Letters to a Young Investigator

How to Write a Successful Grant Application and Research Paper

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The 2 most challenging tasks that every investigator faces are to secure grants and publish papers. In the current funding environment, preparing an outstanding grant proposal is critical, as even minute deficiencies can potentially lead to rejection. Furthermore, publications in reputable journals are crucial to disseminate research findings and promote career development. The purpose of this article is to review some of the key elements that characterize successful grant proposals and scientific papers and to offer advice (based on my own experience) that I hope will be helpful to applicants and authors.

**How to Write a Successful Grant**

Writing a grant application is a demanding process, especially in the current environment of historically low funding levels.1 The current funding rate of the National Heart, Lung, and Blood Institute is 10%, compared with ≈30% funding rate in 2001. When preparing a grant application, the 5 criteria that reviewers will use to score the grant (ie, Significance, Investigator, Innovation, Approach, and Environment) should be kept in mind throughout the process. It is also important to start early and allow yourself at least 4 to 6 months to prepare the proposal.1–3 Of course, the preparation time may vary depending on the applicant’s experience with the process, the extent of the proposal, and time needed to prepare preliminary results. It is generally recommended that the grant application be completed in its entirety at least 1 week in advance to allow for unforeseeable events and issues. Because most agencies have ≤3 submission dates per year, missing a submission date can delay potential funding by several months.

**Initial Steps**

There are several steps that need to be taken for the initial steps of grant preparation. The first and perhaps the most critical step is formulating a study question. The study question on which the overall hypothesis is based should be a testable hypothesis and of high significance. Many reviewers require that your answer to the study question will lead to a substantial improvement in our current medical practice or a significant change in our understanding of biological processes. The hypothesis and the study question should be formulated many months or possibly years before the grant submission date to allow time to perform the required preliminary experiments. The applicant will then have to find the right home for the grant application and identify the funding agencies that would be most suitable for such a proposal.

The applicant should spend as much time as needed to carefully review the grant instructions. This is particularly applicable to new investigators who have little experience with the grant submission process. For the majority of National Institutes of Health (NIH) grant applications, the instructions are >100 pages, but it is important not to skip any sections. The basic formatting instructions, including page limits, font size, and page margins, should be reviewed carefully.

The instructions will also provide details on what should be included in the application. It is important to know these in detail, because including extra and irrelevant information merely to make the application longer and to impress the reviewers normally backfires and may make the grant seem unfocused. Perhaps the single most important piece of information in the instructions is the due date. This due date should be clearly marked on your calendar, and your timeline for the completion of the grant application should be appropriately delineated. However, it is sometimes better to miss a deadline if it is deemed that more time is needed to perfect the proposal.

While reviewing the instructions, it is also important to identify the items that need to be included in the application and who will be responsible for obtaining those items. If collaborators or consultants are needed, they should be identified and contacted early in the process. I recommend that the applicant makes a checklist at this point and checks the items as they become available. A sample checklist for an R01 application is included in the Table.

The applicants are also encouraged to get to know the staff in the Office of Sponsored Research at their institution. The Office of Sponsored Research staff has extensive experience and can help the applicants throughout the grant process. They are generally available to answer any questions related to the grant process and to assist with the administrative aspects of the submission process. Thus, they should be contacted early in the process to determine which sections of the grant application they plan to complete. It should also be kept in mind that the Office of Sponsored Research usually requires the application to be completed several days before the deadline, and their required deadline should be determined early in the process. The applicants may also consider establishing communication with the staff at the funding agency. The application instructions usually have the name and information of person(s) to contact.

**Writing the Grant**

Although it is crucial to submit a complete application and include all of the required nonscientific sections, the most important component of a grant application that will likely determine the success of the grant is the proposal itself. The
proposal needs to be clear, flow well, and not contain any structural or grammatical errors. In other words, the grant should tell a story that is easy to follow, even to someone not familiar with the topic. The applicant should avoid copying sections from previously written grants, because the sections may not be harmonious and may not flow with the rest of the grant. Such applications do not generally go well with reviewers.

The proposal starts with a specific aims page, in which a brief background and rationale for the proposed studies is provided, followed by the hypothesis and aims of the proposal. The specific aims page is probably the most important section of the grant application, because all members of the study section will likely read this page, whereas the assigned reviewers will read the entire application. I suggest: (1) to make the hypothesis statement bold so that its emphasis is highlighted; (2) to have 2 to 3 specific aims depending on the length of the grant activation; (3) to avoid statements such as “To study…” or “To test…” in the aims, because they may indicate lack of focus or a well-defined hypothesis; instead, use statements such as “To determine…” or “To elucidate…”, followed by the hypothesis statement; (4) to ensure that the aims are not dependent on each other; in other words, if Aim 1 does not work, will that nullify the goals of Aim 2 and Aim 3? If yes, then the application is not likely to succeed.

The first section of the grant is Significance. The applicant should have an in-depth knowledge of the field to be able to write a comprehensive but succinct review of the literature. This section should also describe the gaps in the field, which will be a preview of the goals of the proposal. The significance of the proposal should be highlighted, because the reviewers will look for this as part of the 5 criteria they will use to grade a grant application. Finally, innovation should also be described under a different subheading. It is crucial to focus on 2 innovative aspects of the application: scientific novelty and methodological innovation. In other words, if new and novel techniques are used in the application, they should also be highlighted in this section. Additionally, potential clinical implications of the proposal should also be discussed in the Innovation section.

The next section is Approach, which includes the Preliminary Results and Experimental Designs subheadings. In the first section, the applicant has the opportunity to prove to the reviewers that he/she has the skills and the background to conduct the proposed studies, as well as to demonstrate that the proposed studies are feasible. The applicant should not be too modest in this section, but should also strike a balance and not be perceived as too arrogant. Figures and tables that summarize the results should be included, but if any of the results have been published, it is acceptable to reference them. For young investigators applying for mentored grants, it is important that the work performed by the applicant is highlighted by statements such as “The applicant has performed…” Such statements will demonstrate the personal contributions of the applicant to the field. The Experimental Designs section generally constitutes more than half of the grant and should describe the research designs and methods that will be used and the applicant’s proficiency to complete the studies. Each Aim should be included, followed by rationale and experimental design. Details of the experimental approach should be included, but limited application space does not allow for too much detail to be provided. If there are any techniques that the applicant is not familiar with, a collaborator who is familiar with the method should be recruited to serve on the application. Each Aim should end with 3 sections: Summary, Expected Results and Interpretation, and Potential Problems and Alternative Strategies.

General Comments

NIH applications are scored based on 5 criteria:

**Significance:** Does this project address an important problem in the field? How will this project impact the field and how will it improve scientific knowledge?

**Investigator(s):** Are the investigators qualified and experienced to conduct this project? If the project is collaborative, do the investigators have complementary expertise that are appropriate for the project?

**Innovation:** Is the project concept novel and original? Are the experimental techniques innovative?

**Approach:** Are the strategy and study design appropriate for the completion of the study? Are potential limitations and alternative strategies discussed?

**Environment:** Is the institution supportive and are the resources adequate for the project?

As you are writing your grant, always keep the reviewers in mind and think like a reviewer. Reviewers in general are busy and may spend limited time on an application. Furthermore, many of the reviewers may have expertise not related to the subject of your application. Thus, it is important to make the grant easy for them to read and understand. Some reviewers may get the first impression after reading the Abstract, further emphasizing the importance of this section. Make sure the application is structured well and does not contain spelling and grammatical errors, because these errors can sometimes be fatal. Including figures and flowcharts that summarize the aims of the grant application can also be helpful to the reviewers and make their decisions easier. Finally, proofread the grant several times and make sure to ask colleagues with expertise in grant writing to review it for you. It is important to ask those who will have the time and dedication to read the grant.
If you receive feedback along the lines of “it was good,” then it is likely that the person had not read it carefully. In general, the more red marks a grant receives before it is submitted, the more likely it will succeed.

**How to Write a Successful Paper**

Writing a research article and its successful publication in a reputable journal generally requires significant effort and time. This process, however, can become more efficient and productive if simple guidelines are followed and common errors are avoided. The major key to a successful paper is to plan in advance and be clear, precise, and simple in your writing.

**Initial Steps**

Writing a successful paper starts months, and perhaps years, before the paper is ready to be submitted to the journal. I usually ask my mentees to start putting their figures together as they become available and plan what additional experiments should be performed to address the scientific question they are answering. As data become available, analyze them in a timely fashion, organize them so they follow a logical sequence, and plan your next experiments based on those results. It is important to note that the figures in a paper may not necessarily represent the order in which the experiments were performed; it may be better to reorganize them to provide a more logical flow. You may have to consolidate several figures into 1 figure, because many journals have a limit on the number of figures (generally, 6–8 figures in a paper is a reasonable number). The next step is to make a first draft of the paper. It is important that your writing is clear and that your paper can be understood by those who are not in your field.

**Writing the Paper**

A scientific paper generally has the following sections: Title, Abstract, Introduction, Methods, Results, Discussion, Figures and Tables, and References. For the title, compose a statement that is short, attractive, and relays the message of the paper. The Abstract should be succinct and contain enough information to summarize the findings of the paper without the benefit of the text. The Abstract generally contains 4 sections: succinct background and the central hypothesis of the study; what was done (Methods); what was found (Results); and what the results mean (Conclusions).

The Introduction contains a summary of the current state of knowledge before the start of the studies (background) and the purpose and hypothesis of the study. Start the section with a general overview of the topic, followed by 2 to 3 paragraphs that discuss previous work. A brief summary of the findings is also sometimes provided, and only relevant information should be included. The Methods section should be detailed enough so that if someone tries to repeat the experiments they can rely on the information that is provided in the paper. Because several journals now allow supplementary information to be included online, many of the experimental details can be added to the supplemental section. In certain cases, a method can be referenced if it has already been described in detail in other papers. Statements on animal and human subject approval and statistical methods should also be included. The Results section should summarize the findings of the study without comment or bias. The figures and tables are referenced throughout the Results section. The Methods and Results section should be narrated in past tense.

The Discussion section should focus on the analysis of the results and how it relates to other studies. This section generally contains a discussion on whether the results support the original hypothesis, an integration of the data in the paper with data that have been published, and a discussion on the unexpected results. If the results do not agree with previous reports, this discrepancy should also be discussed. It is important to avoid redundancy between the Results and the Discussion sections. At the end of Discussion section, a summary of the principal findings of the paper is usually included; this is your last chance to tell the readers what you want them to learn from your study. Before References, an Acknowledgments section is usually included, in which the funding agencies and colleagues or collaborators who contributed to the study are acknowledged. The references are formatted according to the journal specifications.

The next step involves finding a home for the paper, where the target readers will be reached. Some laboratories focus on the impact factors of journals to decide where the paper should be sent. Although this is a topic that requires extensive discussion (which will not be covered here), it is important to choose a journal that can reach your article to its target audience. After a journal is chosen, find their formatting requirements and format your paper accordingly. Proofread the paper several times and ask colleagues to read the paper for suggestions before submission. It is important for all authors of the paper to read the article and approve the final version.

**General Comments**

Two to 3 reviewers usually review the article, and they generally provide suggestions to improve the content of the paper. If the reviewer misunderstood a point, do not automatically blame the reviewer; it is possible that you did not describe it well in the paper. Do not get discouraged by the decision; read the comments carefully and try to determine how you can address the comments. It is important not to just turn around and submit to another journal if you know that the article suffers from major deficiencies. Sometimes, even rejected papers may be resubmitted to the same journal if all of the concerns of the reviewers are addressed. In your response, be courteous and provide a point-by-point response to each comment. Resubmit the paper when you are confident that you have addressed all of the concerns. It is generally accepted that hand-waving your response will not go well with the reviewers and editors. If the paper gets accepted, you will receive galley proofs, which is your last chance to make minor corrections.

**Concluding Remarks**

Our professional success is partly measured by our publication and funding records. If these processes are approached in an organized way and with a clear plan in advance of submission, the likelihood of success is higher. Although the process of grant and paper review is not perfect, and sometimes unqualified applications or papers are accepted, if your scientific approach is well founded and thorough, you will have a higher chance of success. In general, most grants are awarded based on a careful review process with criteria that everyone has
access to. I encourage young investigators to remain focused and not get discouraged by repeated rejections; this is part of academic life and everybody fails before they succeed.

Acknowledgment
I would like to thank Konrad Sawicki for careful evaluation of this article.

Sources of Funding
H. Ardehali is supported by the National Institutes of Health (grants K02 HL107448, R01 HL104181, and 1P01 HL108795).

Disclosures
None.

References

Key Words: grants ■ manuscripts ■ National Institutes of Health
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Circ Res. 2014;114:1231-1234
doi: 10.1161/CIRCRESAHA.114.303695

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