

# Enhancing NIH Grant Success

Allen Harmsen

Retired Professor of Immunopathology

# Goal of Presentation

- Give you my opinion of what it takes to get an NIH grant proposal funded.
- My opinion is not the only right opinion, talk with other experienced researchers to get other opinions. We have many of these experienced people at MSU, any one of who could be up here instead of me.
- You can access many “how to write a successful NIH grant application” presentations online. I encourage you to do that. These are good for telling you what should be in the different sections of the proposal.
- I will try to give you some information you may not get online. My presentation today will be from the perspective of what you need to accomplish in your proposal to convince the reviewer to give you a fundable impact score.
- Examples.

# Why we are here today, “NIH paylines”

Institute	Non-new invest.	New invest.	ESI	R21
NIAID R01	10%	14%	-	24 imp.
NHLBI* R01	15%	-	25%	RFA on
NCI R01	11%	11%	15%	No R21

\*NHLBI only funds for 4 yrs, except ESI which is 5 yrs

**Do homework on Institute!!!!!!**

# For your application to be successful, you MUST!!!

- 1. Convince the reviewer that the hole in knowledge you will fill will result in a significant increment in improved knowledge/understanding. “SA” and “Significance”.
- 2. Convince the reviewer you have made a significant finding that supports your hypothesis that if proven by achievement of aims, fills the hole in knowledge you identified. “SA” and “Approach”.
- 3. Convince the reviewer you have the needed expertise and are a good investment. “SA”, “Approach” and “Biosketch”.
- 4. Convince the reviewer your approach will accomplish each of your SAs, resulting in a significant increment in new knowledge. “SA” and “Approach”.

1. Convince the reviewer that the hole in knowledge you will fill will result in a significant increment in improved knowledge/understanding.
- Significance is the extent to which the successful completion of the aims change the concepts, methods, technologies or treatments that drive the field.
  - Reviewer begins the assessment of significance in the SA page by the description of the hole in knowledge to be filled and the presumed achievements of the specific aims.
  - Significance section of proposal should be ultimate place where you convince reviewer the significance of project is high. This section needs not be very long as you are just reinforcing what the reviewer should have already decided from SA page. Discuss how achievement of aims adds to significance.

2. Convince the reviewer you have made a significant finding that supports your hypothesis that if proven by achievement of aims, fills the hole in knowledge you identified.

- The significant finding that supports the hypothesis is sometimes referred to as the “hook”.
- The hook should be an exciting finding that you have made that represents a breakthrough that will be built on and that informs the pathway you will take to fill the hole in knowledge.
- A good hook justifies the proposal and gives reviewer confidence in you as an investigator.
- If you have a good hook, you should write a proposal.

### 3. Convince the reviewer you have the needed expertise and are a good investment.

- Your expertise will be judged by the reviewer from your publications and by your approach to accomplish your aims.
- Research does not always go as planned, reviewer needs confidence you have the ability to adapt and make good scientific decisions if your approach needs to be redesigned.
- Whether you are a good investment and can make adaptations, is determined by the reviewer's assessment of your:
  1. publication productivity (trajectory and impact)
  2. scientificity (analytical, rational, critical) should be thread throughout

# Scientificity of PI

Rational and creative approach.

Justifies hypothesis, aims, approach.

Anticipates problems and presents alternatives.

Is critical, discusses what results will mean, and not mean (limitations).

Prolific use of words/phrases such as therefore, thus, because of, if we find, however, this means, this would mean, and alternatively.



4. Convince the reviewer your plan in “Approach” will accomplish each of your SAs, resulting in significant increment in new knowledge.

- Approach is section that is most criticized and probably the most influential in determining impact.
- NIH has tried to get review panels to emphasize approach less but have not been successful. This is where science is criticized.
- Experiments must accomplish aim.
- Must be rational (rationale section). Must utilize most current technology. Must be critical (what experiment results will mean and not mean). Must have alternatives (alternative approaches).

## 4. Convince the reviewer your plan in “Approach” will accomplish each of your SAs. (cont.)

- In my opinion there are two categories within approach the reviewer looks at, technical accuracy and scientific impression.
- Technical accuracy means use of scientific methods creatively, accurately and precisely. Must be familiar with and critical of methods, show that you know their attributes and limitations.
- Scientific impression is how approach flows, smooth transitions, creativity, correct interpretation, and focus. An outstanding approach many times is described as creative, exquisite, innovative, and ingenious; similar to how good art is described.
- If your approach does not accomplish your aim, must change aim or find an approach that does.

# Specific Aims Page

- In my opinion many reviewers form their initial opinion of a proposal after reading the SA page. If reviewer likes the project after reading SA page, they will likely look for positive aspects in rest of application to support this impression. If don't like SA page, will look for things to criticize to support that impression.
- Notice that my list of things you must accomplish in the application all begin in the SA page.
- Should be the first section you write as it should be a blueprint of entire proposal.
- Spend as much or more time on SA page than other sections combined. Write the SA, have it reviewed, rewrite, have it reviewed, rewrite, then use it to guide the writing of the rest of the application.

- Influenza causes substantial economic loss as well as much morbidity and mortality annually. Yet influenza vaccines are only partially effective as they tend to induce resistance mainly to highly variant viral epitopes and thus must be changed as variants emerge. A pan influenza vaccine that protects against all influenza variants by inducing responses to conserved antigens would eliminate the need for yearly immunizations and improve effectiveness. In this regard, we have recently found that placing influenza antigens on the surface of non-infectious viral like particles induces host immune responses to viral epitopes conserved between influenza variants. Thus, we hypothesize that an effective pan influenza vaccine could be made by attaching influenza antigens on the surface of viral like particles.

To test this hypothesis, we will achieve the following specific aims:

# Specific Aims

- Each aim must address hypothesis or goal.
- Aims must be definitive. Start with phrases like to determine, define, understand. Do **NOT** start with phrases like to investigate, describe, study.
- Aims should state what will be accomplished, not what will be done.
- Aims must be shown to be accomplishable in Approach.
- Aims should not be interdependent.
- Each aim should be strong, fewer strong aims better than more weaker aims. Depth not breadth.

- SA 1. To determine which influenza antigens should be attached to surface of viral like particles to induce the most effective protection.
- SA 2. To determine which viral like particle makes the best vehicle for a pan influenza vaccine.
- SA 3. To determine the route of vaccination by influenza decorated viral like particles that generates the best protection.

**Reviewer's confidence that each specific aim's accomplishment represents a significant increment in increased knowledge.**

**PLUS**

**Reviewer's confidence that specific aims will be achieved.**

**PLUS**

**Reviewer's confidence in investigator.**

**EQUALS**

**Impact Factor**

# **Reviewer's confidence that each specific aim's accomplishment represents a significant increment in increased knowledge.**

- Aim will generate results that support a significant hypothesis or goal.
- Aim that is designed to produce a significant increment in knowledge even if results do not support hypothesis or goal.
- Aims that if accomplished will move field forward in a significant increment.



# **Reviewer's confidence that specific aims will be achieved.**

Function of:

- Preliminary data that supports aim
- Approach that will accomplish aim/do-ability.
- Expertise of investigator

# Reviewer's confidence in investigator.

Function of:

PI's publication record

Quality of preliminary data

Co-Investigator's expertise

**Scientificity of PI**

# Most Frequent Problems Reviewers Cite (CSR)

over ambitious

- \*lack of knowledge of relevant published work
- \*lack of sufficient experimental detail, your reference
- \*diffuse superficial approach
- \*questionable reasoning in approach
- \*uncritical approach, pitfalls
- \*lack of new ideas
- \*absence of rational approach
- \*not experienced with methodology
- \*uncertainty about future directions

# Terms you do not want to see in summary statement

\*descriptive

\*confusing

verbose

dense

modest productivity

\*small increment in knowledge

not justified

\*little beyond already done

\*not supported with preliminary data

no increase in knowledge if it doesn't work

\* lacks expertise

\*not hypothesis driven

\*weak aim

\*not well developed

# After Submission

- After submission presume you will not be funded.
- Continue to develop proposal with new preliminary data, especially data that informs hypothesis and aims with more depth.
- If you need to resubmit, reviewers will want you to not only respond to summary statement but also to have further developed the project.

# Thinking Resubmission

- Read summary statement, then put it in the drawer and go for a hike. Wait one week.
- Get other opinion(s) of summary statement.
- Decide whether to resubmit and if so when, was proposal discussed and how well scored, best use of time  
can you make resubmission more developed.

Will resubmission be stronger beyond making changes suggested by reviewers in first review?

# Final Advice

- Be persistent, keep publishing and keep submitting.
- Know when to pull the trigger, get other opinions. Hook and other preliminary data determines when you should submit.
- Don't be afraid to ask for help. Find a mentor.
- Get nuts and bolts review as well as scientific review. You need both.
- Get reviews in plenty of time to make revisions.
- Early Career Reviewer (ECR) Program.

# Final advice (cont.)

- Its all about the science. I have never seen a proposal funded that had weak science, even if well written. I have seen proposals poorly written with outstanding science funded. However, the vast majority of funded proposals are both well written and are outstanding science.
- Spend time starrng out the window, thinking, challenge yourself to solve a hard problem and focus and be persistent. Thinking is a lot of work, takes a lot of time. Creativity does not just fall in your lap.
- Extend yourself, don't settle for doing something easy. Make your project achieve a big increment in knowledge. That will challenge you and force you to be a better scientist.



# It Takes a Village

- Develop programs where grant proposals are reviewed pre-submission.
- Paper showed a departmental proposal review program doubled proposal success rate.
- Reviews by senior and junior faculty
- Takes much effort and time but is well worth it. One additional R01 funded by these efforts can generate one million dollars of IDCs.
- SA chalk talks.
- Work with Nicole's office, need investigators to step up.
- Highly recommend the NIH Early Career Reviewer (ERC) Program- [ERC Link Here](#)