Grant writing

Writing biomedical research grants: strategies for success

Keywords
Biomedical research, grant funding, grant proposals

Presenter: Gail M. Seigel, PhD, is a Research Professor at the State University of New York at Buffalo, where she is Director of the Ocular and Auditory Neuroscience Lab. Her research focuses on novel therapeutic approaches to retinoblastoma, where she has successfully secured a variety of research funds at the federal, state, private, and commercial levels. Dr. Seigel is a recipient of the Cybil Harrington Research Scholar Award from Research to Prevent Blindness, and a Fight for Sight Award of Merit. She is a Fellow of the Association for Research in Vision and Ophthalmology.

Introduction

Obtaining stable funding is one of the most important aspects of running your laboratory. In order to continue your work in the biomedical/cancer field, you need as many tools as possible to secure funding for salaries, cutting-edge equipment, core facility support, and consumables. However, the success rates for research grant applications can be discouraging. An application to the National Institutes of Health (NIH), according to their statistics, has about a 1 in 5 chance of being funded. Although funding rates vary by institute and research area, these sobering numbers are repeated throughout the world, as research funds are scarce these days. However, with the right preparation, strategies, and targeting, your application can stand out from the crowd and have increased chances for a favorable review that could lead to funding success. Here we present some guidelines for writing successful grant proposals that you can use in time for your next grant application deadline.

Getting started

Timing: You can do much to prepare ahead of time before you even begin to work on writing the research plan of your proposal. First, check the timing. Think about the time you need to write the proposal in terms of where you are in your project and other responsibilities (e.g., teaching, conferences) you have on the horizon. At the same time, check the deadlines of your intended sponsors. Some, like the NIH, have fixed deadlines throughout the year, while others have rolling deadlines. As you assess the timing, gather your preliminary results and see if you have enough to convince reviewers of the feasibility of your project. If the timing is not right, it is better to wait than to submit a subpar proposal.

Develop and target your idea:

Make sure your idea is both innovative and feasible, with hypotheses you can test with your facilities and resources.

As you develop your idea, make sure that it achieves the delicate balance between innovation and feasibility. Include hypotheses that you are able to test with your facilities and resources. The most fundable projects contain exciting ideas that are grounded in achievable results. You can improve your chances of success by targeting your idea to sponsors who are most likely to understand and appreciate it.

- Look for potential sponsors in the acknowledgments sections of peer-reviewed publications.
- Look for potential sponsors in the study section pages of the NIH.
- Note the full descriptions of the study sections in your field.
- Note the rosters of study section reviewers and scan for those who match your area of expertise.

Do not worry if there are collaborators on the roster. They will have to recuse themselves from review if and when the time comes.

Recruit collaborators: It is a good idea to find collaborators early on to fill gaps in your expertise or methodologies. Define the roles of these collaborators up front in terms of whether they are a co-principal investigator, co-investigator, or consultant. It is important to avoid misunderstandings about roles further along in the process. While you establish and strengthen the connections:

- Ask potential collaborators for biosketches, methods, and other supporting information.
- Ask potential collaborators for a letter of collaboration.
  - Ideally, you should write the letter of collaboration for the collaborator.
  - The collaborator will then edit and sign the letter and send it back to you.
- Ask your sponsored programs office for budget and subcontract assistance.

Prepare documentation: If you are planning a project that involves human subjects, animal models, or recombinant DNA, this is a good time to get requests in to the intramural approval committees at your institution. It can take a few months of back-and-forth editing for final approval, during which time you can list these approvals as “pending” on the application.

There are other documents or subsections of a grant that can be prepared ahead of time as boilerplates that can be reused with minor adjustments for multiple grant applications. These are “Personnel”, “Resources”, “Equipment”, and “Data-sharing plan”.

Personnel justification for yourself, key personnel, staff, and students is helpful to have handy with name (degrees), role on project, and relevant experience. Your biosketch can be a basic paragraph about your background and why you are qualified to lead this project. This can be modified to fit the project.

The **Resources** section is the opportunity to describe the following points, in glowing terms:

- Available laboratory space, including core facilities
- Available office space
- Available animal and clinical facilities
- Available computing resources

For the **Equipment** section, list your equipment and shared equipment on hand that will allow you to complete the project.

Describe the equipment in sufficient detail for reviewers to understand its capabilities. This is also the time to determine whether you need any new equipment for the project. If you do need any equipment (i.e., durable items greater than $5,000 US in value), you can get price quotes from companies to attach to the application. Some companies can also help you justify the equipment expenditure.

Examples of equipment justification

- You need new equipment with updated technology.
- You have old equipment that is obsolete and not repairable.
- You are using shared equipment that is in use or not easily accessible.

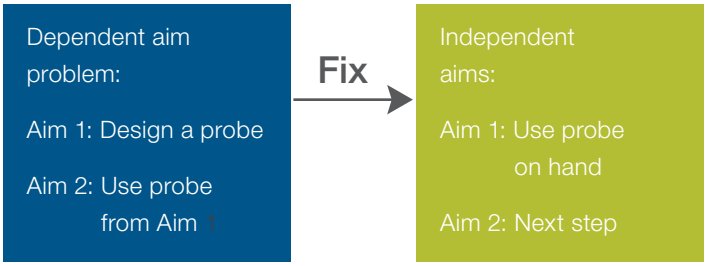
The **Data-sharing plan** can be written as another boilerplate. Some sponsors, including NIH, require an explanation of data sharing. For this section, you need to describe how you will disseminate data to your colleagues around the world. This can include the following:

- Genomic data repositories
- Presentations at national or international meetings
- Peer-reviewed publications
- Laboratory web page(s)
- Newsletters

In a similar vein, NIH also requires you to describe how you plan to authenticate key biological and chemical resources. For example, the authentication plan can include short tandem repeat (STR) testing to verify cell lines, or chromatography or mass spectrometry to validate chemicals.

Writing the research plan

Specific aims: Start with an introductory paragraph to describe the research area and capture the reviewer's attention. Begin with a simple first sentence, add information about what is known, and then present the gap in knowledge and how you will fill that gap. Specific aims are generally one page in length with 2–4 aims. You can include sub-aims (1a, 1b, etc.), but try not to get too complicated. Then, end with a summarizing paragraph that includes innovations, anticipated results, and broad impact. When you write specific aims, be sure that the aims are connected, but can be accomplished independently of one another. One of the most common errors in writing specific aims is making the success of aim 2 or 3 dependent on the aim before it. For example:



Presentation: As you get started on writing the research plan, assume that your reviewer is not an expert in your field. Follow the application's instructions on page limits and margins. Here are some useful tips to improve readability of your application:

- Make it easy for the non-expert to understand what you are doing and why.
- Use bold subheadings.
- Leave "breathing space" between sections.
- Underline important points.
- Use fonts and images that are large enough to easily read.

Aim 1: Quantitatively assess the expression of SWMP in neoplastic tissue.

Hypothesis: SWMP is overexpressed in neoplastic tissue.

Note large clear font and breathing space between aim and hypothesis

Along similar lines, images also need to be large enough to see experimental details, as shown in Figure 1.

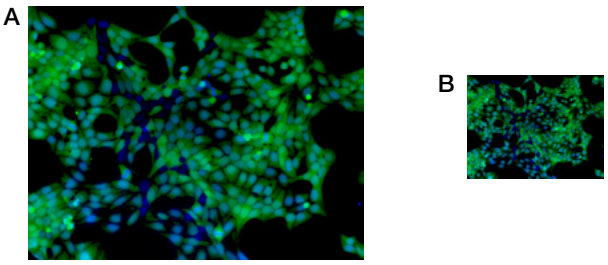


Figure 1. Examples of image quality. (A) Green- and blue-fluorescent cells are readily seen in an image of this size and quality. **(B)** Individual cells are difficult to see here because this image is too small. (Images from Seigel Laboratory, unpublished data).

As you write your research plan, avoid excessive jargon, keeping in mind that the reviewers might not be experts in your subfield. Simplify and define uncommon words when they first appear in the text. Sometimes it helps to read sections out loud to yourself. Define abbreviations the first time they appear. Better yet, some applications ask for a list of abbreviations that the reviewers can use as a reference as they read along. If you have a long list of probes, antibodies, or other research material, a table can help organize and clarify them. Also, state where you buy reagents the first time you mention them (e.g., anti-SWMP antibody from Bigname Biosciences, London UK). This lets the reviewer know that you will be able to obtain the materials needed to complete the project.

Most of the time, you should aim to stay within the page limit and try to save space. There are some approaches you can take that will help save space.

Space-saving tips

- Refer to publications in the text for routine methods.
- Minimize margins (within guidelines).
- Eliminate the word “the” whenever possible.
- Remove redundancy.
- Do not use URLs to circumvent the page limit.

Significance: Significance is a chance to sell your idea. Present the knowledge gaps in your field and how you intend to fill them.

> Little is known about SWMP expression in human tumors. The goal of this project is to develop a robust, quantitative, histology-based assay for SWMP in human tumor samples. The information acquired may lead to new diagnostic strategies and therapeutics for SWMP-associated malignancies.

Innovation: Think about aspects of your project that are especially compelling. It could be anything from a new gene, a new assay, or a particularly synergistic research team.

> - We have unique access to a *SWMP* tumor registry.
> - The *SWMP* marker itself is novel.
> - The PI is the world expert on *SWMP*.
> - Our methods are novel (but feasible).

Methods: Include enough details about the methods to show the reviewers that you can do these experiments. In this example, a reference to the method is used to save space, but some important details are included.

> Slides will be immunostained according to protocols optimized in our laboratory [18]. Briefly, tissues are rehydrated through xylenes and alcohols, rinsed in PBS, boiled in citrate buffer for 25 minutes, rinsed in PBS-Tween, and then incubated in 10 µg/mL mouse anti-SWMP antibody for one hour at room temperature. The samples are then rinsed, incubated in 1 µg/mL secondary fluorescent antibody for 45 minutes, rinsed, and coverslipped for microscopy and image analysis.

For each aim in your research plan, after the statement of the aim and hypothesis, state your rationale. This may refer to previous publications, preliminary results, or other information that can address the feasibility of your approach.

> **Rationale:** We have shown previously that SWMP is expressed in a variety of malignant tissues. We will build on these findings to develop a novel histological assay for SWMP expression.

Each aim also needs anticipated results. These results may or may not come to pass, but this is your opportunity to show that you have thought through the project enough to have an informed opinion about the outcome. You will also want to have a paragraph on pitfalls and alternative approaches you will take in the event that the anticipated results do not materialize.

> **Potential pitfalls and alternative approaches:** In some cases, the SWMP protein is truncated and not detectable by our monoclonal antibody. To address this, we will use additional antibodies that recognize the truncated portion of the protein.

Statistics: Spend enough time on the statistical analysis section to convince reviewers that you have enough statistical power in your hypotheses and are using the right tools to analyze your datasets. If you have doubts about this section, consider adding a dedicated biostatistician to your key personnel list, and pay them as a consultant or even as a co-investigator. This is particularly important for studies involving clinical trials or other large-scale human or animal studies.

There are other miscellaneous sections to address in the research plan and accompanying sections. A timeline, with aims and milestones, can be helpful to the reviewer as another indication that you have carefully thought through the project. Timelines are very fluid because anyone who conducts biomedical research knows that experiments do not follow a rigid schedule. A best estimate will make a good impression on the reviewers as a sign of organization. The research narrative is composed of 2–3 sentences in lay language to convey the gist of the project. Be sure not to include anything proprietary in the research narrative or the abstract, because these sections tend to be made available to the public.

Abstract: The abstract is really the culmination of the research plan in a nutshell. You assemble the key elements from the rest of the document and distill it into a brief paragraph or two.

1. Start with a sentence about the problem.
2. State the significance of your research.
3. Mention relevance to the mission of the sponsor.
4. Include your specific aims and hypotheses.
5. Describe your long-term objectives.
6. Keep to the word limit.

At this point, the grant proposal is ready to be submitted. It can take months to receive notification about a submitted grant. While you wait, try to get additional preliminary results.

Post-review

Ultimately, you will receive notice that your grant has been reviewed and the summary statement is available for viewing. Read the review more than once and take notes. Regard the feedback as constructive; do not take it personally. There are three possible outcomes to the grant review: 1) your research is funded, 2) your research is not funded, or 3) you are in limbo. If your research is funded, congratulations. If it was not funded or you are in limbo, there are steps you can take. If you have questions, contact the program officer (never the reviewers). Ask the program officer what the general opinion was about your proposal and whether a resubmission would be reasonable. If so, what are the most important factors to address? Take the time to think about the information you gather from the program officer and decide whether you are able to address the criticisms. If so, you can prepare a resubmission. If not, you can regroup and send the application to another sponsor.

If you decide to resubmit your proposal, copy and paste the reviewers' comments into a fresh document in bold font. Use this page as a template to address the reviewers' concerns, point by point. This will be your "introduction to revised application" page. You can respond to the comments and complete this page to use as a checklist for actually making the changes in your proposal. Address each point clearly, thoroughly, and respectfully.

Comment: It is not clear whether the PI has enough expertise in histological analysis.

You reply: Since the original submission of this proposal, our group has two additional publications involving histological analysis. We have also added more details about histological analysis in the text (page 15).

At first glance, this reviewer's comment could be somewhat insulting, especially if you have 30 years of experience in histology. The important thing is to answer matter-of-factly, and with sufficient evidence to show that the concern has been addressed. It is also important to thank the reviewers for their helpful comments.

Some of the issues that commonly need to be addressed in resubmissions include the criticism of being "descriptive" instead of "hypothesis-driven", lack of innovation, dependent aims, and even conflicting reviews. In general, reply to these comments with as many positive responses as possible, and try to address the critiques.

Comment: This study should include ovarian cancer tissue.
You reply: Since the *SWMP* gene is not expressed in ovarian cancer, we will include these samples as a negative control.

If you get a conflicting review in which two reviewers make opposing comments, try to mediate by clarifying the issue with something like “We have added more detail to our timeline to clarify the milestones.” On the other hand, pay special attention to any particular comments that are made by more than one reviewer. For example, if two reviewers are unsatisfied with the statistical plan, it is time to contact a biostatistician. In general, for the written response, you want to clearly indicate where you have made changes from the original application. The response needs to address each point with an upbeat attitude. Add new preliminary data if you have anything that supports feasibility. Also, since some time has passed, make sure to update internal approvals and the budget.

In summary:

1. Choose your timing for submission.
2. Develop an innovative yet feasible idea.
3. Target a suitable sponsor.
4. Bring people on board.
5. Get approvals, prepare boilerplates.
6. Present all material clearly and define all acronyms.
7. Specific aims should include a hypothesis, the rationale, pitfalls, and alternatives.
8. Use every opportunity to sell the idea and your ability to do the work.
9. Include controls and statistical analyses.
10. Make the proposal easy for reviewers to follow and understand.
11. Read and review the summary statement.
12. Clarify any questions with the program officer.
13. Determine if resubmission is feasible.