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by Karen Hopkin

PROFESSION

How To Wow A Study Section: A Grantsmanship Lesson

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Morning in Bethesda: The jet-lagged reviewers drag themselves to the hotel conference room for another day of bad coffee and endless grants. The wife of the study section chairman phoned at dawn to announce that she's leaving him for some hotshot postdoc. "Harvard," he reads from your application on top of the stack. "That's where her boyfriend works!" And you can kiss your R01 good-bye.

If this is how you picture a study section, you're in for quite a surprise—a more pleasant one than our fictitious chairman received. Study section meetings are actually civil, efficient, and business-like. Although the coffee may be bad, the reviewers are completely professional. And believe it or not, they're on your side.

On December 16, scientists attending the American Society of Cell Biology meeting in Washington, D.C., got to see for themselves just how a study section operates. "We want to demystify the process," says Gerald A. Greenhouse, the scientific review administrator (SRA) of the National Institutes of Health Cellular Biology and Physiology (CBY1) study section, who assembled a crew of veteran reviewers to publicly critique a pair of real grant proposals. The more familiar you are with the system, he reasons, the better poised you'll be to pen a successful application.

"I had no idea what happened behind closed doors," said Joydeep Mitra, a new postdoc at Harvard Medical School, who attended the workshop at the cell biology meeting.

Ask a successfully funded researcher to critique your grant proposal before you submit it.

Be hypothesis-driven, not technique-driven.

Clearly state what impact your work will have on a field.

Don't be too ambitious; focus on three to five specific aims.

"This was a clear demonstration that grants are judged and scored in a reasonably fair manner. It gives me confidence in the system."

Did Mitra learn anything about grantsmanship? "If I want to be successful, I need to write as clearly as possible," he says. Sounds simple, but where to begin? Seasoned reviewers have plenty of advice on matters as lofty as philosophy and as mundane as font size.

Study sections are looking to recommend proposals that will add something new to a field-grant applications that have what Greenhouse calls "a vector" associated with them. "The work should move the field forward, not sideways," he says.

So remember to stress the impact your study will have on the field. "And show your excitement," says the current chairman of CBY1, Randall T. Moon, a Howard Hughes Medical Institute (HHMI) investigator and a professor of pharmacology at the University of Washington in Seattle. "If you fail to win someone as your advocate, your grant will sink to the middle of the pile." When the study section convenes, the reviewer who gave your proposal the highest relative score presents your application. Your primary reviewers (usually three) discuss the application's strengths and weaknesses, and then announce their amended scores. All told, the discussion that will shape your scientific future lasts 10 to 20 minutes.

That's why you need to write a proposal that is "completely transparent"-logical and clear, says Harvard Medical School professor of immunopathology Hidde L. Ploegh, a member of CBY1 and one of the mock reviewers. "This document is the only interface between you and the reviewer."

"There are no

Always include preliminary data.

Be considerate of reviewers: Use readable fonts and leave space between paragraphs.

Convey your excitement and enthusiasm.

Discuss data interpretation and alternative hypotheses.

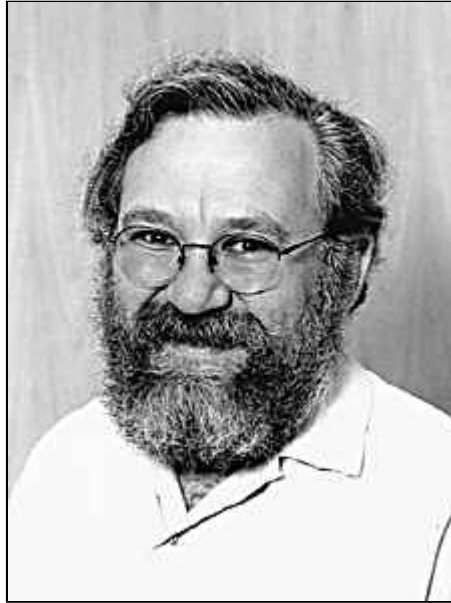
Avoid trying to fill the allotted 25 pages.

Be organized: Use headings and diagrams to help reviewers get oriented.

Call a scientific review administrator (SRA) or search the National Institutes of Health Web page (<http://www.nih.gov>) to determine which initial review group (IRG) or study section best matches your research interests. Include your preference in a cover letter.

Don't be discouraged by rejection. If at first you don't succeed, try, try again.

-K.H.



NO TRICKS: UC-San Francisco's Peter Walter says proposals should be readable and easy to understand.

tricks," says Peter Walter, an HHMI investigator and a professor of biochemistry and biophysics at the University of California, San Francisco, who has served on NIH's Molecular Cytology study section and was on the mock committee. "Just write it so it's readable." Each reviewer receives 12 to 20 grant proposals per round. "I cannot spend a week reading each grant," he says. So your application—which includes sections on specific aims, background and significance, preliminary studies, and research design and methodology—must be easy to understand.

should tell me what you want to do," says Walter. "The background should say why this work should be done. And the experimental section should say how you want to do it," he says. "What, why, and how: If you put everything in the proper section, your logic should be immediately clear."

"Be organized," Moon seconds. Make sure that the headings you use for the specific aims match the headings you use in the experimental section. "I have to be able to read these grants in a nonlinear manner," says Moon. "I jump from the specific aims to the methods," he says. "Then I look at the C.V. and ask, 'Can this person pull this off?'"

And neatness counts, says Anne M. Etgen, a professor of neuroscience at Albert Einstein College of Medicine in New York and veteran of National Science Foundation and National Institute of Mental Health study sections. "Misspellings, grammar errors, and incorrect references all reflect badly on your judgment."

Include diagrams and illustrations to show complex pathways, present preliminary data, or guide readers through your experimental plan. "Like most primates, I like to look at pictures," says Alan Wolffe, chief of



NEATNESS COUNTS: Anne Etgen of Albert Einstein College of Medicine warns against misspellings, grammar errors, and mistakes in references.

molecular embryology at the National Institute of Child Health and Human Development and former chairman of the Biological Sciences 2 NIH study section. "They can help break up page after page of gray type," he says. And use at least a 12-point font, adds Moon, or you may find that your application is returned for reformatting. "A grant doesn't get reviewed if it doesn't get past the font police," he says. Finally, don't feel like you need to fill "every micron of space," he says. Ploegh agrees. "If you can say it in one page, why use four?"

The specific aims section may be the most important section in your grant application, say reviewers. What should you keep in mind as you present your experimental agenda?



GET THE PICTURE: NICHD's Alan Wolffe says that illustrations help make a proposal understandable.

three [and] five years," says Etgen. Focus on three to five aims, Wolffe advises. State each clearly and explain what impact the results will have on the field. "Be hypothesis-driven," suggests Moon. "Your experiments should address specific questions," says Walter. Also, avoid writing a list of specific aims that are all contingent on the successful completion of specific aim No. 1, he adds. "If the first one can't or shouldn't be done, then the rest of the

"The most common mistake that first-time applicants make is proposing to do 20 years' worth of work in somewhere between

Beginning with the next round of study sections, reviewers will be asked to rate grant proposals in the light of five criteria established by the Peer Review Oversight Group, a panel of National Institutes of Health administrators and extramural scientists (R. Finn, *The Scientist*, Aug. 18, 1997, page 1). Although reviewers have always based their appraisal of grants on similar standards, they must now officially assign a score to each criterion (Significance, Approach, Innovation, Investigator, and Environment) before coming to a decision on a global score. You should consider these criteria carefully when you prepare your grant application, says Peter Walter, a Howard Hughes Medical Institute investigator and a professor of biochemistry and biophysics at the University of California, San Francisco.

- Significance: Will the study move the field forward?
- Approach: Are the experiments you

grant will fall apart."

As for the types of experiments you propose in the specific aims section, try to stick with things you can do. "If somebody who's been a gene jock says he's going to crystallize a protein, forget it," says Wolffe. Instead, set up collaborations. But be sure to identify who will be doing what, says Ploegh. "For the first grant, it must be clear that you will be running your own show."

To demonstrate your scientific independence, says Wolffe, "it's also important to divorce yourself from your previous mentor." If you intend to continue working in the same field, get a letter from your former mentor explaining how your proposed project will be novel and fully independent.

Try not to overwhelm the reviewers with too much experimental detail. "Many people think that somehow the concentration of every buffer component must be specified," observes Ploegh. "We're interested in what the experiments seek to establish, what are the controls, and how you will interpret your results."

Successful grant writers also discuss potential experimental pitfalls and provide alternative hypotheses. "You're not supposed to be pushing an agenda," Moon points out. Forgetting to discuss the possible results of your experiment is a "kiss of death," says Etgen. "It gives the appearance that you're not thinking about what you're doing." And if you're a newly independent investigator, Greenhouse says, "you have to give reviewers some feeling for how you think about science."

And remember to present preliminary data. "Reviewers like to see some results that suggest that the strategy you propose will yield something interesting," says Wolffe. A grant application that proposes generating a knockout mouse is not as likely to succeed as one that presents a mouse with an interesting phenotype, explains Ploegh. For example, at the mock study section at the cell biology meeting, the panel assigned a fundable

propose sound and technically feasible?

- Innovation: Are your ideas creative? Is your approach novel?
- Investigator and Environment: Can you accomplish your aims, given your training and the resources and collaborations you describe?

The hard part may be trying to balance feasibility with innovation, says Gerald Greenhouse, scientific review administrator for NIH's Cell Biology and Physiology 1 study section. His advice? "Try to submit an application that includes both solid science and more risky stuff." And visit the Web page of the Center for Scientific Review (formerly the Division of Research Grants) at <http://www.csr.nih.gov> to learn more about the new criteria and other NIH happenings.

-K.H.

score to a resubmitted grant proposal that had been vastly improved by the addition of preliminary results from a simple two-hybrid screen. The experiments gave the revision a focus the original submission had lacked.

"The longer you can wait to submit an application, the better off you'll be," says Greenhouse. If a university can offer you a year or two of support, gather data before writing your first grant. "It's important to show that you are an independent scientist," he adds. "If you can say you've been on your own, your lab is cooking, and you've got some data, it'll save you time in the end."

"I wish I'd heard all this eight years ago," says Jonathan A. Rothblatt, an associate research scientist at Columbia University. Rothblatt, whose first grant got funded on its third submission, said the mock study section at December's American Society of Cell Biology meeting gave him a better idea of what reviewers want to see in a proposal. "It's one thing to say to yourself 'I should do that,'" says Rothblatt. "It's another thing to hear a study-section member tell you the same thing."

If your grant does not receive a fundable score, don't get discouraged, says Walter. "Focus on the big picture and rewrite it from a new perspective." But remember, three strikes and you have to write a different grant.

"Take the re-viewers' suggestions seriously," advises Moon. Reviewers write critiques for a reason—"even if it's the wrong reason," he says. Often they're confused because some piece of logic is unclear. "These people aren't stupid," notes Moon. "So explain yourself more clearly. Don't just ignore the comments and hope that somebody will read your resubmission," he warns. "That'll just tick everyone off."

And don't rush through your revisions to get your application back into the next review cycle. "Wait until you feel you've substantially addressed the criticisms before you resubmit," says Moon. Answering the reviewers' comments often involves doing additional experiments as well as a rewrite. If the criticisms are unclear, talk to the SRA who heads the study section and who supervised the review of your proposal.

You also can turn to SRAs for tips before you submit your proposal. "We won't tell you how to do science, but we can help you organize your ideas," advises Greenhouse. Even better: Have someone who has been successfully funded read your proposal before you submit it. "You get so into what you're writing, you can't always recognize when you're not being clear," says Etgen. So show it to someone you trust, someone who is not intimately involved in the same study, someone who is not afraid to hurt your feelings.

Of course, that requires finishing the proposal well before the last Federal Express pickup on the night before the deadline. "Give it to someone a month or two before it's due, not a day or two before," cautions Etgen.

Which means that you need to start writing a few months in advance, so you have time to write multiple drafts and address your colleagues' critiques.

In the end, it's up to you to write a solid grant proposal that will add to the knowledge of biology. "I can't provide a formula for success; I don't think there is one," says Greenhouse. Even with good advice, writing a fundable grant is certainly not a walk in the park. "Each of us makes the very mistakes that we rail against," says Ploegh. "It requires constant vigilance."

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