

# Principles of Grant Proposal Success

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# Outline

- Factors to consider when selecting and scoping your Aims
- Tips on crafting the written proposal
- Planning the writing process itself
- Additional Questions

# Aim Selection

Staying in your niche, develop 2-4 independent aims that:

- Address significant gaps in knowledge
- Are unique and innovative
- Are feasible given your resources, knowledge base, and available time

Good Aims close gaps in knowledge and open new avenues for future investigation

Good proposals can't come from bad experiments, but worthwhile experiments are not enough for a compelling proposal.

A proposal is a narrative

# Aim Selection Common Pitfalls: Narrowly testing an over-refined hypothesis

"If hypothesis/model X is true, then A, B, and C must be the case...  
I propose to test A, B, and C."

What if you find that A is not the case?

- Contain the consequences of hypothesis falsification to one Aim*
- Give the hypothesis "layers" so there are multiple outcomes*
- Consider "to what extent" phrasing*

# How do these issues play out in a real grant?

R01 - Mechanisms underlying neuronal enhancer specification during postnatal CNS development

**Aim 1: To assess the role of sensory-driven activity in postnatal enhancer selection**

Aim 2: To characterize the molecular mediators of enhancer selection

Aim 3: To test the contribution of enhancer remodeling to postnatal neuronal maturation

# Aim Selection Common Pitfalls: Fishing Expeditions

Examples:

CRISPR/RNAi/Overexpression screens

Looking interacting proteins or post-translational modifications

Profiling for differentially regulated genes or chromatin marks

*--Make a compelling case that interesting hits are out there and that your approach will identify them*

*--Can you reframe as hypothesis-testing?*

*--Don't just end an Aim with a list of hits! What does the pattern of hits tell you?*

# How do these issues play out in a real grant?

R01 - Mechanisms underlying neuronal enhancer specification during postnatal CNS development

Aim 1: To assess the role of sensory-driven activity in postnatal enhancer selection

**Aim 2: To characterize the molecular mediators of enhancer selection**

Aim 3: To test the contribution of enhancer remodeling to postnatal neuronal maturation

# Aim Selection Common Pitfalls: “Crossroads” experiments early in an Aim

Crossroads experiments distinguish outcomes A and B, but the nature of the follow-up study of these two outcomes diverges dramatically.

Placed too early in an Aim, they preclude a straightforward narrative

These issues often when arise following up on a proposed Fishing Expedition

*--Place these types of experiments later in an Aim*

*--Have a good candidate already in hand when following up a Fishing Expedition*

# Value of early phenomenon-characterizing experiments

Further characterization of novel phenomena makes for a great way to begin  
Aims **so long as the studies address genuinely significant questions.**

For example:

Narrowing down the time frame/brain region/cell type involved

Is the process cell autonomous/where does it occur subcellularly?

Structure/function analysis – which domains are necessary/sufficient?

Is the process developmentally intrinsic or dependent on various types of external stimuli?

These studies are defined in scope, with putatively clear-cut answers

# The Specific Aims page - I

## **Introductory paragraph**

- What broad topic are you addressing?
- Capture the reviewer's attention
- What is the basic gap in knowledge?

## **Background paragraph**

- What brings you to this topic?
- Summarize key preliminary findings

## **Outstanding questions paragraph**

- “Taken together, these results show/represent....Despite this progress, several key questions remain to be addressed.”
- List specific questions to be addressed by your Aims
- “To address these and related issues, I propose the following Specific Aims:”

# The Specific Aims page - II

## List and briefly describe Aims

- 2-4 Aims
- General but informative titles set off by numbers or bullets
- 1-2 sentence description of your general approach to orient the reviewer

## Summary

- 2-3 sentence closing
- Re-excite the reviewer: what will the research provide to the scientific community? Take a wide-lens view, like in the intro paragraph

# The Significance section

- ~3/4 of a page
- Move from general to specific
- Provide additional needed background and context for the reviewer
- Be scholarly
- Shape the narrative to illustrate how the issues addressed by your research have been historical impediments in the field

# Writing the Aims themselves

Aims should be ~3/4 of the proposal

For each Aim:

- Rationale

- Preliminary data (if applicable)

- Experimental subheadings

- Future directions

# How to present an experiment

Rationale: What exactly are you testing and why?

“To this end...” What will you do?

Make sure it comes across as feasible:

Preliminary results?

How many samples, animals, etc.?

Intermediate steps where you can confirm it is working?

Rigor and reproducibility – how many samples, control for batch effects etc.?

Controls, Controls, Controls! Especially in the first Aim.

How do you interpret various possible outcomes? Why are the different outcomes significant?

Why might this approach not work technically, and what parameters will you optimize if there are problems? What if you have no answers here?

Potential Pitfalls & Alternative Approaches

# Tips for the writing process itself - I

- Give yourself time – ideally identify major holes and fill them with preliminary data
- Don't just focus on the experiments, but also on their order and the transitions linking them
- Expect to have to adjust the Aims once you start writing
- Save all your versions!!
- Be concise but clear – reviewers will not re-read if confused!

# Tips for the writing process itself - II

- Get examples of successful proposals from colleagues
- Check for changes in the instructions
- Create a checklist of all the needed components
- Ask for recommendation letters early and offer to write drafts yourself
- Get feedback from as many people as possible
  - Get feedback on ideas before writing and later on well-written drafts
  - Get feedback from both experts in the field and outsiders