to revise and re-submit (perhaps multiple times).



Review Process

- You need to understand the review process.

Review Process

- Leave as little to chance as possible.
- Know the review process and possible review groups.
- Try to direct your application to an appropriate institute and review group.
- You **CANNOT** recommend potential reviewers to NIH.

Overal Impact or Criterion Strength	Score	Descriptor
High	1	Exceptional
	2	Outstanding
	3	Excellent
Medium	4	Very Good
	5	Good
	6	Satisfactory
Low	7	Fair
	8	Marginal
	9	Poor
Other Designations for Final Outcome		
AB		Abstention
		Abstention
CF		Conflict of Interest
DF		Deferred
ND		Not Discussed
NP		Not Present
NR		Not Recommended for Further Consideration

Review Process

- Your application will be reviewed by multiple individuals.
- Different scientific review officers (SRO) have different philosophies about the expertise of these individuals.
  - All are experts
  - One is knowledgeable but not an “expert”

Who are the reviewers?

- Accomplished, respected and busy scientists
- Hardworking, dedicated and conscientious individuals
- Individuals who are providing a valuable service for little monetary remuneration.
- Above all, they are fair and genuinely concerned that their respective fields are moving forward.

Who are the reviewers?

- They are human beings.
- Their behavior is influenced by many factors.
- Each reviewer will have several applications (e.g., 8-12) to review per cycle.
- Each application takes 4-8 hours to review.
- They must do these reviews over about 4 weeks in addition to their other responsibilities.

Responding to Reviews

My application was discussed and/or got a good score, what do I do?

- Speak to the funding agency to determine if the score is good enough to be considered for funding.
- Not all applications with a good score get funded (not compatible with mission of agency).
- Some applications with scores that do not seem good might eventually get funded.

Review Process

I did not get a good score, or my application was not discussed, what should I do?

- The funding agencies will provide you with written comments.
- Wait to see these comments before doing anything.
- For NIH applications, it is difficult, but not impossible, to move an application from not discussed to a fundable score with a single revised submission.

Review Process

Why should you seriously consider submitting a revised application?

- The success rate for revised applications is about three times better than for original submissions.

Analyze the Feedback

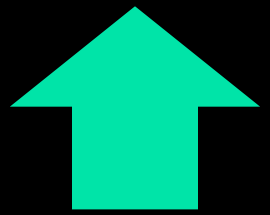
- Analyze the individual criterion scores
  - Significance
  - Innovation
  - Investigator
  - Approach
  - Environment
- Analyze the overall impact score (if discussed)
- Analyze the critiques from the reviewers
- Share the summary statements with co-investigators, peers, mentors, senior investigators, colleagues with experience on study section

Review Process

Significance: 7	Significance: 2
Investigators: 2	Investigators: 5
Innovations: 7	Innovations: 2
Approach: 2	Approach: 6
Environment: 2	Environment: 5
Overall: 4	**Overall**: 4

Review Process

Significance: 7	Significance: 2
Investigators: 2	Investigators: 5
Innovations: 7	Innovations: 2
Approach: 2	Approach: 6
Environment: 2	Environment: 5
Overall: 4	**Overall**: 4



Common Mistakes

- The problem is not significant.
- The hypothesis/basic premise is flawed.
- The investigator lacks sufficient expertise in the area of proposed study.
- The Specific Aims are not carefully thought out and logical.
- The aims are interdependent and cannot not stand alone.
- The proposal is overly ambitious (common for early-career investigators).
- The methods are difficult to follow, too detailed or do not provide enough details.
- The proposal does not acknowledge alternative approaches.
- The scope of the work does not fit the funding mechanism.
- Proofreading is poor, including references and figure legends.

Responding to Reviews

Contact the program officer

- Start with a pleasant e-Mail that explains your understanding of the reviews. This is not a time to “plead your case”.
- Arrange to talk with the program officer on the phone.
- You need to be careful and not appear to be overtly “lobbying” for you grant. This can earn you a poor reputation.
- If this is your first time, consider having a more senior investigator on the phone so he/she can interpret the comments of the program officer.

Responding to Reviews

After analyzing these factors, you must answer four questions affirmatively:

- Are you committed to submitting a revised application?
- Can you make changes to respond to the criticisms?
- Are you willing to make the necessary changes?
- Do you have time to commit to preparing an appropriate response (writing, gather additional pilot data)?

Responding to Reviews

- You get one page to respond
- **BE RESPONSIVE**!
- **DO NOT** be argumentative or combative!
- Be apologetic if points were not clear! You need to take responsibility.
- Correct any other errors (e.g., grammatical or typographical) you find.
- **DO NOT**, obviously planning to delete, write insulting comments (e.g., “this reviewer is stupid”).
- The resubmission will go back to the same study section and likely back at least one of the original reviewers.

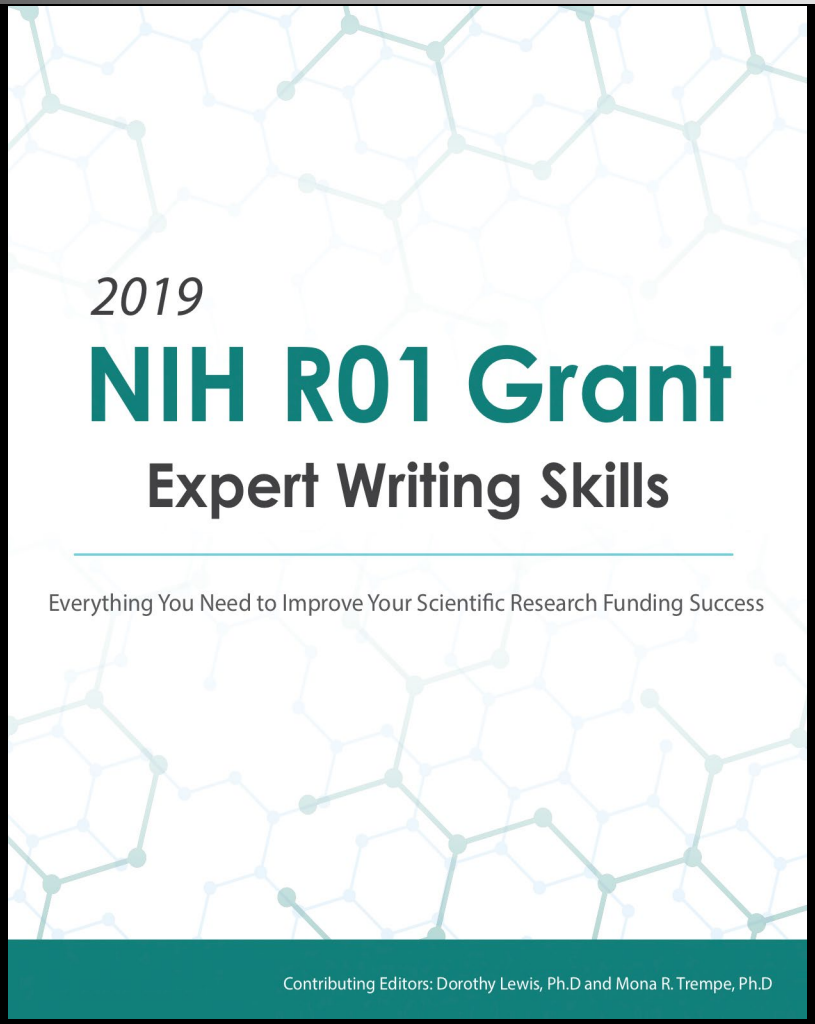
Responding to Reviews

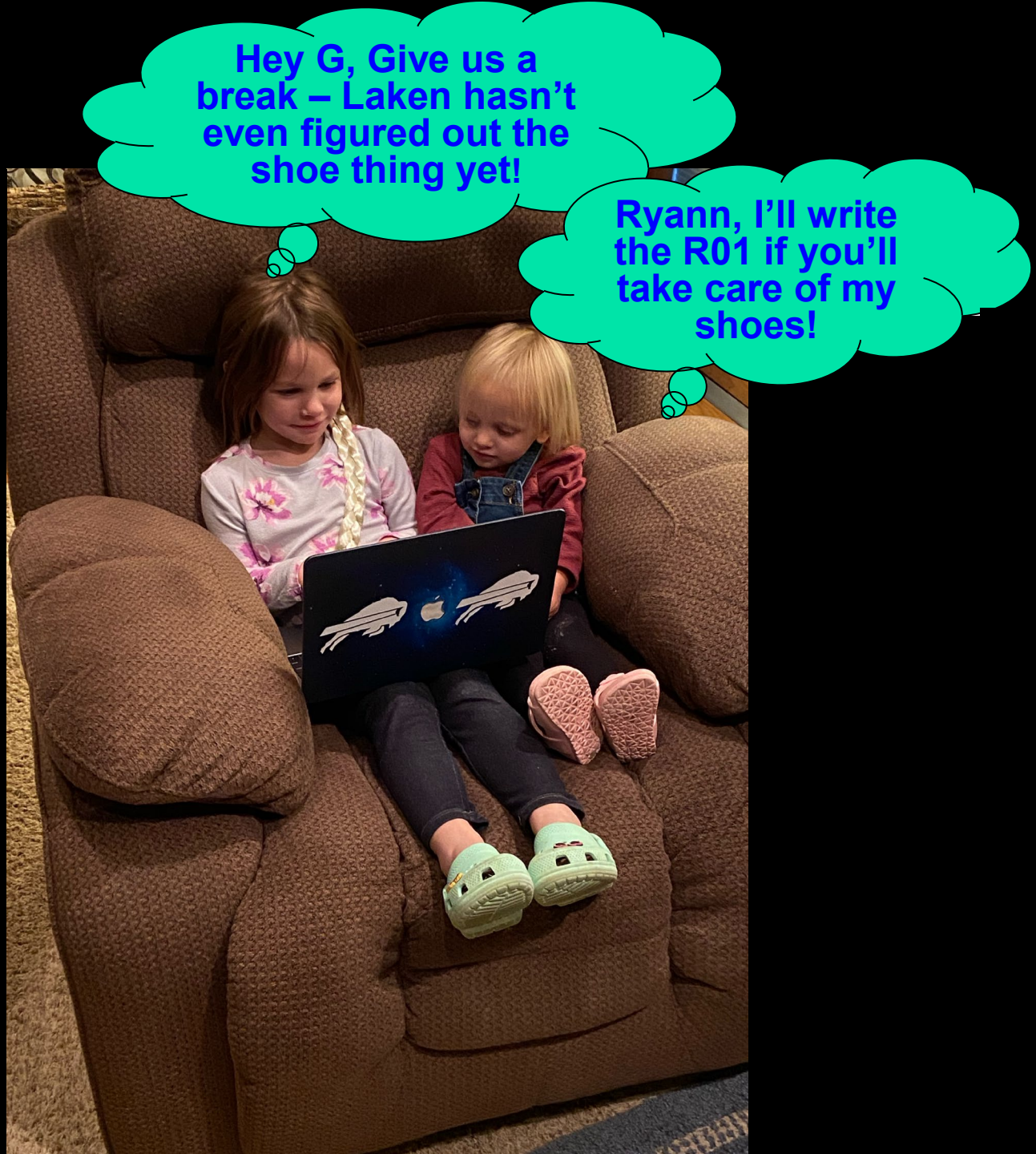
- You must address every concern.
- Comply as fully as possible with the recommendations of all reviewers.
- Correct any other errors (e.g., grammatical or typographical) you find.
- Mark changes in the text (e.g., line in the margin).

Responding to Reviews

- Disagreeing with a reviewer
  - When possible, **DON'T**!
  - Doing so is, of course, at your own **PERIL**!
- If you decide to do so:
  - Realize this is the risky alternative.
  - Obtain other input (co-investigators, peers, mentors, senior investigators, colleagues with experience on study section).
  - Find all available data, publications, or conference presentations to support your position.
  - Provide additional preliminary data to support your position.
  - Be diplomatic (i.e., put a positive spin on it when possible).
  - Have many others read your response.

Recommendation




Hey G, Give us a break – Laken hasn't even figured out the shoe thing yet!
Ryann, I'll write the R01 if you'll take care of my shoes!

Questions