

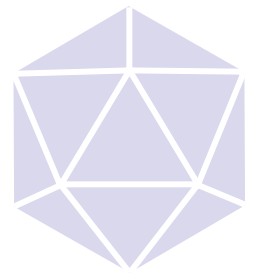
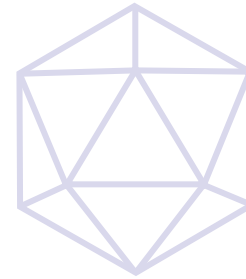
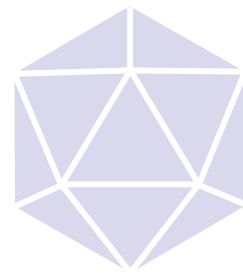
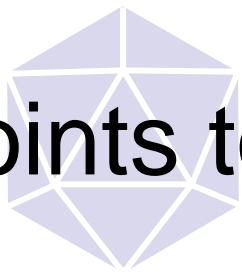


Strategies for Getting Your First NIH Grant Funded

American Society for Virology
Madison, Wisconsin
July 2006

Cathy Laughlin
Roz Sandri-Goldin
Sandy Weller
Chris Beisel

Points to Consider



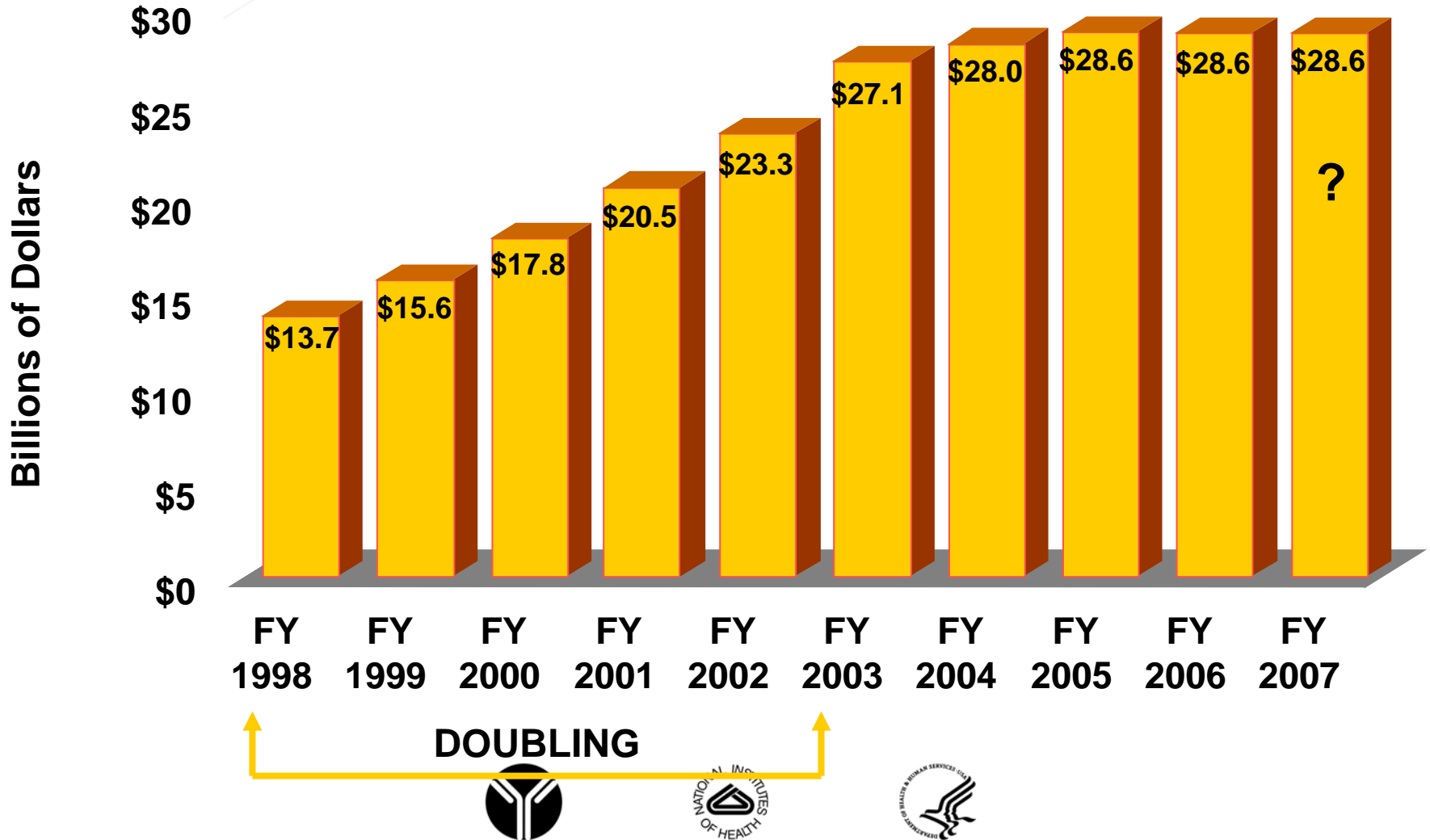
- ◆ NIH Organization & Budget Issues

- ◆ Hypothesis

- ◆ Presentation



NIH Congressional Appropriations

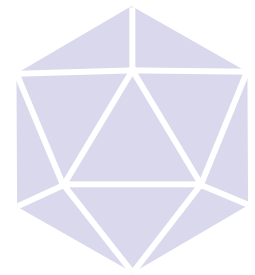
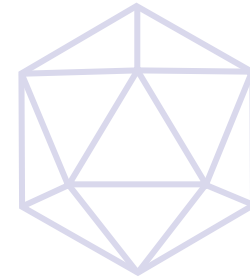
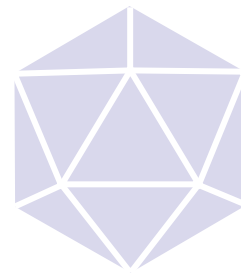


Budget Doubling & Falling Paylines

- ◆ Since 1995:
 - ◆ The NIH budget up > 150%
 - ◆ NIAID R01 spending up almost 180%
- ◆ BUT...
 - ◆ The size of the average grant has increased almost 40%
 - ◆ The number of applications has increased
 - ◆ Recent NIH budgets have not kept pace with these increases.



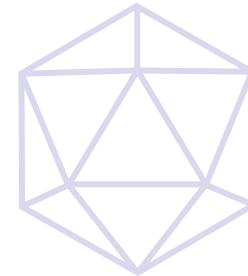
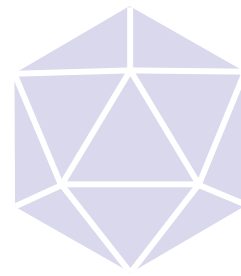
R01 Paylines



FY	Payline
2001	22
2002	22
2003	22
2004	20
2005	18
2006	14
	16 for new investigators
2007	?



Who's Who at NIH

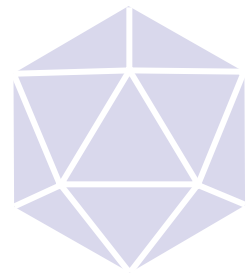
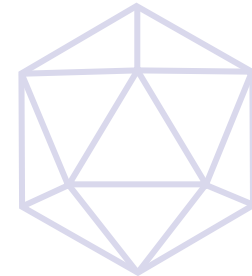
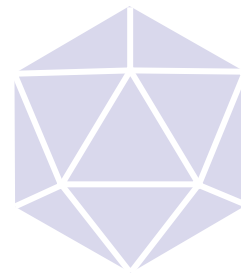


Institutes/Programs	Review
<p>NIH grants are funded by 24 <i>Institutes & Centers</i></p>	<p>All grant applications undergo <i>peer review</i> for scientific merit. Most reviews are conducted by the <i>Center for Scientific Review (CSR)</i></p>
<p><i>Program officers</i> are responsible for an Institute's extramural activities in a scientific area, and manage all the related grants</p>	<p><i>Scientific Review Administrators (SRAs)</i> manage all review activities</p>



Grant Mechanisms

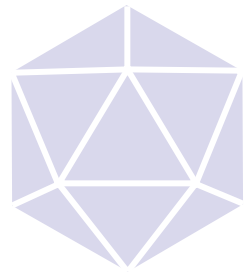
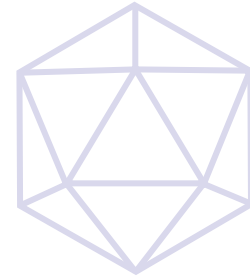
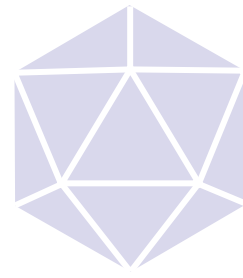
Research Projects



- R01 Research Project
- R03 Small Research Grant
- R21 Exploratory/Developmental Grant
- R15 Academic Research Enhancement Award
(AREA)
- R43, R44 Small Business Innovation Research Grant
(SBIR)
- P01 Research Program Project
- K99 Pathway to Independence Award (PA-06-133)



Hypothesis is Key



“There is no grantsmanship that will turn a bad idea into a good one, but there are many ways to disguise a good one.”

William Raub, Former NIH Deputy Director

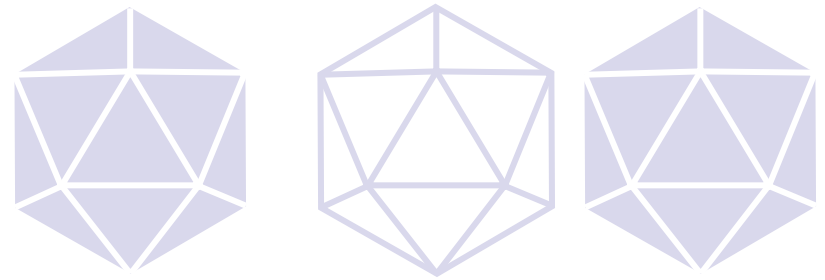


The Basics

- ◆ The Research Plan should include sufficient information needed for evaluation of the project, independent of any other document. Empathize with your reviewers.
- ◆ Be specific and informative, and avoid redundancies. Watch your ambition. Address your independence.
- ◆ Organize the Research Plan to answer these questions:
 - ◆ What do you intend to do? (Specific Aims)
 - ◆ is the work important? (Background & Significance)
 - ◆ What has already been done? (Preliminary Results)
 - ◆ How are you going to do the work? (Research Design and Methods)
 - ◆ What will the results mean? (How will you interpret the results)
 - ◆ Expect to Revise at Least Once



Specific Aims



- ◆ The Specific Aims are the first part of the proposal that the reviewer reads. Include a short description of problem and background summary (one paragraph)
- ◆ The Specific Aims should address an hypothesis and the hypothesis should be clearly stated
- ◆ They should be bulleted and clearly and succinctly outline the proposed research.



Formulate Sound Hypotheses

1. Specific Aims

- Use different synthetic and plasmid constructs to target plasmid based Enhanced Green Fluorescent Protein (EGFP) expression for RNAi destruction [REDACTED] [REDACTED] to validate RNAi constructs for activity [REDACTED]
- Use validated RNAi constructs to reduce expression of EGFP in the EGFP constitutively expressed [REDACTED] line, [REDACTED]
- Report RNAi effect on EGFP expression [REDACTED]

What's the hypothesis here?



Brief summary
of background

SPECIFIC AIMS

The manner whereby [redacted] the etiologic agent of [redacted] [redacted] can chronically infect both humans (21, 22) and animals (26, 28, 31) in the face of a vigorous and specific immune response continues to be an enigma. Especially intriguing is the long-term survival of [redacted] despite the presence of a strong antibody response that is directed against [redacted]. A novel mechanism of immune evasion [redacted] was recently proposed.

Long term goal

The long-term goal of this proposal is to examine several [redacted] antigenic targets of host antibody responses. [redacted] Our central hypothesis is that [redacted]

Hypothesis

[redacted] is a major immune evasion mechanism that contributes to [redacted]

[redacted]. The rationale behind the proposed research is that the expression of these antigens *in vivo* over time [redacted]. Therefore, we propose the following specific aims:

A) *Generate antigen and antibody reagents to assess antigen expression.*

Clone, express, and purify the specified antigens as glutathione S-transferase (GST) fusion proteins. Generate specific antibodies. To obtain sufficient amounts of antibody for passive immunization, purified recombinant antigens will be used to immunize mice, and polyclonal antibodies will be produced. The ability of these antibodies to [redacted] will be tested *in vivo* by passive immunization experiments [redacted]

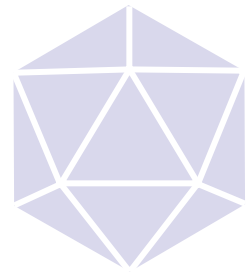
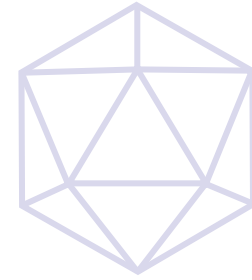
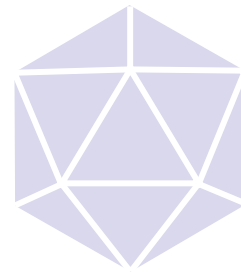
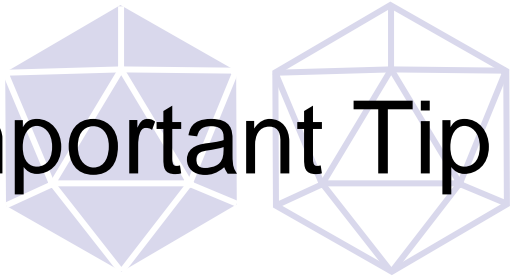
B) *Comprehensively assess expression [redacted] in vivo, and [redacted] of specific antibody.*

Assess expression of the chosen antigens in a variety of different [redacted] [redacted]. Transcripts will be quantified by RT-PCR; antibody titers will be determined by ELISA.

C) *Assess [redacted] to explain the observed [redacted] expression in the host.*

[redacted] will be assessed *in vitro* by [redacted] [redacted]. These experiments will directly demonstrate the role of specific antibody [redacted]

Important Tip



- ◆ The specific aims should be interrelated but should not totally depend on the success of one aim to perform the others.
- ◆ Example:
 - ◆ Aim 1 proposes to identify and clone the cellular receptor that restricts HXV infection to humans. In Aim 2, there are plans to construct transgenic mice expressing the receptor to develop an animal model for HXV to study pathogenesis.
 - ◆ What if there is more than one receptor? Or you are not successful in identifying putative receptors? Or infection is also blocked at a stage past entry?



Background and Significance

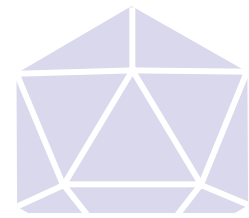
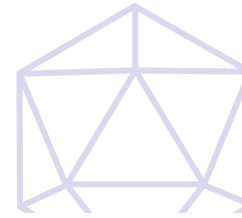
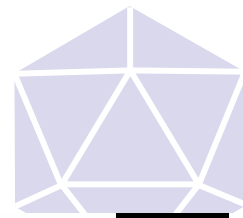
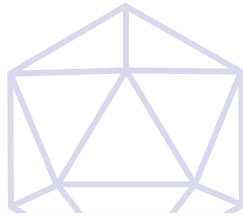
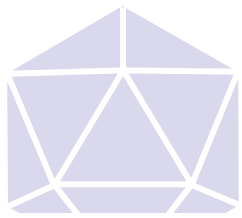
- ◆ Summarize what is known about the research problem being investigated in the proposal.
- ◆ Describe unresolved questions.
- ◆ Explain why this is an important problem.
- ◆ Describe how your studies will contribute to answering the outstanding questions.



Tips on Background & Significance

- ◆ Don't review the literature. Cover only those areas that directly pertain to your proposal.
- ◆ Do critically evaluate the literature in terms of what is known and generally accepted and explain how your proposed studies will advance the field.
- ◆ Include a one paragraph summary at the end of recaps why the proposed studies are important. Don't assume the reviewer should be able to glean the significance of your proposed work.





→ These studies are important because [redacted] is a key player in [redacted] infection. [redacted] is multifunctional and has been implicated in all aspects of gene expression [redacted]

[redacted] we are focused on probing the molecular mechanisms by which [redacted] functions, including how [redacted] affects cellular and viral gene transcription [redacted]

→ cytoplasm. In this proposal, we hope to define [redacted] functional domains [redacted] and to elucidate [redacted] its intermolecular interactions. A model [redacted] showing the known functional activities and interactions [redacted] is shown in Figure 1. It is currently unclear which of these activities and interactions are essential [redacted] These studies will help to determine which activities [redacted] are actually directly mediated [redacted] and which are mediated indirectly, for example by [redacted] Further, these studies will help to determine which interactions [redacted] are crucial to [redacted] infection. [redacted]



Research Design and Methods

Do provide the rationale for each experimental approach

- ◆ Discuss possible outcomes and how these will be interpreted
- ◆ Discuss potential pitfalls and alternative approaches

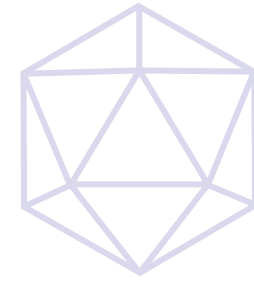
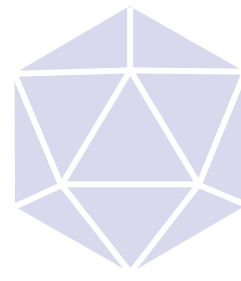
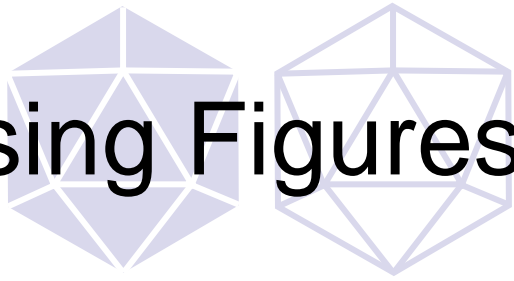


A Picture Can Be Worth a Thousand Words

- ◆ Illustrate models instead of describing them in the text
- ◆ Use schematics to summarize
- ◆ If data figures or schematics are inserted into the Preliminary Studies or Research Design sections, make sure both the figure and the legend are legible and easily readable by the reviewer



Using Figures



involved in these various activities and functions are shown in Figure 2A.

A) Functional regions

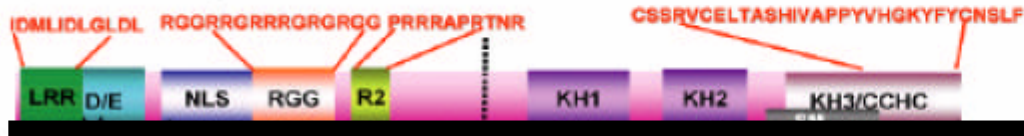


Figure 2. Schematic showing structural motifs based on sequence homology to other proteins. The motifs include:

Both the figure and legend can easily be read by the reviewers.



Using Figures

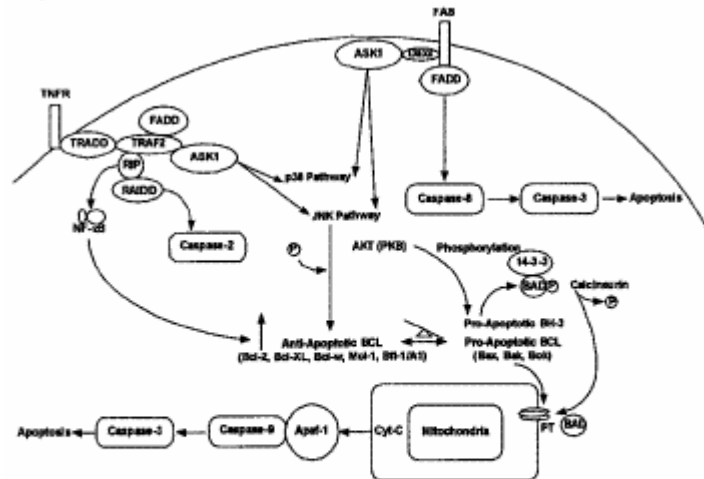


Figure 1. Simplified model of Fas/FasL and TNFR induced caspase activation and apoptosis.

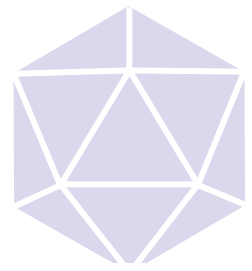
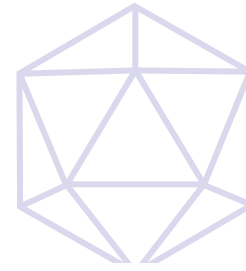
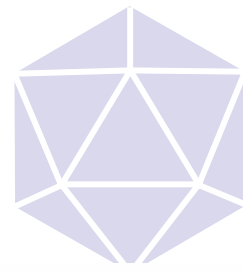
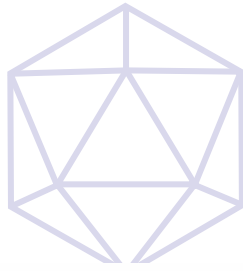
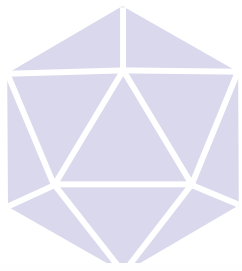
The legend can be read but the schematic cannot be read.



Useful Tip

- ◆ Add a short summary at the end of the Research Design and Methods section to drive home what will be learned from the studies and why that is significant. Future directions can be included briefly.





Taken together, the aims of this proposal will further elucidate current knowledge of [REDACTED] during mammalian cell cycle entry. An expanded understanding of the DNA replication process will yield novel insight into cell growth control and potential therapeutic strategies for the inhibition of cancer cell proliferation.



Have Colleagues Critique the Application

- ◆ Have at least two colleagues read and critique your application
 - ◆ One of the readers should be outside of your field to gauge general clarity and comprehension of the proposal.
 - ◆ One of the readers should be knowledgeable about the area to give informed advice.
- ◆ Plan to complete your proposal with enough time (weeks before it is due, not days) for your colleagues to do a good job.

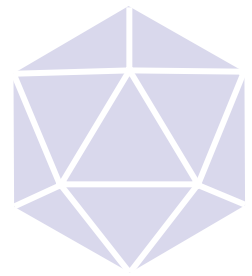
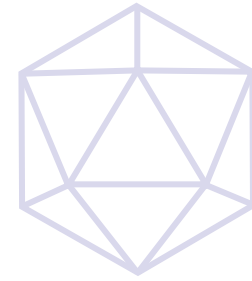
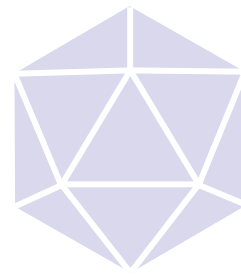


Include a Cover Letter

- ◆ Suggest appropriate Institute(s)
 - ◆ Multiple Institute assignments
- ◆ Suggest appropriate Study Section(s)
 - ◆ Go to the CSR web site <www.csr.nih.gov> for a description of Study Sections & rosters
- ◆ Suggest reviewer expertise(s). *Do not* suggest specific names!
- ◆ Identify potential reviewers who may be conflicted, mortal enemies, etc. *Explain why!*



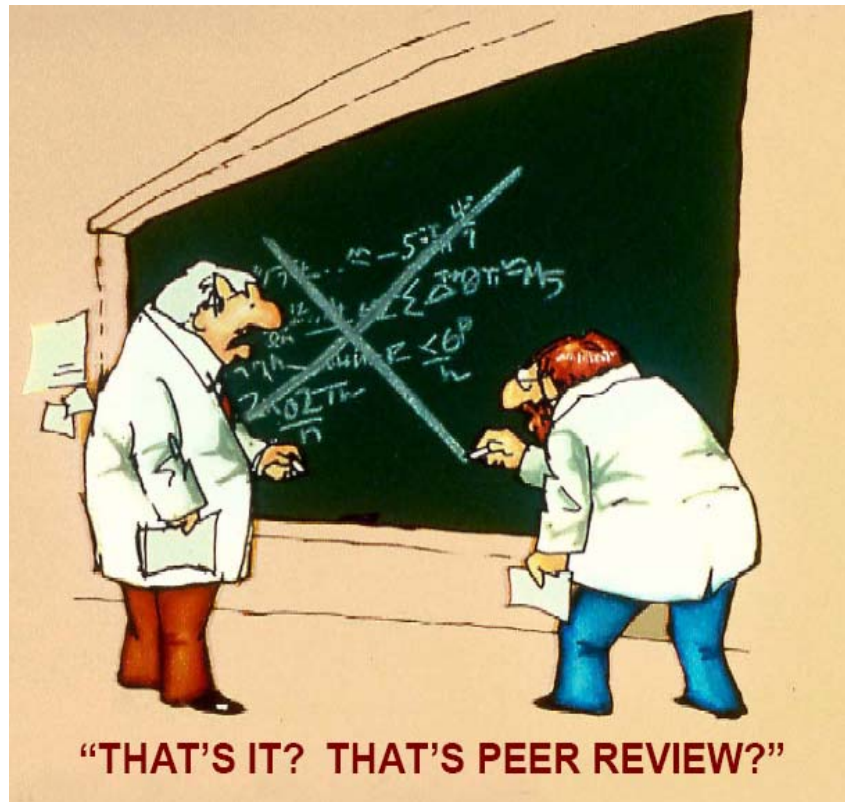
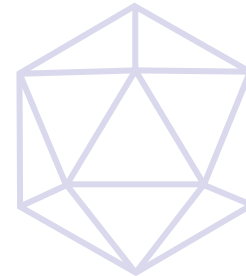
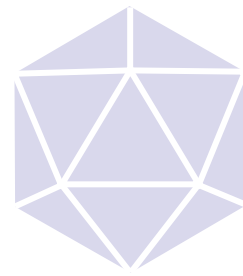
Streamlining



- Reviewers put applications in the “upper half” or “lower half”
- Any reviewer (not in conflict) may remove an application from the “lower half”
- Upper half applications:
 - Discussed fully at the study section meeting
 - Receive a priority score
 - Taken to Advisory Council for second-level review
- Lower half applications:
 - Not discussed or scored
 - Written critiques are provided to the applicant
 - Not taken to Advisory Council



In the “lower half” ...



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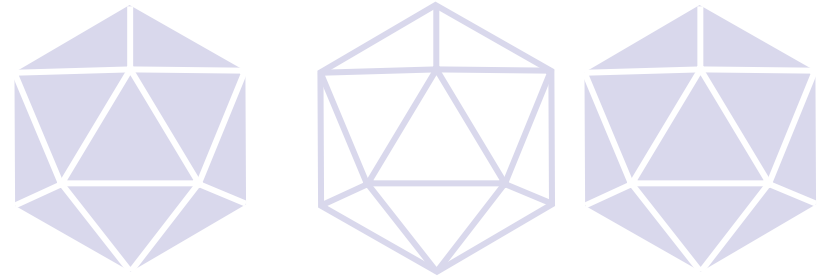
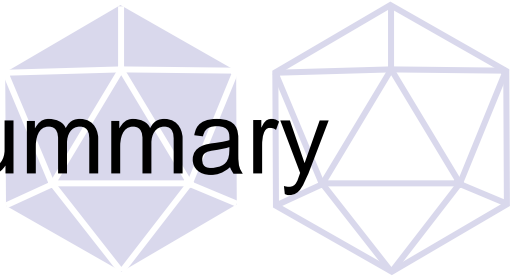


Getting the Review Results

- ◆ The NIH Commons
 - ◆ Score & percentile
 - ◆ Summary Statement
- ◆ Program staff:
 - ◆ Payline information
 - ◆ Advice on revision



Summary



- ◆ Plan your application carefully
- ◆ Write to clearly communicate your plans and sell their feasibility and significance
- ◆ Network!
 - ◆ Have colleagues critique the application before submission
 - ◆ Know your Program Officer and SRA and call with questions or for advice
- ◆ If at first you don't succeed...

