

MDF Grant Writing Training

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MYOTONIC
DYSTROPHY
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Care and a Cure

Overview

- Rigorous Science: improving the quality of what we produce & the challenge of valuing being right in the long run above being published quickly
- Competing for Funding: know the system & use absolutely every crutch that you have available

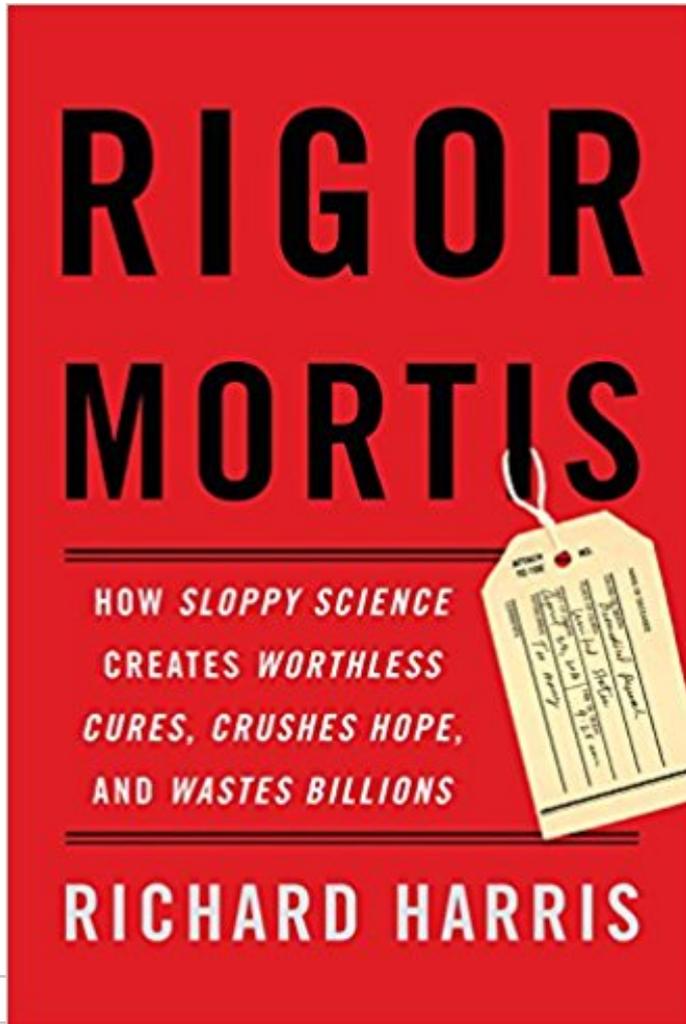
Evaluation of Scientific Rigor Now Required by Many Funders & Publishers

Unintentional Bias is a Serious Problem
& Much More Frequent than Scientific Fraud

Reproducibility is a Problem

- Bayer validated only 25% of published preclinical studies sampled (*Nat Rev Drug Discov* 10: 712, 2011)
- Amgen published similar data...
- NCE Phase II clinical trial success rates have fallen from 28% to 18% (*Nat Rev Drug Discov* 10, 328–29, 2011)
- After 30 candidates failed in trials, ALS TDI failed to replicate *any* of the prior mouse efficacy study results for 70 cmpds (“...effects are most likely measurements of noise...”)
- Cliché (but also true): Integrity & credibility are the currency of science...**if others can't believe your work, you're dead**

Rigor Mortis



- Author: Richard Harris (NPR Science Reporter)
- Written during 1 year sabbatical
- Distilled from extensive interviews & careful analysis
- Crux: flawed research is a key cause of failed clinical trials
- Eye opening in how non-scientific much of science has been

NINDS Rigor Criteria

- Rationale for models/endpoints/delivery
- Sample size/power
- Blinding/Randomization
- Missing data/reporting all results
- Independent replication
- Level of effect ($p < 0.01$, but so what?)
- Biodistribution/PD
- Dose-response
- Alternative interpretations
- Literature support (or denial)
- Effect size re potential clinical benefit
- COIs

NIH Rigor/Reproducibility Standards

- Now in application instructions & instructions to reviewers (see NIH Rigor & Reproducibility site)
- Scientific Premise of Proposed Research (skepticism until proven otherwise)
 - Strengths/weaknesses of foundational research
- Rigorous Experimental Design
 - Including methodology, analysis, interpretation, & transparent reporting
- Consideration of Gender & Other Relevant Biologic Variables
 - Biological variables factored into research designs, analyses, & reporting
- Authentication of Key Biologic or Chemical Resources
 - Key resources regularly authenticated to ensure their identity and validity

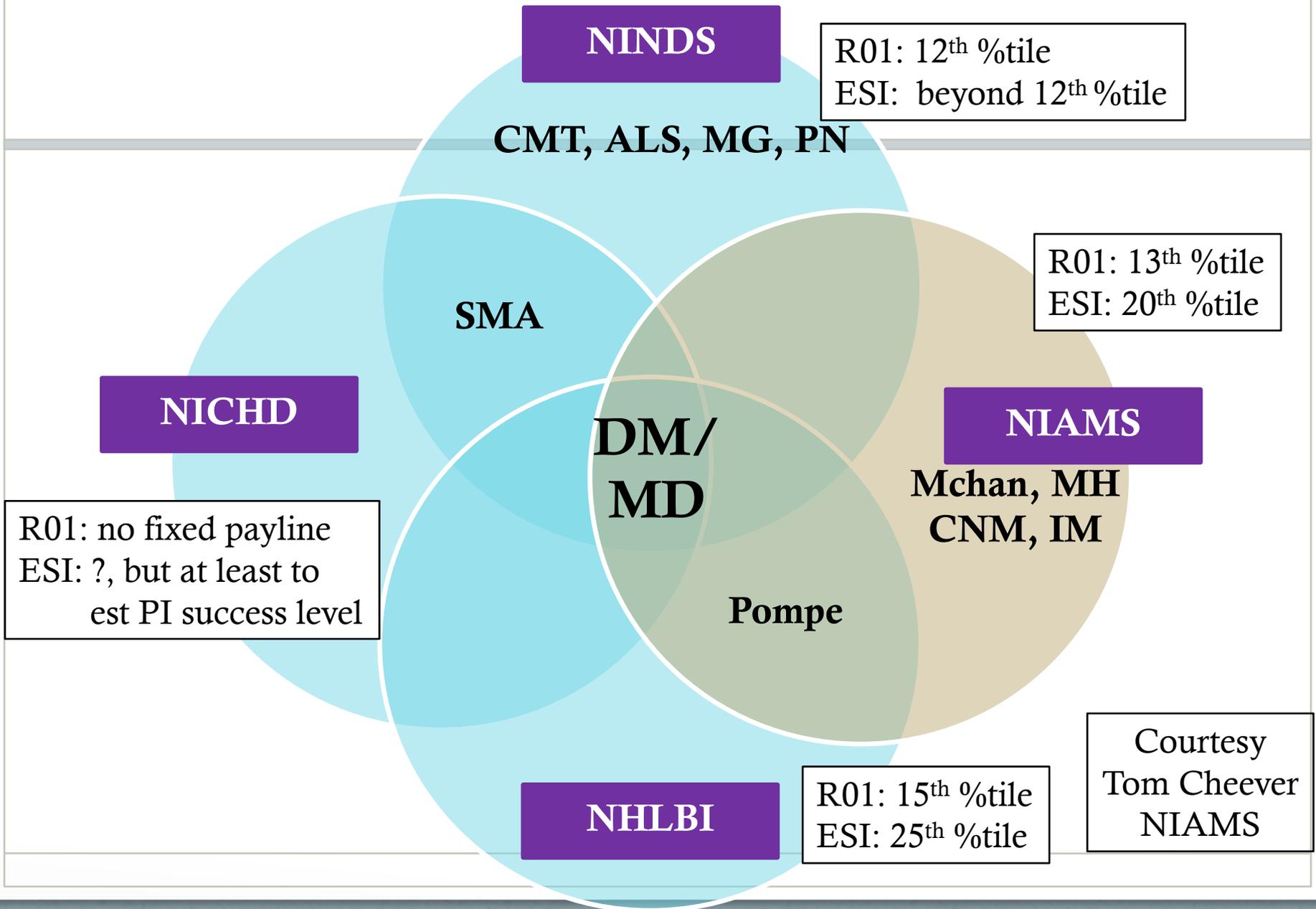
Competing for NIH Grants

(with some advice that works for
any funder)

NIH 101: Basics

- NIH: 27 Institutes and Centers (ICs)
- Grant review at each of 2 levels (Study Section & Council) is by peers, with decisions based on outcome of peer review
- IC “pay lines” vary, sometimes widely (see IC websites—Google “ IC name & funding strategies”)
- IC Program Directors are your interface point (filter & facilitate)

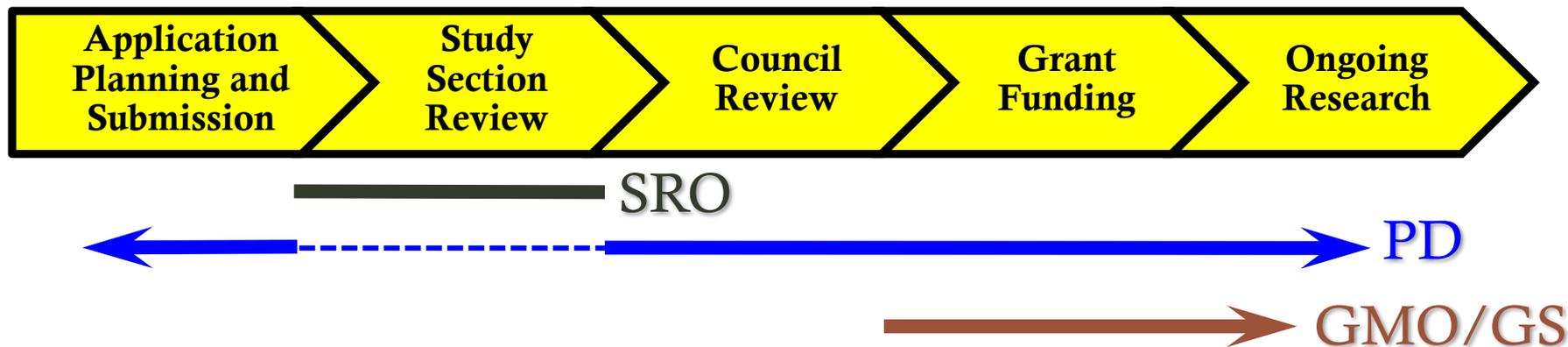
NIH Institute Homes for Neuromuscular Diseases



Study Sections

- Most NIH applications are investigator-initiated (80% of budget; don't get hung up on finding 'special initiatives')
- Understand the grant mechanism (R01, R21, U01...), FOA type (PA, PAR, PAS, RFA), & locus of review
- +/-: PAR = special review; PAS & RFA = special review & set-aside \$\$s; many RFAs are one shot only
- CSR vs IC-Specific
- SS descriptions & rosters are on CSR website
- Assignment Request Form: Can *suggest* institute, study section, expertise needed and/or names of potential conflicts

Who to Talk with at NIH?



Scientific Review Officer (SRO)

- Manages, coordinates & conducts initial peer review
- Ensures fairness & administrative compliance of applications
- Prepares summary statements

Grants Management Officer/ Specialist (GMO/GS)

- Sets up & issues awards
- Interprets & ensures compliance with grant policies
- Reviews grant business activities

Program Director (PD)

- Advises on funding opportunities & requirements for applications
- Observes review meetings & interprets summary statements
- Approves funding & monitors scientific progress
- Anticipates future scientific directions, assesses research opportunities

Writing Applications for Reviewers 1

- Criticality of Niche: NIH RePORTER for what's funded (and insights into what's 'fundable')
- Pay strict attention to the SF424 and FOA instructions & deadlines
- Exude confidence—if you don't believe in yourself...
- Avoid jargon; achieve clarity with brevity; judiciously use figures for clarity; don't assume that the reviewer will "get it" (reviewer often not expert in your field)
- Focus, focus, focus: "over-ambitious," "descriptive," "incremental," & "fishing expedition" are easy "kills" for a SS member

Writing Applications for Reviewers 2

- Synergy among aims, strong rationale, & significance are all critical
- Preliminary data always essential (don't buy the 'not needed for R21' line; R01s need preliminary for every aim); NINDS--ESI/NI R21 recommendations & IC withdrawals from parent R21
- Cover your bases on expertise—document yours & collaborators
- Always have others read and red-mark your application—you're too close to it (your true friends leave the most red ink)
- Never argue with review on re-submissions—you always thank them for their helpful insights (even when they're wrong)
- Talk with your Program Director early and often

Make the Reviewers Lives Easy

OVERALL IMPACT

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five scored review criteria, and additional review criteria. An application does not need to be strong in all categories to be judged likely to have major scientific impact.

Overall Impact Write a paragraph summarizing the factors that informed your Overall Impact score.

SCORED REVIEW CRITERIA

Reviewers will consider each of the five review criteria below in the determination of scientific and technical merit, and give a separate score for each.

1. Significance

Strengths

•

Weaknesses

•

2. Investigator(s)

Strengths

•

Weaknesses

•

3. Innovation

Strengths

•

Weaknesses

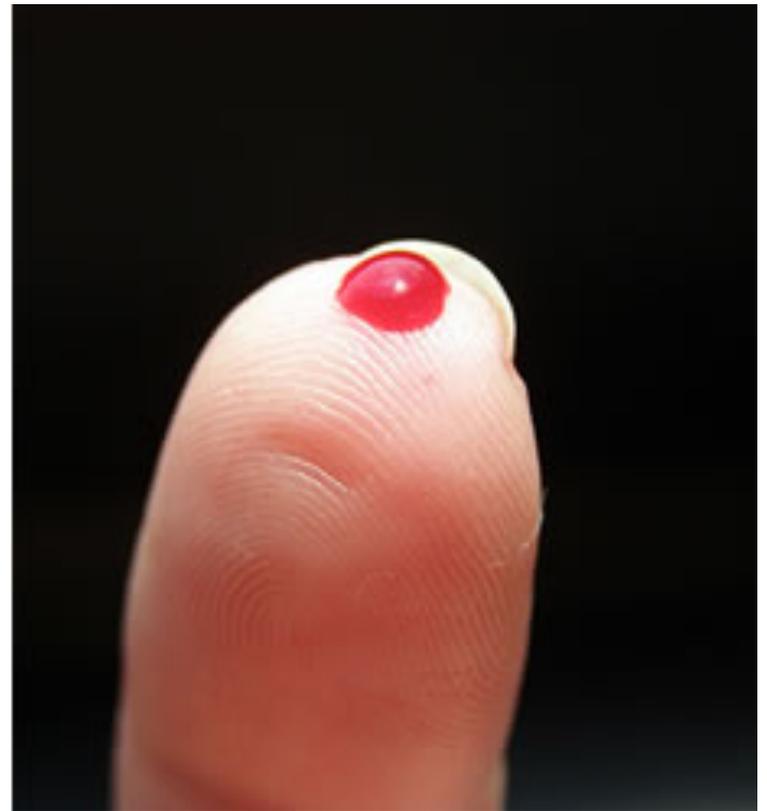
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4. Approach

- Most of the “ball game” is your Specific Aims page (SA page is not about methods, but why this is important to fund
- “Help” them fill out the rating sheet
- Give them the bullet points for each review criterion to cut & paste from your application

Study Section: Fatal Hemorrhage Starts with a Pin Prick

- Cover all bases in feasibility, preliminary data, & expertise so reviewers can't find openings
- Ask for help from mentors, colleagues, & Program Director
- Bleeding can start slowly (e.g., over a detail in a data figure). Even your strongest proponents on Study Section sometimes can't stop fatal hemorrhage once started



I'm Not Funded, Now What?

- Understand the System: you didn't talk with your Program Director? Now it's even more important
- You may think you "know" who your reviewers were; it's very likely you don't "know" who gave you the good or bad scores
- Mentoring—have a mentor(s) & use them
- Exactly what did the reviewers *say*? Attention & responsiveness to critiques matter, not arguing
- Did you have preliminary data for each aim?
- Revised vs. new application? Study Section assignment?
- Shotgunning (many, different applications) vs. focusing

I'm Funded, Now What?

- What the hell was I thinking when I wrote this?
- Deliver on what you proposed (publications), but also necessity of gathering hypotheses/preliminary data for the renewal
- Annual progress reports (“type 5’s”)—value in gauging progress toward the renewal
- Speed of the cycle—5 years of funding doesn’t mean 5 years before renewal (time to hire, time to complete work, publication lag, application deadlines...it goes by fast!)
- Develop lab management skills (personnel, resources, ideas)
- Use a career mentor(s)

Traits of The Fundable Grant

It's About the Reviewers, Not You!

- They understand every aspect of the proposal (*clarity*)
- They recognize that the work has impact (*significance*)
- They recognize that the work has novelty (*niche*)
- They recognize that you can direct the work (*feasibility*)
- They recognize that you have the necessary resources (*environment*)
- They feel good about and gain new insights from your clear explanations (*educational*)
- **Most importantly:** they don't have to work hard to draw these conclusions from *what you write for them!*

NIH Grants are a
Persistence Game:
Submit, Learn, Revise,
Resubmit

(the only truly failed application is one
that you learn nothing from)