How to Write a Successful National Institutes of Health (NIH) Grant Proposal

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ABSTRACT

KEYWORDS: NIH, grant proposal, funding

Most academic research laboratories in the U.S competitively apply for grants from the National Institutes of Health to acquire funding for their research site. Therefore, it is important that individuals working in the research field have a basic knowledge of grant writing and understand how to write one effectively. The aim of this paper is to help future PhD students investigate the components, and the writing style and techniques of grant proposals, specifically to the NIH, that helps maximize funding opportunities for scientific research projects. This was accomplished by conducting face-to-face interviews with grant-writing experts in the field of Biochemistry, whose perspectives are also well-supported by various secondary sources from the NIH and other experienced grant writers. The result of this study shows that there are five main criteria that must be incorporated and strictly organized into eight principle components of a NIH grant proposal. In addition to the content of a grant application, text and paper formatting must rigorously follow various requirements set by the NIH. The findings of this article also give an in-depth description of grantsmanship in terms of scientific arguments and writing styles.

INTRODUCTION

Besides intellectual manpower, funding is an essential, determinant factor for keeping academic research laboratories well-resourced, in turn contributing to numerous groundbreaking discoveries happening around the world every year. The funding is utilized to buy new, highly expensive machines that can cost hundreds of thousand dollars, and other basic equipment that is disposed and replaced on a daily basis. In addition, the laboratory funding is served as the source of salary payments for employees in the lab.

Academic scientific research laboratories in the United States are mostly sponsored by federal agencies, such as the National Institutes of Health (NIH) and the National Science Foundation (NSF). In the field of Biological Sciences, the research sites receive funding mainly through the NIH's grants. In order to acquire such a grant, in the submitted proposal, the principle investigators must substantiate the significance of their research projects, and the practicability and the relevant importance of the results. In 2014, the NIH experienced a decrease by approximately 2 billion in funding[1]. In addition, "inflation has resulted in a 25% reduction in NIH purchasing power over the last decade and ultimately a 20% reduction in annual funded projects." [1] Due to the declining available research funding from the NIH, the grant application process has become more challenging and highly competitive.

As a science-major student who plans to pursue a PhD degree, you might be confused by the concept of grant writing. You might feel distressed because you would potentially have to write grant proposals in order to obtain funding that supports your ongoing and prospective projects, either as a PhD candidate or a postdoctoral scholar. In this article, I plan to provide you with a clear summary of the skeleton and writing strategies for a scientific grant proposal. By the end of the article, I hope you can have a better understanding about the NIH grant writing as well as become more confident to write a successful one in the future.

METHODS

Two professors, Dr. Jawdat A and Dr. X (pseudonym), of the Department of Molecular and Cellular Biology at University of California, Davis were interviewed face-to-face. The two interviewees have years of experience in writing NIH grant proposals in the purpose of obtaining funding for their own research labs. In addition, Dr. A has recently joined the grant peer review panel of the NIH and thus has insights into the scoring system of NIH grants.

The two interviewees were asked to explain the basic components of a NIH grant proposal, to describe the writing style of grant writing in general and required by the NIH in particular, and to provide samples for each section of the grant proposal.

The interviewees' responses were recorded, transcribed and re-organized for a better flow in the results and discussion section. In addition, various secondary sources were analyzed and integrated with the findings of the primary research to compare and contrast the arguments.

All figures used in this article are original unless stated otherwise. In all writing samples adapted from Dr. A's proposal, important scientific contents were blurred out per his request. Relevant key words and phrases to description in text were highlighted.

RESULTS AND DISCUSSION

NIH PEER REVIEW PROCESS

Similar to any genres of writing, a grant proposal also has its specific audience. In order to compose an effective grant application, it is important to know who will be reading and evaluating it. According to the NIH Office of Extramural Research, in order to receive a NIH research fund, an application, or a grant proposal, must be approved by two levels of NIH peer review.[2]

1. The first level of review is "an assessment of scientific and technical merit and is conducted by a Scientific Review Group (SRG) composed primarily of non-federal scientists who have expertise in relevant scientific disciplines and current research areas."[2]
2. The second level of review is performed by IC National Advisory Councils or Boards. Members of the councils consist of both scientific members and public representatives. They contribute to decisions of awarding research funds by making "recommendations on priority areas of research, pending policy, and funding of particular applications."[2]
3. The IC Director then makes final determinations of research fund awards.

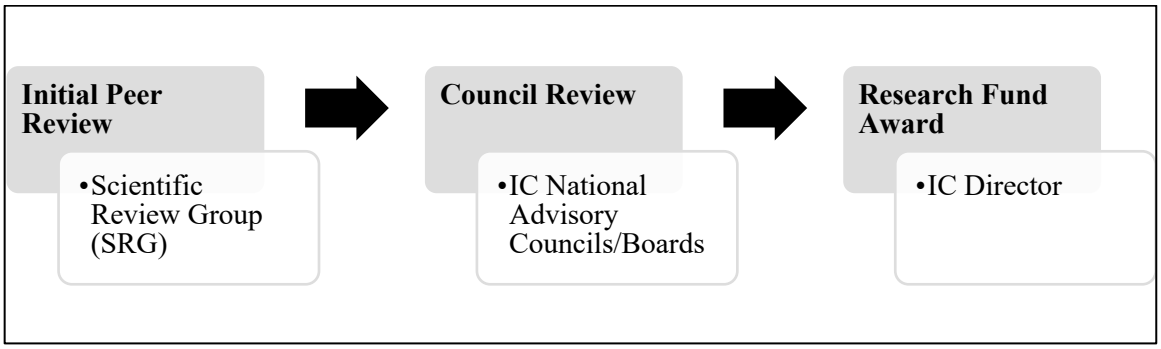


FIGURE 1: SUMMARY OF THE NIH PEER REVIEW PROCESS.

BASIC COMPONENTS OF A NIH GRANT PROPOSAL

NIH Review Criteria

According to my two interviewees, Dr. X and Dr. A, and the NIH's grant and funding information page[3], grant applications submitted to the NIH will be reviewed and scored based on five main criteria. Therefore, grant writers must incorporate these specifications in their grant proposal and describe how their project fits the expectations and deserves the funding.

1. *Significance*: the project has important impacts on the field and the society.
2. *Approach*: the study design and methods of the project is feasible and appropriate.
3. *Innovation*: the project is original and develops or uses novel techniques or ideas.
4. *Investigators*: the project's investigators are experienced in performing the study with the availability of a principle investigator.

5. *Environment*: The project has appropriate institutional support and facilities.

Liu et al. formulate the overall impact score of a grant proposal based on the above five criteria and describe the common pitfalls for each requirement (shown in Figure 2).[1]

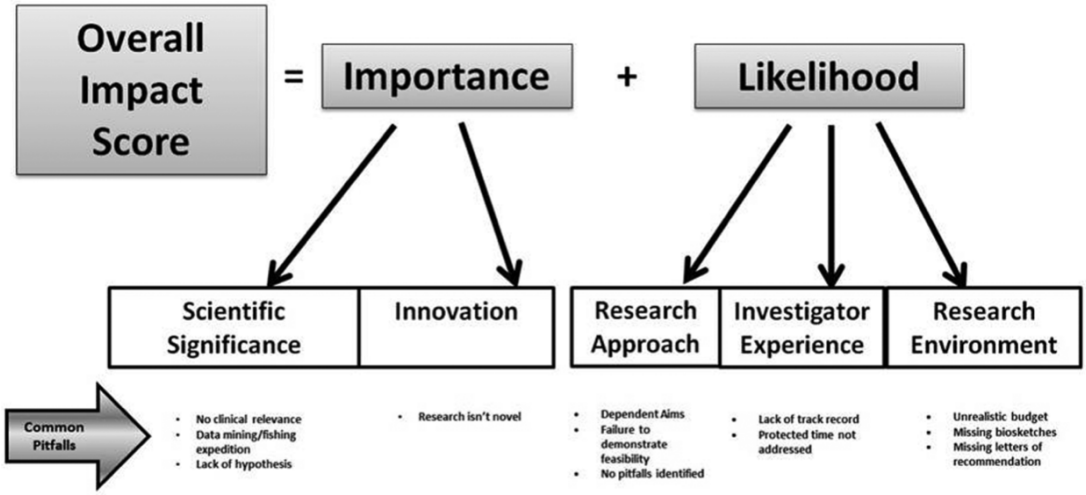


FIGURE 2: FIVE CORE CRITERIA IN GRANT SCORING WITH ASSOCIATED PITFALLS (LIU ET AL.)[1]

Outline of a NIH grant application

From my primary research study, I acknowledge that a NIH grant submission must include (1) an abstract, (2) an introduction, (3) an assertion of specific aims including the significance, innovation and approach of the study, (4) a background and significance, (5) a description of preliminary studies, (6) an outline of research design and methods, (7) an acknowledgement of limitations, and (8) a reference list. During the interviews, the two professors of my primary research thoroughly explained the contents of the grant proposal's components and their strategies for writing them, as well as provided a copy of their approved NIH grant applications serving as samples.

1. The a*bstract* is a comprehensive summary of the entire proposal. My primary research interviewee, Dr. A, emphasized the importance of the abstract: "This is where investigators would want to make a good first impression." He explained that only a few reviewers will actually read the full proposal while most of them will rely on the abstract. Therefore, the abstract must be carefully crafted and polished before submission. Another interviewee of my research, Dr. X, stated that the abstract is usually written after the content of the proposal is finalized because the abstract summarizes key points of the proposal. He furthered that since the abstract must be clear and concise, investigators should avoid using jargon and explaining technical details here, and that they should use lay terminology instead.

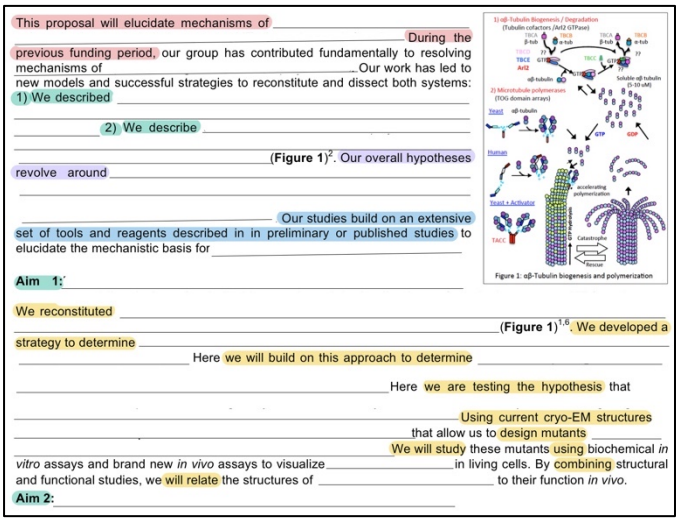
2. According to Dr. A and Dr. X, an *introduction* is not specifically required in a NIH grant proposal. They noted that investigators typically include an introduction when submitting a revised proposal. Below is an introduction sample taken from Dr. A's previous revised grant application to illustrate how an introduction is written.

   "I thank the reviewers for their constructive comments that helped to significantly improve our revised proposal. The comments suggest strong enthusiasm for our proposed studies, extensive preliminary data, trajectory of our research, scientific environment, and my qualifications as an investigator. This proposal was extensively revised to address concerns raised about: 1) Significance of studies in relation to other models in

the field. 2) Collaborators' Commitment. 3) Scientific productivity and accomplishments during the previous period."

3. *Specific aims* contain the research questions or hypotheses of the project that investigators are requesting the grant for. Specific aims are typically the first section of the body of the grant and in fact the most important section of the proposal.[4] According to my two interviewees, a grant proposal can have multiple but no more than four specific aims, each of which must describe its significance, innovation and approach (three of the five NIH review criteria). The specific aims section is limited to only one page where grant writers explicitly state the purpose (significance) and methods (innovation and approach) of the proposed projects. Dr. A described the specific aims section as a summary of the entire body of the proposal. He furthered that throughout the subsequent sections, investigators should constantly remind reviewers of the aims by making frequent reference to them.

   In figure 3, I used Dr. A's specific aims to illustrate how this section is well-written accordingly to the above description. In the first paragraph of the page, he stated the overall purpose of the project (red), introduced the aims (green), summarized the hypotheses (purple) and claimed the innovation and approach (blue). Next, each of the following paragraphs focused on a specific aim (*note*: only aim 1 is shown in figure 3). In each individual aim paragraph, Dr. A explained more explicitly the aim's hypothesis and the approaches that his lab would perform to investigate the question (*note*: key words are highlighted in yellow).


This proposal will elucidate mechanisms of _____ During the previous funding period, our group has contributed fundamentally to resolving mechanisms of _____. Our work has led to new models and successful strategies to reconstitute and dissect both systems: 1) We described _____ 2) We describe _____ (**Figure 1**)[2]. Our overall hypotheses revolve around _____ Our studies build on an extensive set of tools and reagents described in in preliminary or published studies to elucidate the mechanistic basis for _____

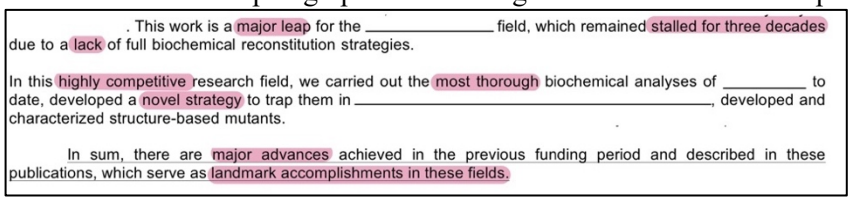
Aim 1: _____

We reconstituted _____ (**Figure 1**)[1,6]. We developed a strategy to determine _____ Here we will build on this approach to determine _____ Here we are testing the hypothesis that _____ Using current cryo-EM structures _____ that allow us to design mutants _____ We will study these mutants using biochemical *in vitro* assays and brand new *in vivo* assays to visualize _____ in living cells. By combining structural and functional studies, we will relate the structures of _____ to their function *in vivo*.

Aim 2: _____

FIGURE 3: SPECIFIC AIMS SAMPLE (ADAPTED FROM DR. A'S PROPOSAL)

4. The next section of the proposal is *background and significance* which "demonstrates an in-depth knowledge of the important history and current state of knowledge of the field."[4] In this section, investigators present the existing knowledge and its remaining limitations in the literature, then explain how the proposed project will fill these informational gaps. As the title of this section indicates, investigators must show the reviewers the importance of the project by explaining its potential impacts on the world, the society or the scientific field. Dr. X gave examples of projects' significance: "Some studies focus on finding a potential cure for either rare or prolonged diseases. Others investigate questions in specific fields that have remained for decades." Dr. A used a paragraph from the significance section of his proposal to show how he


. This work is a major leap for the _____ field, which remained stalled for three decades due to a lack of full biochemical reconstitution strategies.

In this highly competitive research field, we carried out the most thorough biochemical analyses of _____ to date, developed a novel strategy to trap them in _____, developed and characterized structure-based mutants.

In sum, there are major advances achieved in the previous funding period and described in these publications, which serve as landmark accomplishments in these fields.

FIGURE 4: SIGNIFICANCE SAMPLE (ADAPTED FROM DR. A'S PROPOSAL)

stated the importance of his project (Figure 4).

5. The *preliminary studies* section is focused on the last two NIH review criteria – the principle investigator and the environment. According to Chung et al. (2008), "it provides an opportunity to demonstrate to the reviewers an expertise with the field of research."[4] They furthered, "it also shows that the project is feasible and there is sufficient institutional support to bring the project to completion."[4] In this section, investigators present data of previous work that is directly related to the proposed project and describe how the pilot data indicate the merit of the hypotheses. In addition, Dr. X commented that one should avoid including so much pilot data that project will appear to have already been conducted because reviewers do not want to approve funding for a completed project.

6. The *research design and methods* section is accounted for 50% of the page allowance.[4] It is the largest section in terms of page number and content. The aim of the section is to describe how the proposed project, more particularly the specific aims, will be designed and studied. Chung et al. (2008) explained, "the organization of this section should flow from the general study design to participant recruitment, to data collection, to data analysis."[4] Dr. A and Dr. X both admitted that this is where the majority of errors appear, and that the problems are typically found within study sample, outcomes, and data analysis. They furthered that investigators must show reviewers their proficiency in performing the study, and, as Dr. A said, "attention to the most minute details of the study protocol" to assure reviewers that investigators are thoughtful in designing the studies. Dr. A compared this research design and method section of grant proposals to be as detailed as published primary research articles including an appendix.

7. Although the *limitations* subsection is limited to one-half page, it is a critical component of the proposal. As mentioned in the above section (section 6), investigators must assure the reviewers that they have thoroughly anticipated pitfalls and limitations associated with the proposed project. In this section, grant writers present potential problems and how they can be resolved, as well as, "address possible confounders and biases and their solutions."[4]

8. As secondary sources in the literature are always used throughout any scientific papers, scientific grant proposals also include a *reference* list. The NIH does not require a specific citation format but recommends investigators to follow their own organization's standard.

WRITING STYLE OF A SCIENTIFIC GRANT PROPOSAL

Typography and Readability

Following the instructed text formatting, such as page limits, font sizes, margins, and indentions, is a critical element of grant submissions. A NIH grant proposal will be returned if there is any typographic error. In a report on grants that were submitted to the NIH, 20% of proposals had formatting errors for which the directions were clearly written in the NIH grant writing booklets.[5]

According to the NIH's formatting instruction[6], in order to ensure legibility, text in the submission must follow certain requirements. Firstly, font size must be 11 points or larger, except for small text in figures as long as it is readable. Secondly, to maintain an appropriate text density, there must be no more than 15 characters per linear inch (including characters and spaces) and no more than six lines per vertical inch. Lastly, although there are no restrictions on text color and font, it is highly recommended to use black or high-contrast text color with a traditionally professional font such as Ariel, George, Helvetica, Palatino Linotype, etc.

In addition to text format, paper settings of grant applications are also strictly coded by the NIH.[6] Paper size must be no larger than a US standard letter with margins of at least one-half inch at top, bottom, left, and right for all pages. Furthermore, no headers nor footers are allowed as the NIH grant review committee will compile and organize the complete application in their way upon submission. Hyperlinks and URLs are also prohibited in any part of grant proposal, and reviewers are not obligated to view linked sites. Similarly, markups are not allowed in the grant attachment.

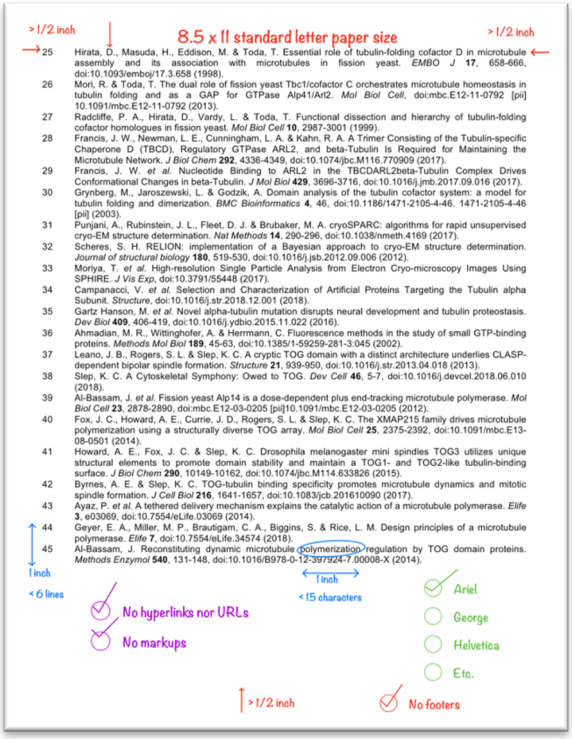


FIGURE 5: EXAMPLE OF THE APPROPRIATE FORMAT OF A NIH GRANT SUBMISSION (ADAPTED FROM DR. A'S GRANT PROPOSAL)

Finally, one of the most important typographic aspects of a NIH grant application is page limit. The number of page limit depends on the type of grants that writers are applying for. My interviewee, Dr. A, commented that a good researcher should be able to confidently and concisely describe their research projects in a way that excites but does not overwhelm reviewers. He also stated that the page limits required by the NIH are reasonable as they give grant writers enough space to effectively persuade reviewers to approve their grant application.

Language and Tone

As the NIH is a federal grantor agency of the United States, English is required to be used in grant applications.[6] Although NIH grant submitters must be U.S permanent residents or citizens, they could come from various ethnicity backgrounds, cultures and social communities. Therefore, it is important that grant

writers carefully proofread their proposal before submission to ensure that they did not use different languages, jargons, or abbreviations without previous introduction.[6]

During my interview with them, Dr. X and Dr. A explicitly described the writing style, language, and tone used in their grant proposal. As mentioned earlier about the page limit, Dr. A added that in order to ensure the page number restriction, he tended to use fairly short sentences, and minimum to no filler phrases. He explained that every sentence should always have an independent argument and can serve its own purpose when standing alone. This technique not only helps writers present their ideas to reviewers more constructively and concisely, but also diminishes confusions that might rise within long sentences. In terms of language and tone, Dr. A and Dr. X both agreed that it should be appropriately formal as reviewers are experts of the field as well as prestigious scientific and non-scientific government representatives. Unlike typical scientific research articles where passive voice is preferred, first-person narrative is widely used in grant proposals as writers want to demonstrate their work's innovation as well as to subtly claim their authorship and efforts on the project. Having said that, the language of the grant writing must not be personal, meaning that no words or phrases describing writers' intimate emotions should be included. For example, the use of the italic words in the following sentence is inappropriate: "*Fortunately*, the method worked, and we are *thrilled* to proceed with the next step."

CONCLUSION

Crafting an effective grant proposal is a long process that requires careful and detailed planning. According to my interviewees, the time for writing a grant proposal ranges from three months to a year depending on the type of preliminary research and the availability of manpower contribution. Therefore, investigators should start early, follow the directions from the NIH, and organize checklists. Below in Figure 6 includes a flow chart demonstrating writing steps and strategies for a NIH grant proposal, a summary of important considerations at each step, and two suggesting checklists.

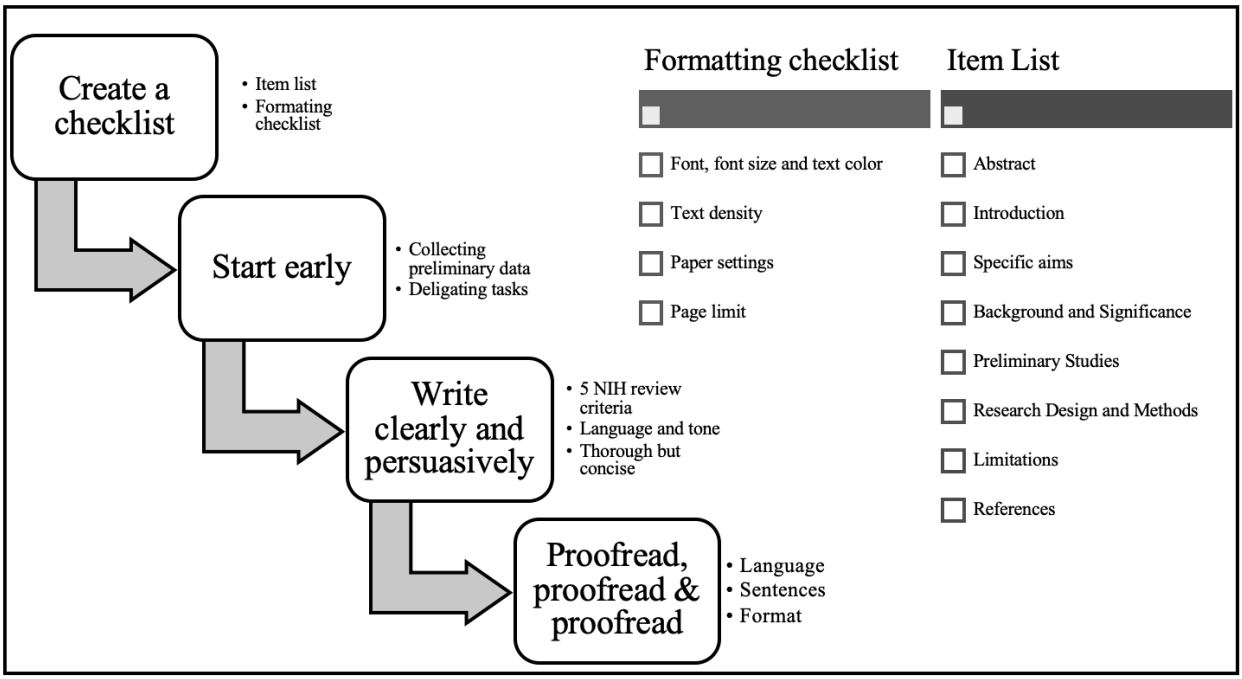


FIGURE 6: WRITING STRATEGIES FOR A NIH GRANT PROPOSAL

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