

Grant Proposals



Pamela Derish
Publications Manager
Department of Surgery

1. Getting Started

Writing Grant Proposals: The First Word...

Never forget that your proposal is a work of persuasion and not a collection of disparate facts. It isn't merely a description of the work you want to do; **you are making an argument that it is work that needs to be done and that you are the right person to do it.** Make your argument convincingly.

~ **Science (NextWave) 2001**

Understand that Effective Grant Writing Requires Lots of Preparation

Start early:

1. Define project
2. Identify funding sponsor
3. Read proposal instructions
4. Know submission deadline

To Define a Project...

1) You must be knowledgeable about your...

interests (may require some soul searching)

future goals (future area of specialization?)

expertise (be honest about strengths and deficits)

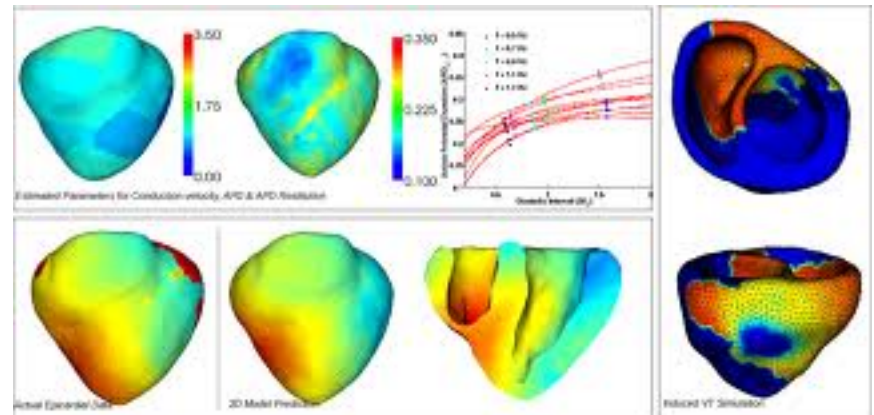
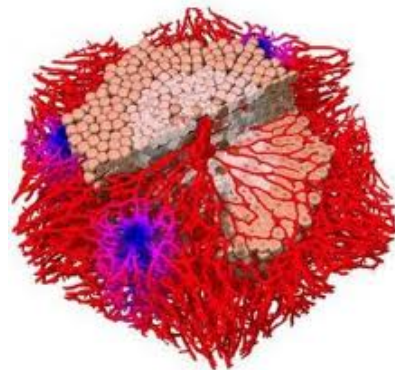
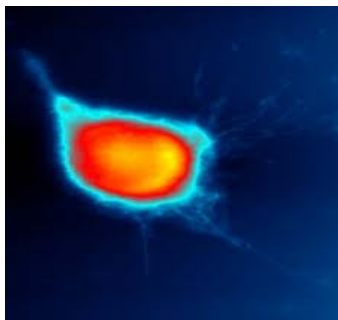
mentor (track record of supervising mentees, etc)

workplace environment (facilities, equipment, etc)

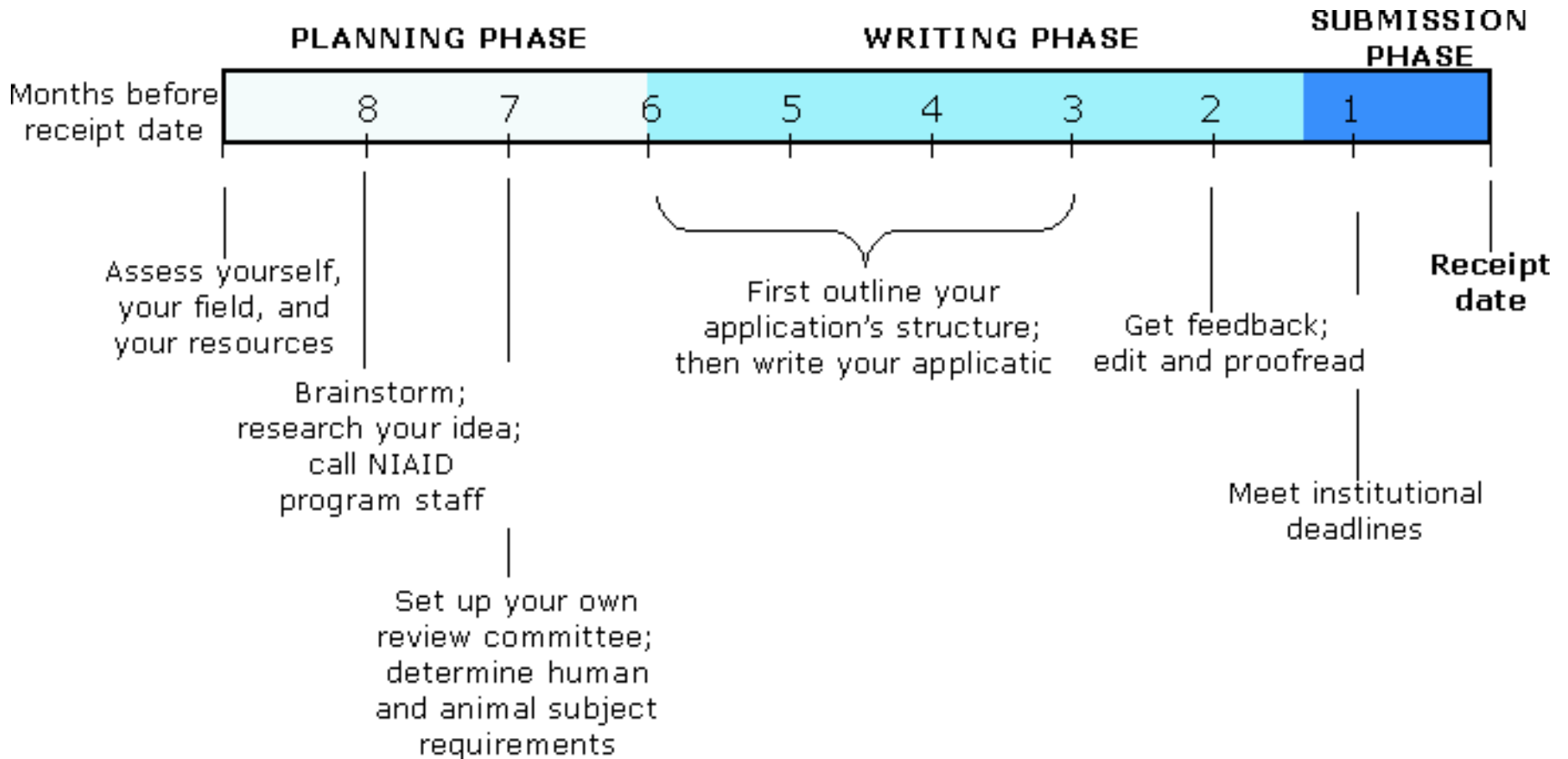
Understand that to Write A Clear, Concise, and Focused Proposal, Good Science is not Enough

You must also...

- Understand the mission statement of the funding agency to which you are applying. **The strongest proposal is tailored especially for the agency it is directed to.**
- Identify funding agencies whose priorities are similar to your interests.



Allow Enough Time to Prepare a Great Application (Pre-Submission Planning Timeline)



NIH slide

Contact UCSF Research Administration as Soon as You Think You Want to Apply for a Grant

Your Pre-Award Analyst will:

Read the agency guidelines and let you know exactly the sections you will need to complete for your application and which sections they will complete for you.

Complete all internal forms, obtain approval signatures, make copies of hard-copy submissions and submit your final application to UCSF's Office of Contracts & Grants or directly to the funding agency.

2. The Format of the Proposal

Snapshot of Format for Many Agencies

Each section describes something important about the proposed research. Length may vary (3 pp – 25 pp):

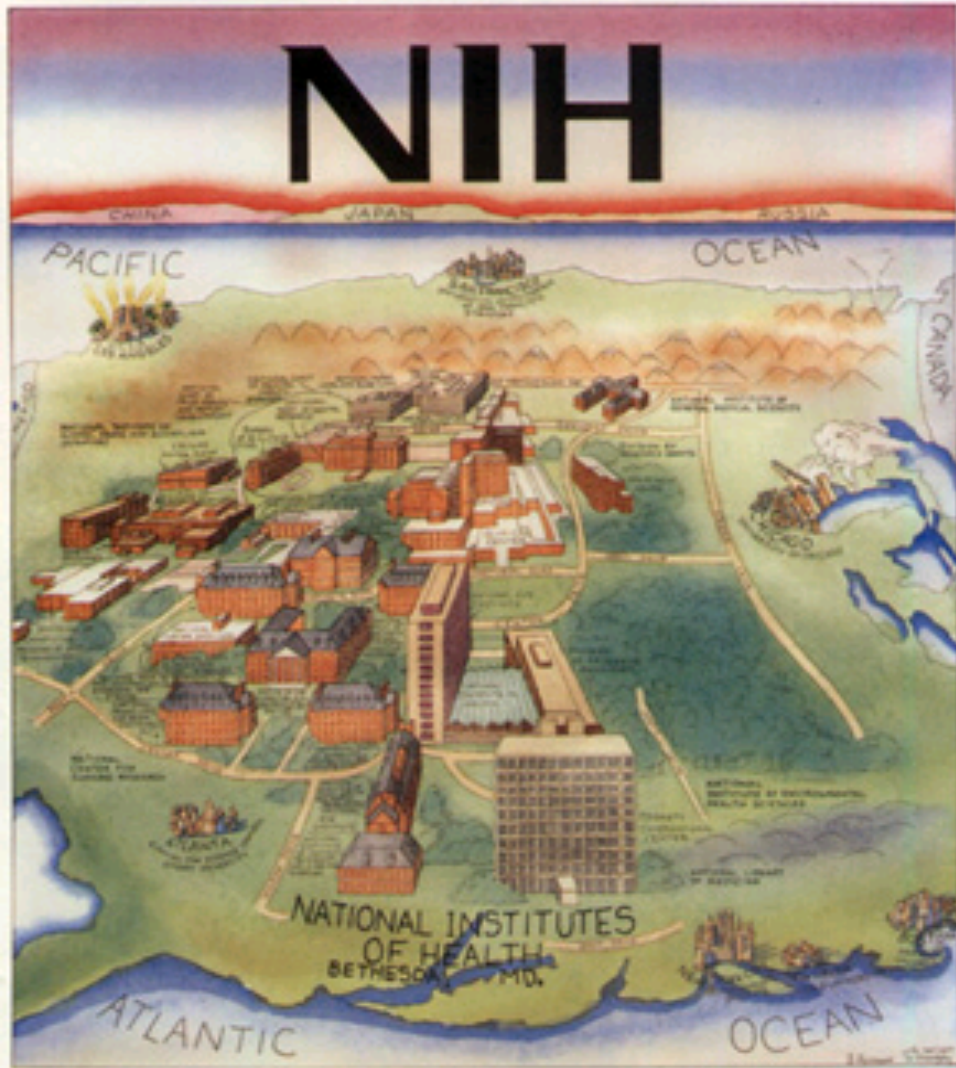
Specific Aims: goals of the research you intend to conduct

Background and Significance: importance of the research to science and public health

Preliminary Studies/Progress Report: data showing the viability of your proposal

Research Design and Methods: detailed description of your planned experiments

NIH



Snapshot of the NIH Format

SPECIFIC AIMS (1 page)

RESEARCH STRATEGY (6 or 12 pages)

A. Significance (0.5-0.75 page)

B. Innovation (0.5-0.75 page)

C. Approach

Needs to cover, for each aim:

Justification & feasibility

Research design

Expected outcomes

Potential problems and alternative strategies

Preliminary data gets tucked in here.

Literature cited throughout, as needed.

For All Funding Agencies, the Proposal Provides Answers...

- What do you intend to do?
- Why is this worth doing? How is it innovative?
- What has already been done *in general*, and what have other researchers done in this field?
- What will this new work add to the field of knowledge?
- What have you (and your collaborators) done to establish the feasibility of what you are proposing to do?
- How will the research be accomplished?

Know Who The Reviewers Are



Don't Make Reviewers Work Hard

Explicitly address the Agency's review criteria.

*“This proposed work is significant for three reasons.
First, Second, Third,*

Generate excitement about your project.

Use strong active verbs.

Be interesting and clear, even to the non-specialist.

Avoid abbreviations & jargon.

Write a Proposal that is “Reviewer Friendly”

Make your proposal easy to follow:

- ✓ leave white space
- ✓ Include legible figures
- ✓ Use informative subheadings
- ✓ highlight important key points **using bold-face type sparingly, underlining, and *italics***
- ✓ edit & proofread



3. Writing a Clear Specific Aims Section

THE FOLLOWING **PREVIEW** HAS BEEN APPROVED FOR
ALL AUDIENCES
BY THE MOTION PICTURE ASSOCIATION OF AMERICA, INC.

www.filmratings.com

www.mpa.org



The “Preview” Covers a Lot of Ground

- introduces **the problem** you are addressing; indicates if your research has contributed
- identifies the **specific gap** in knowledge that the proposed research will fill.
- identifies the long-term goal (beyond the current proposal).
- introduces hypotheses to be tested; describes the basis for the hypothesis.
- states the **aims or objectives** of project
- briefly **describes the main techniques** you will use to answer questions;
- highlights your qualifications to do the research
- describes **the advance** your study represents.

4. Review of a Specific Aims Section (Exercise 1 in Supplemental Handout)

Eukaryotic innate immune systems act as effective barriers to infection by microorganisms. Understanding the mechanisms that bacterial pathogens employ to circumvent innate immune systems will improve our ability to control disease. Plants and animals use specific pattern recognition receptors (PRRs) to recognize conserved molecules of microorganisms (known as PAMPs). Plants have numerous PRRs that can recognize specific virulence proteins specifically present in pathogens (known as Avr proteins). Many Gram-negative bacteria use type III protein secretion systems to inject effector proteins into host eukaryotic cells. We have shown that a primary role for many *Pseudomonas syringae* type III effectors is to suppress innate immunity. However, the enzymatic activities and the mechanisms that type III effectors use to suppress innate immunity are not well understood. Identifying the enzymatic activities of type III effectors and their substrates is essential to identify important components of innate immunity and to improve strategies to control bacterial diseases.

Our long-term goal is to elucidate the molecular basis for suppression of innate immunity by type III effectors. The objective of this application is to identify targets of the P. syringae type III effector HopU1, a mono-ADP-ribosyltransferases (ADP-RTs), and to determine its roles in bacterial pathogenesis. The central hypothesis of the proposed experiments is that the targets of the HopU1 ADP-RT type III effector will be components of innate immunity. We formulated this hypothesis based on the literature and on our research on other type III effectors as well as our preliminary data showing that HopU1 suppresses outputs of innate immunity. Based on our preliminary data, one of these proteins, AtGRP7, plays a role in innate immunity.

We are prepared to undertake the proposed research because we have extensive experience in manipulating type III systems, and we were among the first to report that certain type III effectors suppress innate immunity. In addition, our preliminary identification of HopU1's substrates has positioned us well to perform the experiments described in this application. Our research team includes experts in the following areas: type III secretion systems, proteomics and mass spectrometry, Affymetrix microarrays, plant glycine-rich RNA-binding proteins, and animal pathogen ADP-RTs. This qualified group of investigators will insure that our discoveries are linked to basic concepts of pathogenesis and immunity in both plants and animals.

The Specific Aims of this application are as follows:

- 1. Determine the molecular consequence of ADP-ribosylation on the function of AtGRP7 and elucidate the role this protein plays in innate immunity.** *Our working hypothesis* of this aim is that AtGRP7 binds to immunity-related RNAs to enhance the innate immune response and that ADP-ribosylation by HopU1 disrupts its function.
- 2. Identify additional substrates of HopU1 and verify their involvement in innate immunity.** *Our working hypothesis is* that the plant targets for the HopU1 ADP-RTs will be important components of plant innate immunity.
- 3. Analyze the affect that HopU1 has on host-microbe interactions.** *Our working hypothesis of this aim is* that HopU1 type III effector suppresses innate immunity. This is based on our preliminary data and in this aim we will determine to what extent this occurs with HopU1.

The proposed research is innovative because, to date, ADP-RTs have not been implicated in the suppression of innate immune surveillance systems. Moreover, RNA-binding proteins have not been described as substrates for ADP-RTs and, therefore, represent novel substrates for this important group of bacterial toxins. Collectively, we expect the outcomes of these experiments will greatly add to our understanding of the activities and roles of type III effectors, particularly in how they suppress innate immunity in eukaryotes.



The Components “Map” into a Template

Phenomena X or disease X is... A characteristic feature of this process is... Although ABC has been shown to...it is unknown whether...**Preliminary studies** [or **Recent studies** from our lab] show that... Therefore, **the overall hypothesis** behind the proposed research is that... The basis for the hypothesis is... This hypothesis will be tested by the following **specific aims**:

Aim 1 will determine... Aim 1 will use X and Y methods to... In Aim 1A we will... In Aim 2A we will... We hypothesize that...

Aim 2 will determine...

Aim 3 will determine...

The results of this study will lead to a better understanding of...

Specific Aims Section: Hook the Reader in 4 Paragraphs...

1. "Set-up" (Introductory) Paragraph
2. Hypothesis Paragraph
3. Specific Aims Paragraph
4. "Pay Off" Paragraph (emphasize significance, innovation IF earlier paragraphs don't do this)

...or Less!

If you've got ½ a page, you can't have 4 paragraphs; instead, think of 4+ sentences:

1. 1 or 2 sentences of introduction
2. 1 sentence of hypothesis.
3. Aims statements
4. Maybe a short concluding sentence about significance, innovation

Step 1

✓ Develop Your Proposal's Hypothesis or Objective

A focused objective or hypothesis must be

- Logical
- Relevant to a gap in recent scholarship and/or assessed needs
- Feasible
- Stated precisely

From Description to Hypothesis-Basic Science

1. **We hope to observe how** tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.
2. **We propose to determine how** tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.
3. **We propose to determine the mechanisms by which** tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.
4. **We will test the hypothesis that x is the mechanism by which** tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.

based on Israel Goldberg, PhD, Health Research Associates

From Description to Hypothesis: Clinical or Epidemiological

1. **We hope to observe that** HPV infection is a risk factor for heterosexual HIV infection among women in Zimbabwe.
2. **We propose to establish a relationship between** HPV-mediated cervical lesions and the incidence of HIV infection among women in Zimbabwe.
3. **We will test the hypothesis that HPV-mediated cervical lesions are not only more prevalent but enhance** the acquisition of HIV in HIV+ women.

*based on Sarah Averbach, MD, “the effect of cervical HPV infection on HIV acquisition among women in Zimbabwe (UCSF Pathways to Discovery Program, 2009)

What are the problems with the following hypotheses?

Can you revise them?

(Exercise 2 in Supplemental Handout)

Analogs to chemokine receptors can be biologically useful.

A wide range of molecules can inhibit HIV infection.

Understanding the strategies of *Escherichia coli* to subvert host cells will allow for improved ways of preventing and treating *E. coli* - related diseases.

Rheumatoid arthritis patients with active disease show many alterations in their immune profile.

Step 2

✓ Develop your Specific Aims

A specific aim should *describe concisely and realistically what the proposed research is intended to accomplish*:

test a stated hypothesis

create a novel design

solve a specific problem

challenge an existing paradigm or clinical practice

address a critical barrier to progress in a field

develop a new technology

Develop Your Specific Aims

A general (or long-term) goal is not the same thing as a specific aim:

General goal (goes beyond the scope of the proposed study): To improve the quality of alcoholism treatment

Specific aim: To determine the relative efficacy of Treatment A vs. Treatment B for increasing abstinence among alcohol-dependent patients

Develop Your Specific Aims

General Goal: Our *long-term goal* is to elucidate the molecular basis for suppression of innate immunity by type III effectors.

Specific Aims:

1. Determine the molecular consequence of ADP-ribosylation on the function of *AtGRP7* and elucidate the role this protein plays in innate immunity.
2. Identify additional substrates of HopU1 and verify their involvement in innate immunity.
3. Analyze the affect that HopU1 has on host-microbe interactions.

Develop Your Specific Aims

They should...

- ✓ be logically connected to the rest of the Aims page (*usually through the central hypothesis; each aim often has its own subhypothesis*).
- ✓ go from most developed to least developed.
- ✓ complement each other and should NOT be contingent on each other.
- ✓ each have a concrete outcome.

Develop Your Specific Aims

Write them early. Incorporate feedback from your mentor. Essential to leave enough time for this!

2-3 Aims are the norm. For post-doc fellowship, ok to propose 3 aims, but be sure the 3rd aim will fit into your timeline (2 years).



Specific Aims: Reviewer-Friendly Format

In addition to choosing words carefully, help reviewers make the connections you want to make *by telling them using **explicit language***:

Our long term goal is/ What is not known is/

The overall objective of this proposal is/ Our central hypothesis is/

The rationale behind the proposed research is/

With respect to expected outcomes, the work proposed in Aim 1 is expected to

No abbreviations (or as few as possible)

Use *italics* and/or underlining (sparingly) to highlight key points. (Be very sparing of **boldface**)

White space!!! (open line after each paragraph, at a minimum)

Specific Aims: Reviewer-Friendly Format

Explicit language (from the example in Exercise 1):

Our long-term goal is to elucidate the molecular basis for suppression of innate immunity by type III effectors. *The objective of this application* is to identify targets of the *P. syringae* type III effector HopU1, a mono-ADP-ribosyltransferases (ADP-RTs), and to determine its roles in bacterial pathogenesis. *The central hypothesis of the proposed experiments* is that the targets of the HopU1 ADP-RT type III effector will be components of innate immunity. We formulated this hypothesis based on...

Reviewing a Sample Proposal: Work in Groups

See handout for Exercise 3:

Grant Area: Pilots for Junior Investigators in Basic and Clinical/
Translational Sciences

Project Title: The Role of Natural Killer T cells in Sarcoidosis

Amount Request: \$30,000

P.I. Name: Laura Koth, M.D.

5. Background and Significance

Back to that Outline

Specific Aims: goals of the research you intend to conduct

✓ **Background and Significance:** importance of the research to science and public health

Preliminary Studies/Progress Report: data showing the viability of your proposal

Research Design and Methods: detailed description of your planned experiments

Background and Significance

Is its own section for many funding agencies:

Specific Aims

Background and Significance

Preliminary Studies

Research Design & Methods

Background and Significance

Is sometimes two separate sections:

Specific Aims

Background

Significance

Preliminary Studies

Research Design & Methods

For some agencies, the Significance section comes *before* the Background section.

Background and Significance

Not a section of an NIH Proposal. Significance is included in the Research Strategy Section, as is Innovation.

Specific Aims (own page, separate section)

Research Strategy (consists of several parts)

Significance

Innovation

Approach

Preliminary Studies (for new applications)

Progress Report (for renewal and revision applications)

source: NIAID

Background and Significance

Purpose:

Build enthusiasm for your work by establishing several things in more detail than the “capsule” version of this in the Specific Aims section.

Background and Significance

Background:

- 1) Brief and focused history of what has been done about the problem
- 2) Current state of knowledge in the field
- 3) Gap(s) in the field that your project will fill (*the ones that you highlight in your narrative should be the ones you address in your proposal!*)
- 4) Theories and concepts that will guide your approach

Significance:

Why the study is important.

Background and Significance

Position your project in relation to other efforts and show how your project:

- will extend the work that has been previously done
- will avoid the mistakes and/or errors that have been previously made
- will serve to develop stronger collaboration between existing initiatives

or

- is unique since it does not follow the same path as previously followed

Background and Significance

Not an exhaustive literature review!

You don't need to show that you've read everything.

Be selective, deal with contradictions, cite your own work and that of the reviewers.



Background and Significance

In outline form, for all aims (or each one individually), include what you know about the following:

importance

existing knowledge

gaps in knowledge to be filled

innovation

Outline for Organizing the Key Information

	Importance	Existing Knowledge	Gaps to be Filled	Innovation
Specific Aim 1				
Specific Aim 2				
Specific Aim 3				

"Research Image", N. Bell

Background: It's about synthesis

There is **much** more background material than can possibly be included.

Content depends on precisely what hypothesis is to be tested, or what objective is to be attained. Be sure to...

1. Define the current state of knowledge in the field (using current, appropriate citations; refer to recent reviews).
2. Identify important gaps, discrepancies, questions.
3. State how the proposed research will address these gaps and increase knowledge by weaving your specific aims into the narrative.

Don't just *rehash* what's been written—*interpret* it!

Writing Tips

- ✓ **Write in paragraphs; 1 main idea per paragraph.**
- ✓ **Start with a topic sentence.** (e.g., *The pathogenesis of X is poorly understood.*)
- ✓ **Add the supporting sentences** (e.g., the reasons for this poor understanding)
- ✓ **Use transitions within paragraphs to indicate the logical progression** (e.g., *however, in contrast, next, although, nevertheless, likewise*)

Background: Synthesis not Rehash

Example: Topic sentence first, then details:

Currently, the standard treatment for congenital hematopoietic stem cell disorders is postnatal bone marrow transplantation. The treatment efficacy using this approach is often limited by transplantation complications, such as graft versus host disease and graft rejection, by the availability of few HLA-matched donors, and by the morbidity of host myeloablation preceding transplantation (**reviewed in 2**). The induction of donor-specific tolerance to transplanted allogeneic stem cells without long-term immunosuppression would therefore have important clinical applications.

Background: It's about synthesis

- ✓ **Within (and between) paragraphs**, use **transitions** that make logical connections explicit.

Transitions can be words or phrases:

therefore * thus * for example
first * second * third * last
in addition * in contrast * however
because * furthermore * moreover
in brief * although * whereas

Background: It's about synthesis

✓ **End paragraphs with closing sentences:**

"These studies demonstrate the importance of...
(elaborate)..."

"These studies provide the important background for
this study in..."

"The proposed project will build on this previous work
*[or address limitations in the previous work by
(elaborate)]*..."

Background: It's about synthesis

✓ Focus on the ideas, not the names & dates

Names break up the narrative flow:

BAD: Jones *et al.* (2010) first found . . ., then Liu *et al.* (2011) reported...

Only drop names if it will really help.

Do drop your own name because it gives you credibility:

Your relevant published work gets cited here: “*We previously showed...*”

You can also direct readers “forward” by telling them to “*see preliminary data*”.

Background: It's about synthesis

- ✓ **Focus on the ideas, not the names & dates**

Example

Numerous studies have shown that inflammation increases SQ RBC adhesion (5, 30, 34, 40) but few have provided direct evidence linking inflammation to vaso-occlusion. **In the most convincing study to demonstrate this link (30)**, platelet activating factor increased SQ RBC-endothelial adhesion and vaso-occlusion in the artificially perfused rat mesentery, and blockade of the pro-adhesive integrin $\alpha_5\beta_3$ attenuated these events.

Background: It's about synthesis

- ✓ **Describe key findings from previous studies as concisely as possible.**

Example

Ectopic expression of *nkx2.5* in *C. elegans* body wall muscle
directly **activated expression of the endogenous *myo-2* gene.**

Describe the method in a sentence that presents **the results** = 2 for the price (space) of 1

Background: It's about synthesis

Example: Tying it all together (**subheading**, paragraph with **topic sentence**, supporting sentences, **transition words/phrases**), **explicit link to the proposed work**.

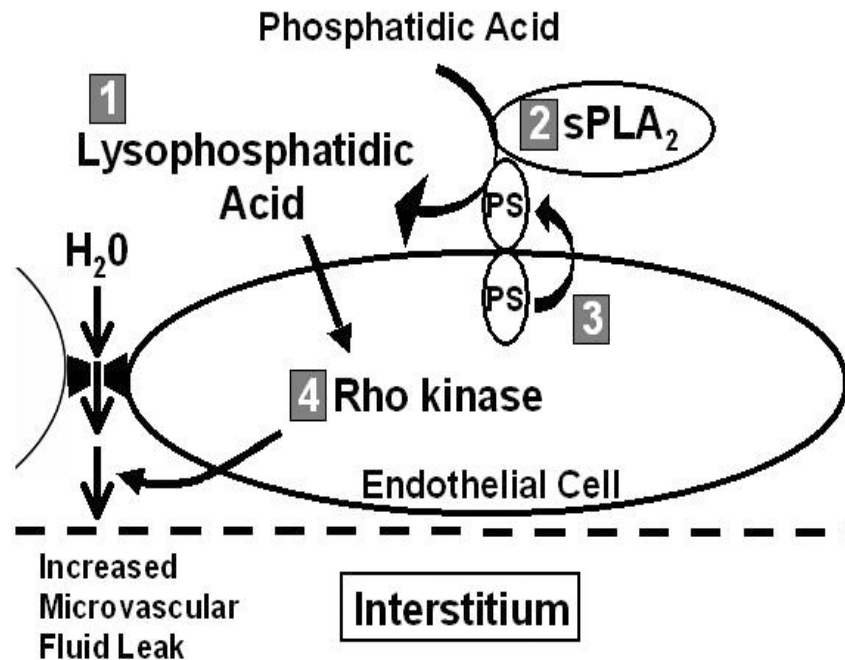
NOTE: No names & dates!

Regulatory T cells (Tregs) have been implicated as critical regulators of the immune system, responsible for maintaining immune self tolerance.⁹ Through the production of inhibitory cytokines and/or direct inhibition with cell to cell interactions, Tregs function to inhibit immune activity and thereby maintain self tolerance. **Furthermore**, recent evidence has demonstrated the ability of Tregs to promote tolerance following allogeneic postnatal bone marrow transplantation.¹⁰ **Little is known, however**, regarding their involvement in allogeneic IUHSTx and **this proposal will address the application of Tregs to improve host engraftment after IUHSTx.**

Source: Amar Nijjal, UCSF Dept of Surgery

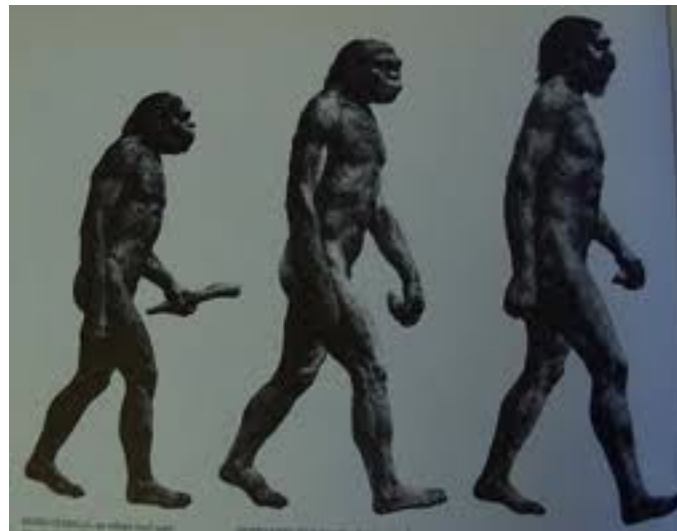
Background: Illustrate

Use figures to make key points, illustrate hypotheses and aims (many reviewers are “visual”).



Significance

1. Can your research move the field forward?
2. Will progress in this endeavor make a difference in human health?



Significance

Convinces reviewers that your research addresses an important, clearly defined question that pertains to health/mechanisms of disease.

Explains why your proposed experiments are an important extension of your preliminary studies.

Significance of your research **is not the same** as significance of the disease!

How to Communicate Significance

Establishing the source of tumorigenesis is a **fundamental and unresolved issue** in pancreatic cancer research. The cells of origin may solely determine pancreatic tumor phenotype.

Alternatively, it may be the unique combination of genetic “hits” amassed by pancreatic cells, rather than the cells of origin, that determines tumor phenotype. It is the goal of my proposal to distinguish between these possibilities.

Source: Sam Wang, UCSF Dept of Surgery

Reviewing a Sample Proposal: Work in Groups

See handout for Exercise 3:

Grant Area: Pilots for Junior Investigators in Basic and Clinical/
Translational Sciences

Project Title: The Role of Natural Killer T cells in Sarcoidosis

Amount Request: \$30,000

P.I. Name: Laura Koth, M.D.

6. Preliminary Studies

Back to that Outline

Specific Aims: goals of the research you intend to conduct

Background and Significance: importance of the research to science and public health

✓ **Preliminary Studies:** data showing the viability of your proposal

Research Design and Methods: detailed description of your planned experiments

Preliminary Studies

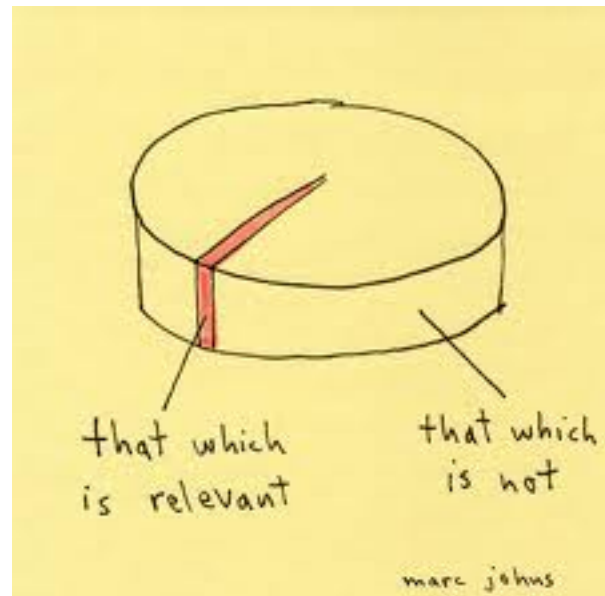
- ✓ Shows that you know what you're doing
- ✓ Shows that the work is feasible
- ✓ Shows suitable groundwork has been done (by you/ your mentor)
- ✓ For clinical studies, shows pilot data on proposed intervention and availability of study participants

Preliminary Studies: Guidelines

- 1) Recommended length = follow agency guidelines!
- 2) Include references.
- 3) First section provides an overview of preliminary data collected.
- 4) Subsequent sections **(with informative subheadings to guide the reader)** describe preliminary studies that support each specific aim.

Preliminary Studies

- ✓ Show only data that is relevant to the current proposal. Make it obvious how the data is relevant to what you propose to do.



Preliminary Studies: Organization (Basic Science)

In each section describing preliminary data to support a Specific Aim...

- Describe central experiments and the subsidiary experiments done to advance or exclude alternative explanations.
- Cite relevant publications and unpublished work.
- Make it clear why you did the studies and what the results mean (but avoid sweeping claims).

Preliminary Studies: Organization (Clinical Research)

In each section describing preliminary data to support a Specific Aim...

- Indicate which studies provided experience with the proposed methods (e.g., study design, intervention, enrollment strategies, assessment tools) of the current study, even if they are on a different topic.
- Cite relevant publications and unpublished work.

Preliminary Studies: Example

1. Begin with a brief introduction that gets right to the **gap in knowledge** and an **overall statement of what you did** in the preliminary studies for the current grant:

Both Hedgehog (Hh) and Wnt have long been known to play an important role in embryonic development, **but the exact nature of their contributions to cancer development remains obscure.**

Previous histological studies on human tumor samples **and recent work from our laboratory** have implicated the Hh and Wnt signaling pathways in pancreatic tumorigenesis [6, 7]. **Based on this work, we have developed mouse models of several pancreatic tumors.**

Source: Sam Wang, UCSF Dept of Surgery

2. Next, describe in detail what you did and **your interpretation of what it means**, and refer to tables and figures as needed to show your data:

In PanIN-PDAC lesions, we found that k-ras activation led to Hh signaling, that in turn activated the Wnt pathway. **These results imply a step-wise relationship** from k-ras activation to PDAC formation, via Hh and Wnt signaling (Figure 1) [8]. **This model suggests** that Hh or Wnt activation would also produce PanIN-PDAC. While simultaneously activating k-ras and Hh (via GLI2, a downstream mediator of Hh) resulted in PanIN-PDC, triggering Hh alone led to only undifferentiated tumor formation [9] (Table 1).

2. More about **what you found** and **what it means**:

When we perturbed the Wnt pathway, the results were also confounding. **Triggering Wnt alone via an activating mutation of β -catenin (β -cat^{ex3}), which is the downstream effector in the Wnt pathway, led to formation of solid pseudopapillary tumors (SPT), a rare and indolent type of pancreatic neoplasm, without evidence of PanIN-PDAC. More interestingly, when k-ras and Wnt were activated together, acinar cell carcinoma-like tumors (ACC) formed without PanIN-PDAC (unpublished data, Table 1). Like SPT, ACC is rare and comprises less than 1% of pancreatic tumors. However, it is more malignant in nature. **This finding is notable because** k-ras activation in the absence of exogenous Wnt activation results in PDAC formation.**

3. Summarize...and end at the “doorstep” of your first specific aim (or the proposed study).

Even though our early work suggested that Hh and Wnt act as intermediaries in a k-ras-PanIN-PDAC progression model, our recent studies suggest a more complicated relationship. **Currently, it is unknown** whether each type of pancreatic tumor arises from a unique cell type that is transformed when certain signaling pathways are perturbed. Alternatively, the tumors may originate from the same cells but the phenotype is determined by the combination of genetic changes. **The objective of the proposed study is** to establish the role that each pancreatic cell type plays in the formation of various pancreatic tumors.

Preliminary Studies: Details

All tables and figures necessary for the presentation of preliminary results must be included in this section.

Legibility is critical or figures (in particular) **are a waste of space** and source of frustration for reviewers.

A figure or table that accompanies the text should be inserted ***after*** referring to it in the text. If there's no room at the bottom of the page after a table or figure is first mentioned, moved it to the top of the next page, with a note on the preceding page that says '(see Figure 6, top of next page)'.

Preliminary Studies: Details

Figures should include legends and footnotes.

The first part of the legend should include whatever description is relevant to making the figure intelligible and include the meaning of all symbols, including error bars.

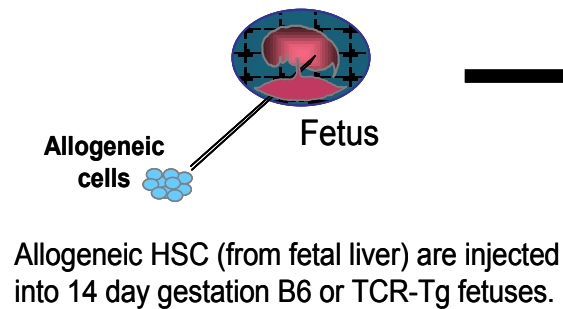
The second part of the legend can take advantage of the fact that figure legends (and footnotes for tables) ‘must be readily legible’, (whereas text must be 11 pt font). You can therefore provide methodologic summaries in figure legends and table footnotes, using 9 pt font. That way, reviewers can read it if they want to, but you don’t take up a lot of text space

Source: *“The Grant Application Writer’s Workbook. A Guide to a Successful Proposal, National Institutes of Health (Beta Edition), by SW Russell and DV Morrison. 2009*

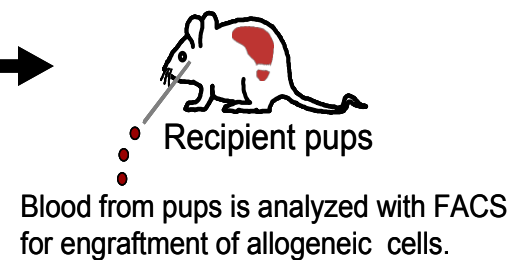
Preliminary Studies: Details

Figures should include legends and footnotes.

1) Fetal stem cell injection



2) Analysis of chimerism



sacrifice

3) Allospecific T cells and their cytokine profiles

- Lymphoid organs are analyzed to detect
- Allospecific T effector cells by Elispot assay (expect deletion in chimeras)
 - Allospecific T regulatory cells by suppression assay (expect increase in chimeras).

Fig 2. Experimental Design for Aims 1a and 1c.

Source: Amar Nijjal, UCSF Dept of Surgery

7. Research Design and Methods

Back to that Outline

Specific Aims: goals of the research you intend to conduct

Background and Significance: importance of the research to science and public health

Preliminary Studies: data showing the viability of your proposal

✓ **Research Design and Methods:** detailed description of your planned experiments

Research Design and Methods

Purpose of this section: to describe how you will carry out your specific aims.

Usually the longest section; approximately half the research plan.

Research Design and Methods

Content:

- experimental design
- specific methods used
- data collection & analysis
- any new methods & why they are better
- potential problems & how to mitigate them
- expected results
- alternative approaches
- timetable for completing project

Research Design and Methods

Design = the way in which you conceptualize your experiments.

Methods = detailed discussion of exactly what you will do to carry out your experiments.

Discuss them separately.

Design and Methods: Writing (Basic Science)

Structure is provided by the science itself:

- Experiments proposed should flow logically from the specific aims.
- Aims usually are achieved through a central experiment and subsidiary experiments (to confirm or exclude potential interpretations of the central experiment).

Design and Methods: Writing (Basic Science)

Cover Five Items Critical to Each Experiment :

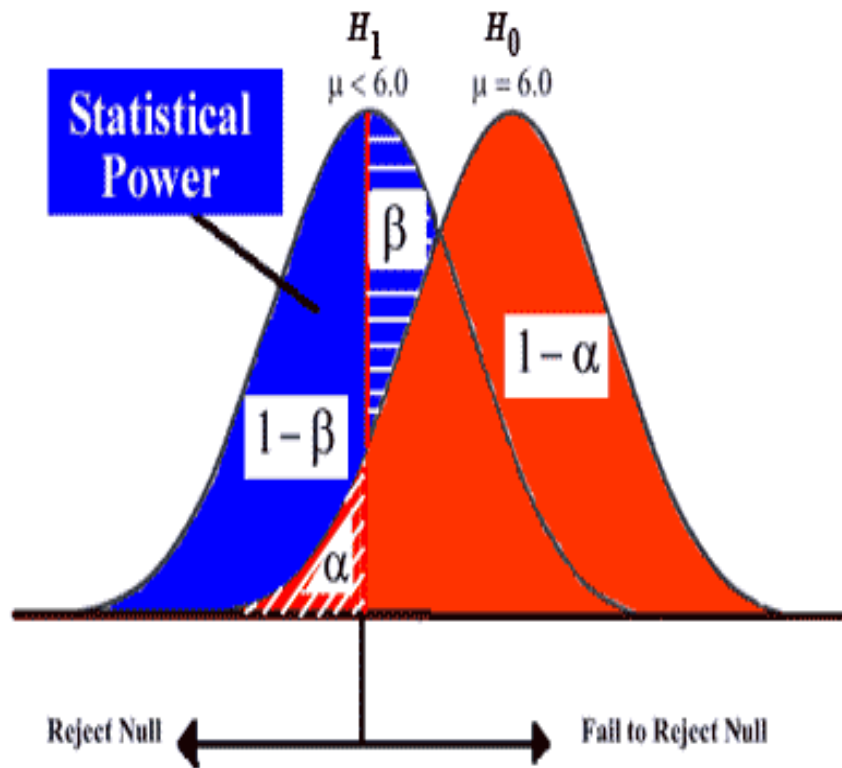
- 1) Rationale and Design
- 2) Expected Results
- 3) Statistical Evaluation
- 4) Pitfalls
- 5) Alternatives

Design and Methods: Writing (Basic Science)

Organize each subsection as follows:

- Specific Aim
- Hypothesis
- Rationale
- Experiment(s)
 - For each one:
 - 1) Rationale and Design
 - 2) Expected Results
 - 3) Statistical Evaluation
 - 4) Pitfalls
 - 5) Alternatives
- Methods

Design and Methods: Writing (Basic Science)



Include Power Calculations:

Do you have enough statistical power to find effects if they exist?

Design and Methods: Writing (Basic Science)

If you can, include a concluding paragraph:

Example: The single greatest obstacle to widespread clinical practice of islet transplantation for Type I diabetes is a critical shortage of islet tissue. Means to augment islet cell mass *in-vitro*, coupled with means to efficiently utilize islets obtained from existing donors, would have a major impact on the field. Techniques for *in-vitro* expansion and cryopreservation adult human islets offer a potential solution for these barriers to transplant, but require further testing in animal models before application in humans. We aim to characterize and test such techniques in a diabetic murine model of human islet transplantation as a prelude to future human trials.

Source: Jon Carter, UCSF Dept of Surgery

Design and Methods: Writing (Basic Science)

Methods: Some Rules of Thumb

- ✓ Describe in detail all methods that have not been published.
- ✓ Give a brief overview of methods that have been fully described previously in published articles and cite the reference.
- ✓ Write short paragraphs.

Design and Methods: Writing (Clinical Studies)

Cover the Following Topics:

Study population

Subject recruitment, enrollment, and retention

Study procedures

Study measurements

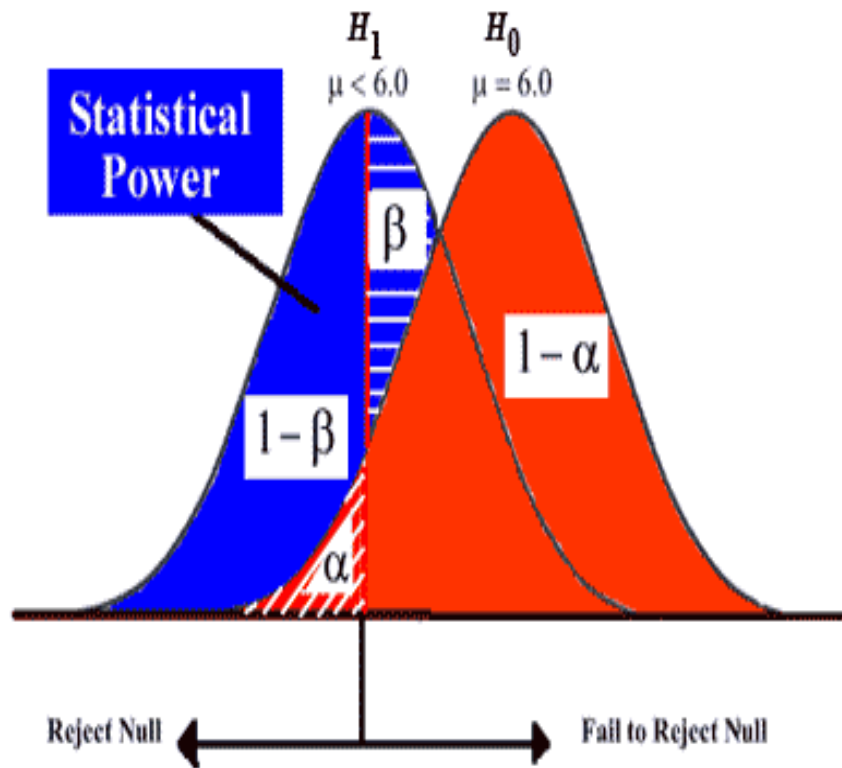
Data quality & management

Data analysis

Potential problems and alternative approaches

See Inouye and Fiellin article for details and examples
(citation is in the Supplemental Handout)

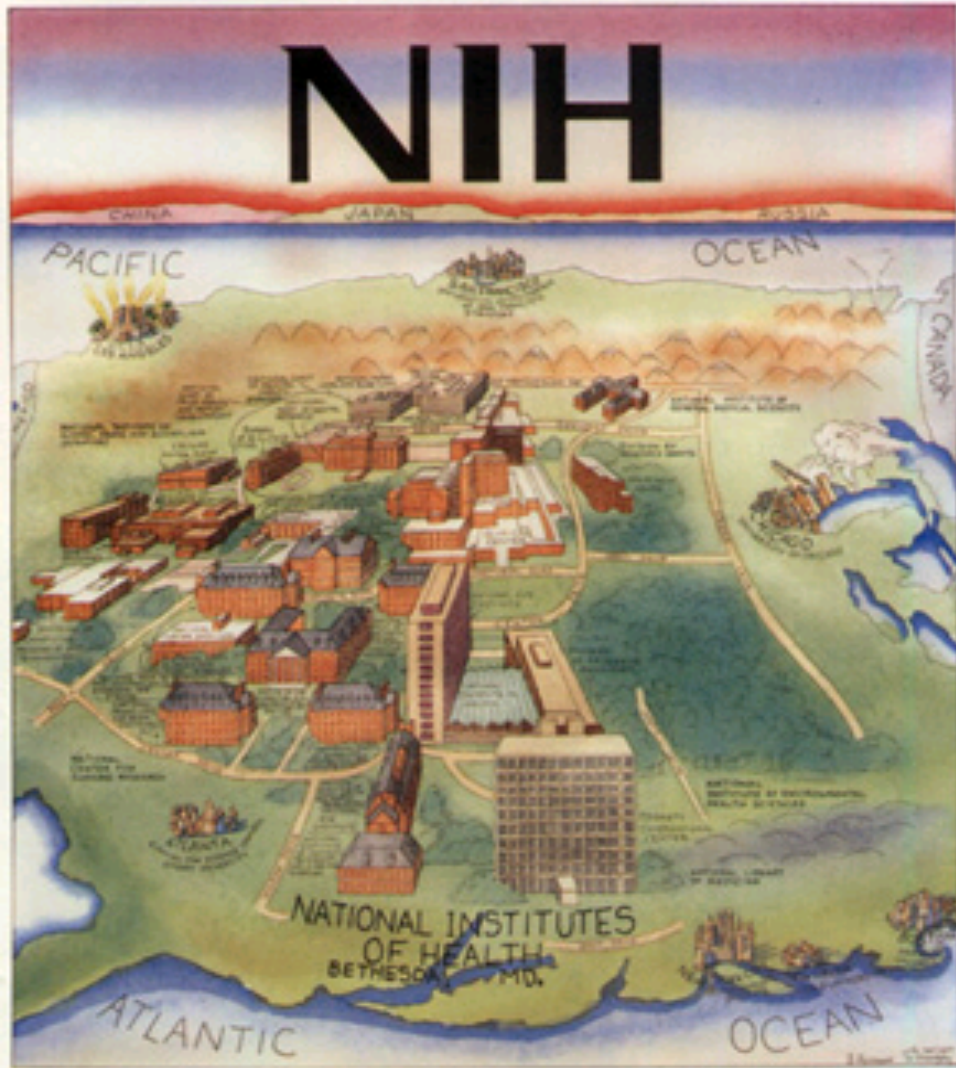
Design and Methods: Writing (Clinical)



Include Power Calculations:

Do you have enough
statistical power to find
effects if they exist?

NIH



Research Plan: Recap of the NIH Format

SPECIFIC AIMS (1 page)

RESEARCH STRATEGY (limited to 12 pages for R01)

A. Significance (0.5-0.75 page)

B. Innovation (0.5-0.75 page)

C. Approach

Needs to cover, for each aim:

Justification & feasibility

Research design

Expected outcomes

Potential problems and alternative strategies

NIH Format: *Thoughts* on How to Organize the Research Strategy Section

Example 1: Organize under each Aim

a. Specific Aim (restated)

b. Significance (of that aim)

c. Innovation (of that aim)

d. Approach (for that aim)

Expected Results, Potential Problems, Alternative Solutions

e. Preliminary Studies (for that aim)

Example 2: Organize more broadly

a. Significance (for overall study)

b. Innovation (for overall study)

c. Approach

c1. Overview and specific aims

Aim 1 (restated), followed by overall approach (1 paragraph)

Aim 2 (restated), followed by overall approach (1 paragraph)

Etc.

c2. Preliminary studies

“The following preliminary data support our aims and demonstrate our ability to do the following: 1)...2)... etc.

c3. Methodology and analysis (describe for each aim, using additional subheadings as appropriate)

c4. Potential problems and alternative strategies (describe for each aim, using additional subheadings, as appropriate)

c5. Timeline

Writing Your Research Plan: Examples to Follow

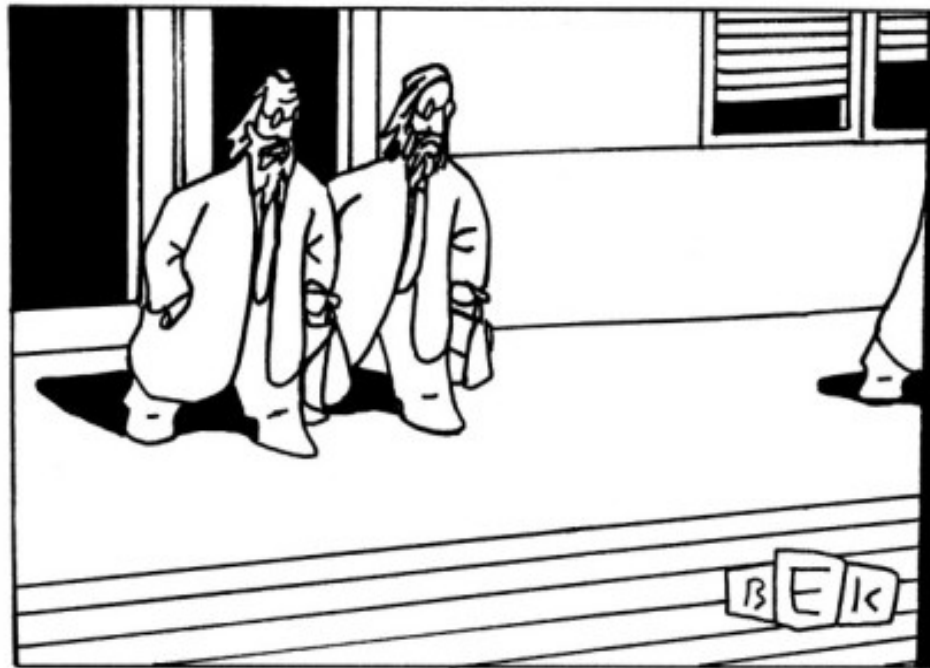
Sample grants sent to you (including the UCSF RAP proposal we looked at earlier)

See the Supplemental Handout for:

- Inouye and Fiellin article for clinical proposals
- Sample grant proposals at NIH NIAID website
- Sample grant proposals at the CLIMB website

ASK YOUR MENTOR FOR EXAMPLES!

8. The Abstract and Title



"I've been reading the trasbiest scientific abstract."

The Abstract

- 1) a brief background of the project
- 2) hypothesis and specific aims
- 3) the unique features of the project
- 4) the methodology to be used
- 5) expected results
- 6) evaluation methods
- 7) description of how results will affect other research areas
- 8) the significance and health relevance of the proposed research

The Abstract

View the abstract as your advertisement.

Be complete, but brief.

Use active voice and strong action verbs.

Write it so it can be made public without revealing intellectual property.

Use all the space allotted.

The Abstract

Look for examples!

✓ **Your mentor's proposals**

✓ **NIH:** <http://projectreporter.nih.gov/reporter.cfm/>

Excellent guidance:

[http://blog.citizen.apps.gov/NIAIDFunding/
2011/02/tips-for-other-application-parts/](http://blog.citizen.apps.gov/NIAIDFunding/2011/02/tips-for-other-application-parts/)

Last But Not Least: The Title

Research intent and value should be communicated clearly, in plain English:

Before: G-PROTEIN SIGNALING IN SYMPATHETIC OVEREXCITABILITY

After: THE ROLE OF ABNORMAL G-PROTEIN SIGNALING IN HEART DISEASE

Look for examples:

* NIH's

[RePORT Expenditures and Results \(RePORTER\)](#)

query tool

9. What is the #1 piece of advice from successfully funded investigators about writing a grant proposal?

Allow Enough Time to Prepare a Great Application!



Allowing Enough Time Can Help Prevent Fatal Mistakes



Allowing Enough Time Can Help Prevent Fatal Mistakes

Mistake #1: No mastery of the literature

The applicant has not considered the recently published research on determinants of risk behaviors predicting graft survival in transplant patients who have HIV/AIDS infection, whereas the much older literature has been discussed.



Allowing Enough Time Can Help Prevent Fatal Mistakes

Mistake #2: The Research Plan is overly ambitious

There are some concerns as to the likelihood of completing aims 2 and 3 within the allotted time given the pilot nature of the work and the number of techniques that need to be mastered.



Allowing Enough Time Can Help Prevent Fatal Mistakes

Mistake #3: There are problems with the hypothesis, study design, experiments, data analysis...

- Hypothesis is ill-defined, lacking, faulty, diffuse
- Methodology is questionable, unsuited or flawed
- Inconsistency in level of detail from one experiment to the next
- Agents, clinical interventions, high tech procedures are not adequately described
- Are there alternatives worth mentioning
- Data collection procedures are not clear
- Power calculation isn't included
- Data management plan is unclear

It is unclear that the analytic techniques will yield the anticipated outcomes.

Allowing Enough Time Can Help Prevent Fatal Mistakes

Mistake #4: Resources and/or mentorship not adequately described

It appears that the lab does not have established techniques, models related to the applicant's training and research goals. There is insufficient supervision by the mentor.



Allowing Enough Time Can Help Prevent Fatal Mistakes

Mistake #5. The proposal is messy, ergo the research will be messy too.

The committee commented on the less than stellar grantsmanship throughout the proposal. There were many misspellings, typos, and grammatical errors. Some members commented on whether the investigator would approach research and publication in a similarly sloppy fashion.



10. Revising Your Prose (A Few Reminders)

Revising

Words *in scientific writing should be:*

1. Precise (increase/decrease NOT change; dog, mouse, NOT animal)

2. Simple (prior to→before, following→after, initiate→begin)

3. Necessary (fewer words = less “noise” and more message)

4. Familiar

Do not invent words (endorphinized→injected endorphins)

Avoid jargon

Limit use of abbreviations

5. Humane (*patients do not fail therapy*)

Revising: Use Passive Voice Selectively

Use active voice when you are talking about your aims, hypotheses, inferences, or assumptions, and when you need to distinguish that previous findings or studies or models are *yours*:

- ✓ Our hypothesis is that cotransplantation of donor-specific Tregs with donor cells will improve host engraftment.
- ✓ We have established the previously described fetal mouse model in our laboratory.

Use passive voice to describe methods when you just want to emphasize what was done, rather than highlighting *who did it*:

- ✓ DNA was extracted from the sample.

Revising: Put the Action in the Verb

Verbs express action in English.

If the action of a sentence is expressed by the main verb, the sentence is natural and direct and easy to understand.

Genomic DNA was eliminated.

As opposed to this:

Elimination of genomic DNA was performed.

Revising: Liberate Imprisoned Verbs!

Look for "increase" and "decrease" as nouns.

Look for weak verbs, such as...

occurred
was achieved
was observed
was noted
was seen

Look for nouns made from verbs:

-tion	prolongation, formation
-ment	measurement, assessment
-ence	occurrence, existence
-al	removal, disposal



Revising: Mentor Review



To submit the most polished proposal possible, allow time for review by mentor(s).

- Have mentor(s) “vet” Specific Aims first.
- Then go on to write other parts of the narrative.

Writing Grant Proposals: The Last Word...

Never forget that your proposal is a work of persuasion and not a collection of disparate facts. It isn't merely a description of the work you want to do; **you are making an argument that it is work that needs to be done and that you are the right person to do it.** Make your argument convincingly.

~ **Science (NextWave) 2001**

Sources

Faculty and Residents, UCSF Dept of Surgery

www.northwestern.edu/climb/resources/written-communication/index.html

http://www.ninds.nih.gov/funding/write_grant_doc.htm#problems

<http://www.nimh.nih.gov/research-funding/grants/common-mistakes-in-writing-applications.shtml>

http://principalinvestigators.org/pdf/5_Common_Mistakes.pdf