Writing Your Thesis Proposal
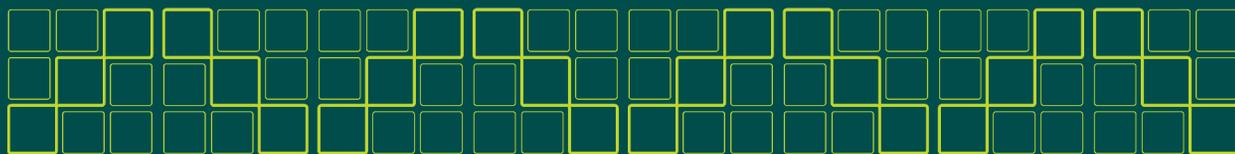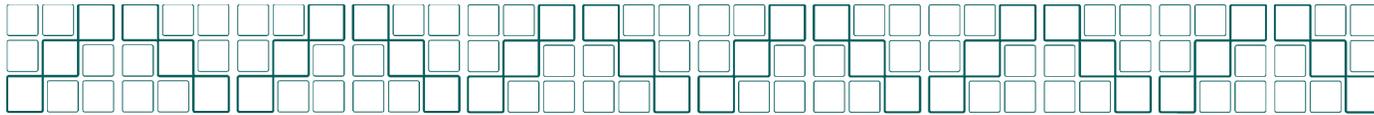
**Sharon L. Milgram
milgrams@od.nih.gov**

Why?

- Insures that you have focus and direction

- Initiates dialogue with your mentors and committee

- Assures that you have a good grasp of the field, including important questions, current controversies, gaps, broad relevance, etc

- Assures that you know (or can learn) techniques required to succeed

- Helps you envision potential problems and devise solutions in advance

- Helps you develop writing/grant writing skills

- Can be used as a "gate keeper"
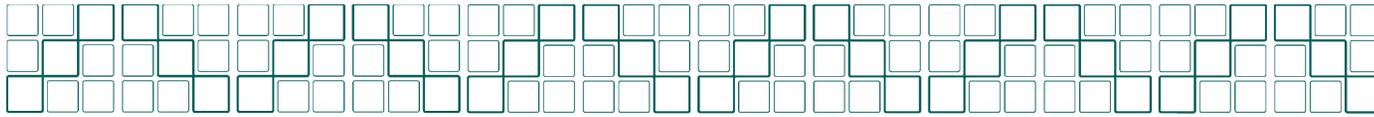
The Organizational Process

"Many of us when confronted by a writing deadline, skip the organizational phase of writing. This is akin to leaving on a trip to unknown parts without a road map, hotel reservations, or plans of any sort."
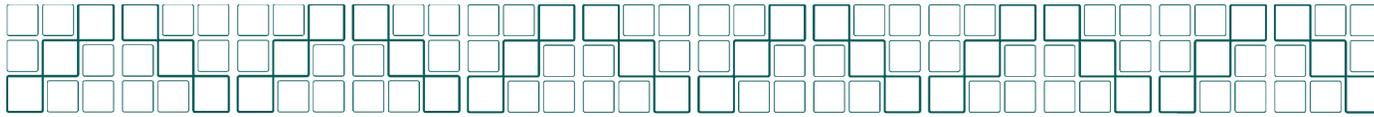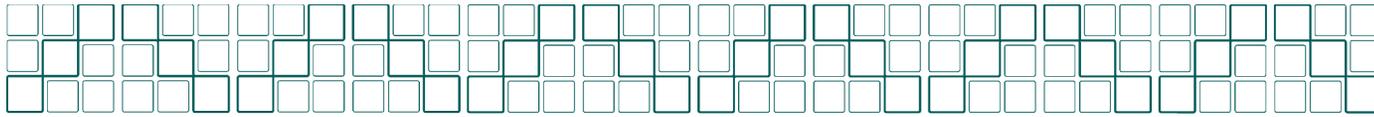
Getting Started: Program Issues

- Start by reading the instructions CAREFULLY

- Talk with your program directors

- Find 2-3 examples from senior students

- Communicate with your mentors and let them know WHAT help you will need and WHEN you will need it
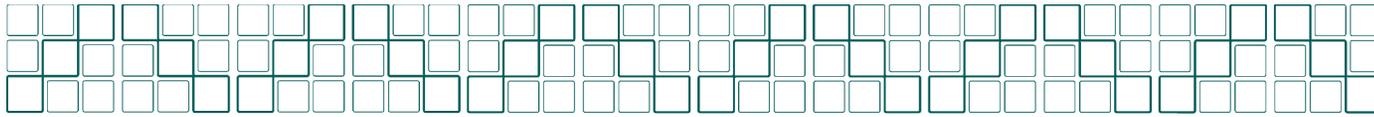
Getting Started: Science

- Don't start writing immediately - spend time thinking & talking first
- Read the literature broadly - not deeply - save important papers for later
- Engage your lab and mentors in the brainstorming process
- Find outside experts to talk with - but go prepared
- Make lists of methods you need to learn and reagent, cell type, animal, or human subject issues you need to deal with

Getting Started: Personal Issues

- Find resources to improve your writing
    - OITE writing courses or courses at your university
    - Watch George Gopen workshop on-line
    - Books in the OITE Career Library
- Set a daily writing schedule (and stick to it!)
- Form a writing group to help with proof-reading, procrastination, writer's block, etc
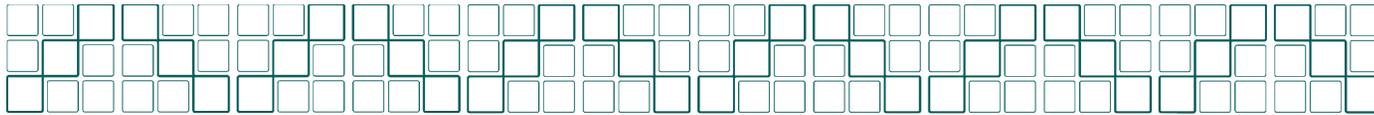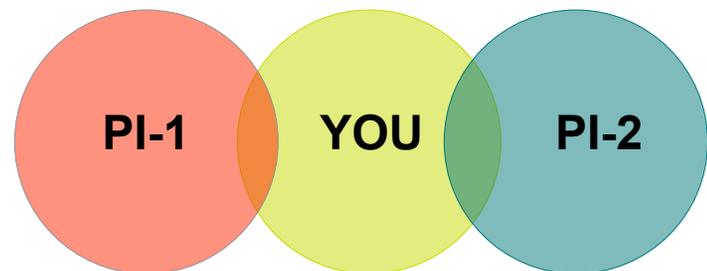
Negotiating Content
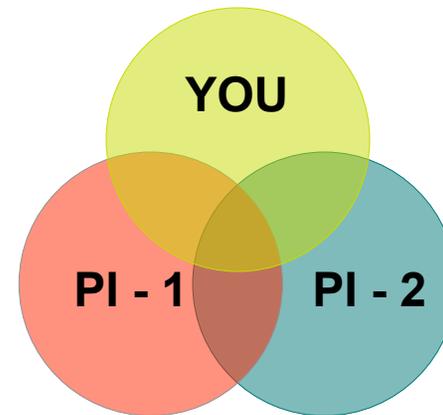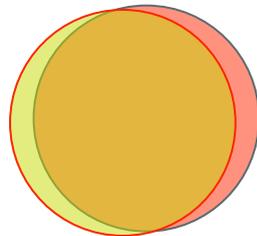
- Start talking with your mentor(s) before you get too far along

- Agree on the Aims before beginning other sections

- Be aware that the proposal is not a contract written in stone, so be willing to compromise
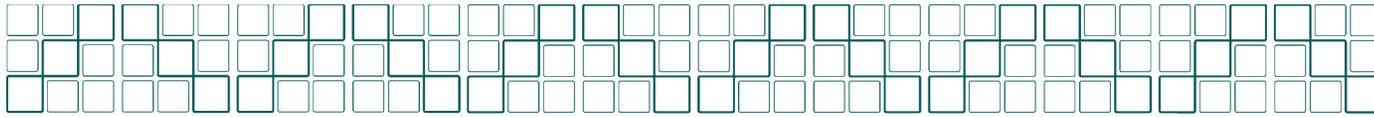
Whose Project Is It?
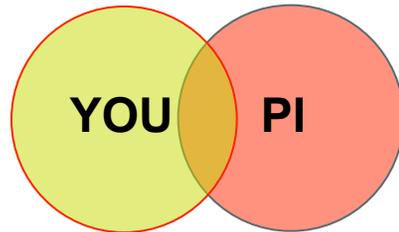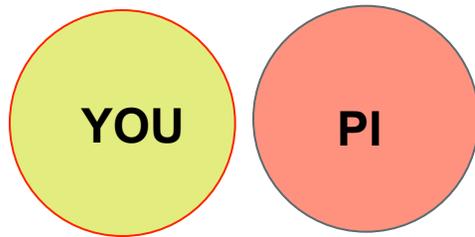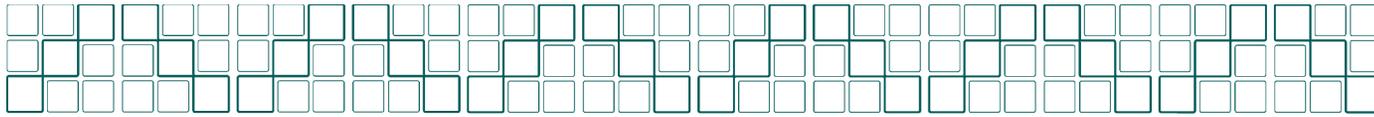
Example: #1

My interest: regulation of CFTR trafficking by NHERF-family PDZ proteins

Bill's interest: identification of protein-protein interactions using mass spectrometry

Bill's thesis: Using mass spectrometry to identify novel regulators Of CFTR trafficking, turn-over, and activity
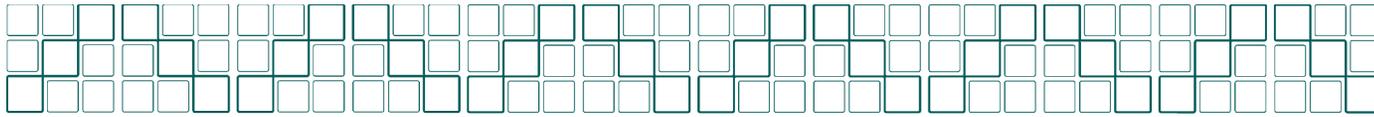
Example: #2

My interest: regulation of CFTR activity by protein kinases

Larry's interest: regulation of ciliary beat frequency

Pat's interest: compartmentalization of cell signaling pathways

Pat's thesis project: Identification and characterization of signaling proteins in human respiratory axonemes
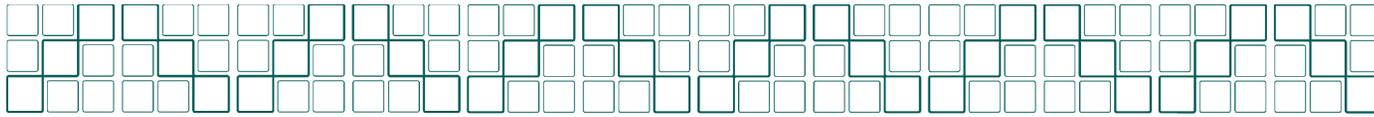
A Typical Thesis Proposal

- Title
- Abstract
- Specific aims
- Background & significance
- [Preliminary data]
- Research design & methods
- [Timeline]
- References

- But in any order and format
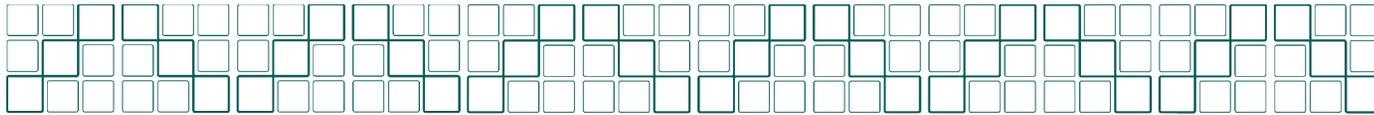
Aims

- The "opening statement" -- tells what your proposal is about
- Should generate enthusiasm & excitement for your ideas - should grab the readers attention
- The reader MUST finish this section convinced that the work you propose is significant and that you have a feasible approach; they should want to read on…
- Should end with a list Aims (and subaims)
- No more than 1/2 to one page
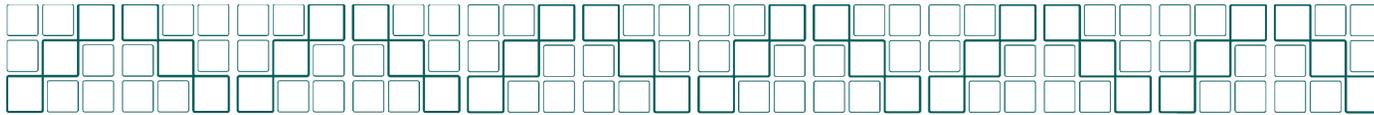
An Example

The goal of this research is to characterize the unique renal function of two proteins IKEPP and PDZK1, which I hypothesize regulate solute transport via interactions with ion channels, transporters, and signaling proteins. IKEPP and PDZK1 are composed of four tandem PDZ domains, protein-protein interaction modules, involved in organizing multi-protein complexes. Both proteins are expressed in the nephron and have been shown to interact with and regulate the activity of proteins involved in ion transport in other epithelial tissues. While IKEPP and PDZK1 share similarities in domain organization, I predict that each protein has a unique function in the kidney. Preliminary immunohistochemical analyses indicate that IKEPP localizes to multiple nephron segments in both the cortex and medulla, while previous reports suggest that PDZK1 expression is restricted to the proximal tubules. Furthermore, my data shows that PDZK1 binding partners do not necessarily interact with IKEPP. Therefore, I propose to determine the specific localization of IKEPP and PDZK1 in the nephron, identify interacting proteins, and study the functional implications of these interactions. This research will help elucidate the mechanisms underlying regulated solute transport which are fundamental to our understanding of basic renal physiology and disease. Specifically, I will:
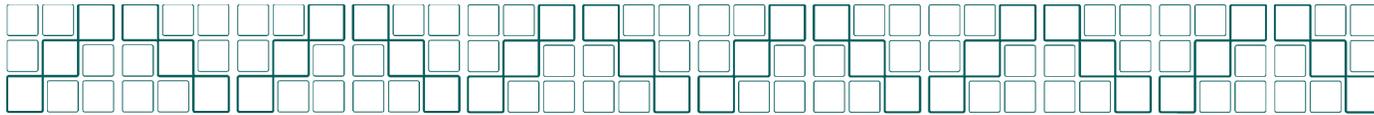
Example, Continued

Specific Aim 1:   Identify and characterize IKEPP-associated proteins in the kidney. Rationale: The proteins most similar to IKEPP (PDZK1, EBP50, and E3KARP) are known to associate with proteins involved in solute transport and cell signaling. Thus, I hypothesize a similar function for IKEPP. I will identify IKEPP-associated proteins and will characterize the functional implications of these interactions. Specifically I will:

A. Purify IKEPP-associated proteins and identify them using mass spectrometry (MS)

B. Study the physiological relevance of new IKEPP-interacting proteins in cell culture model systems using dominant-negative and knock-down strategies
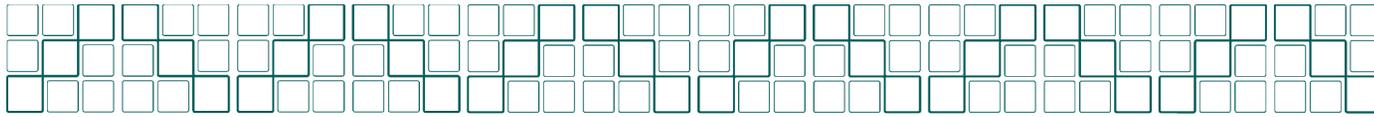
Background & Significance

- The place to clearly state the importance of the proposed research

- Looks both backward & forward

- Should be appropriately referenced with an honest & balanced discussion of others' work

- Points out controversies and discrepancies that your work will address

- Convinces the reader that you know what you are talking about & that your proposed work is the OBVIOUS next step

- Ranges from 1 - 3 pages depending on proposal length; no more than one or two figures
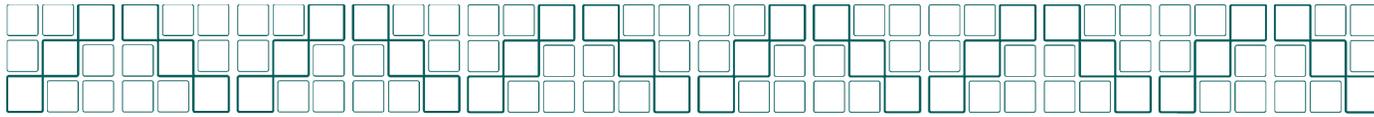
Preliminary Data

- Key pieces of data to generate excitement and enthusiasm for the proposed studies

- Demonstrates that what you propose is feasible

- Shows you are a careful scientist who does controls and does not over-interpret data

- Important to include data and to make the data easily viewed and interpreted

- Ranges from 2 - 8 pages depending on overall proposal length and time of the proposal
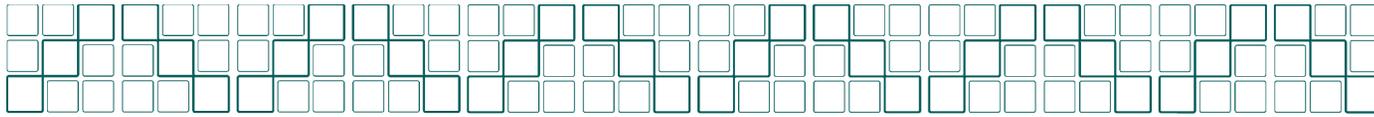
Research Plan

- Organized by Aims
- Balanced between over-view of approaches, rationale for specific experiments & the specific details
- Clearly discuss controls (positive & negative) for all experimental approaches
- Show you have thought through issues of feasibility, sample size, data analysis, etc
- Discuss data interpretation, potential pitfalls & alternate approaches
- Include a timeframe & discussion of critical collaborators if appropriate
- Include discussion of animal use or human subjects if appropriate
- Can put basic methods at the end or leave them out

Strong Research Plans:

- Explicitly state the rationale for the proposed studies

- Never assume the readers will "know what you mean"

- Use flow diagrams for overview, and for complex experiments and protocols

- Include well-designed, easy to follow tables and figures

- Address priorities if patient samples, reagents or resources will be limited

- Include a discussion of how the data will be analyzed and interpreted

- Includes realistic discussion of pitfalls and provides alternate approaches
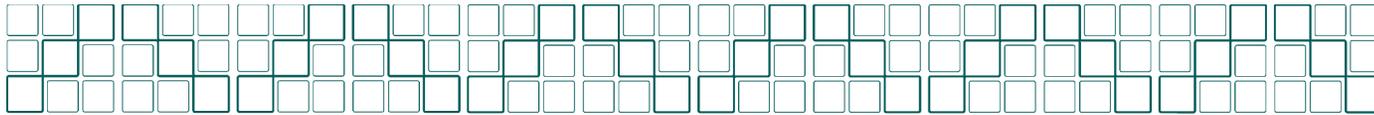
Abstract

- The Reader's Digest condensed version of your story
- Should begin by stating the problem & end by stating the impact of the work if successful
- Should stand alone
- Should not contain abbreviations or jargon
- May follow strict word limits
- Write it last but leave time for it!
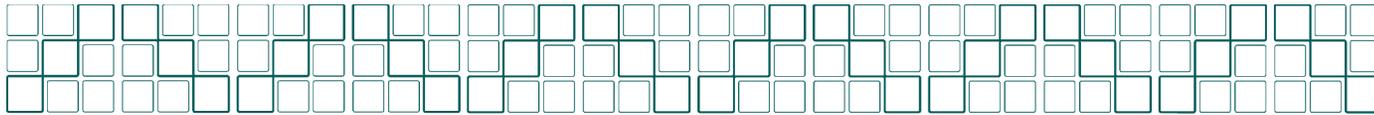
Help the Readers

- Format your application to present the proposal in "bite-sized bits" i.e. use section headings and bold type to identify section and subsection breaks

- Walk the reader through the experiments

- Repeat important points at several points in the proposal
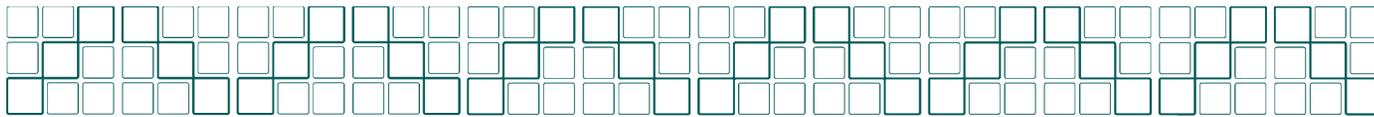
Key Features of A Successful Proposal

- Novel, important, and interesting experiments (but novelty is not
- Advances knowledge in the area of study
- Specific aims well defined and clearly related
- Experimental design well detailed
- Preliminary data support hypothesis
- Overall an "easy" read
- Student-driven elements are obvious but relationship to the mentor's work is clear
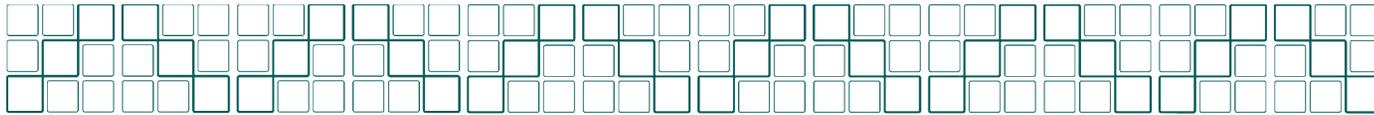
Common Criticisms

- Diffuse, unfocused or superficial examination of the field
- Poorly written with typographical errors and grammatical mistakes
- Lack of knowledge of published work
- Unrealistic amount of work
- Lack of experimental detail
- Too many irrelevant experimental details
- Mediocre preliminary data that is over-hyped
- Lack of experience in required methodologies
- Not enough discussion of potential pitfalls & alternate approaches
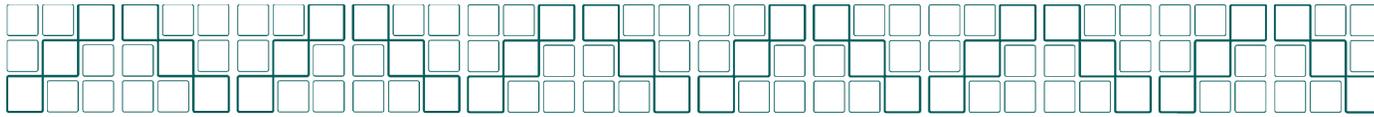- Competent but unexciting science
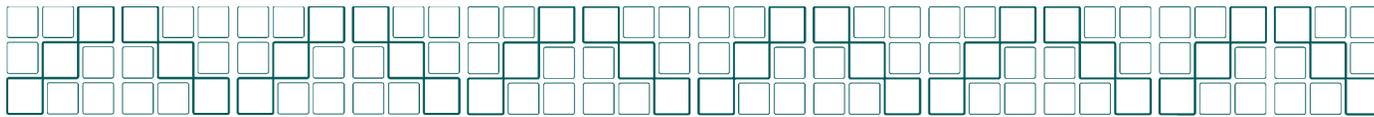
Remember: Strong writing can not compensate for bad ideas, but weak writing can easily ruin good ones
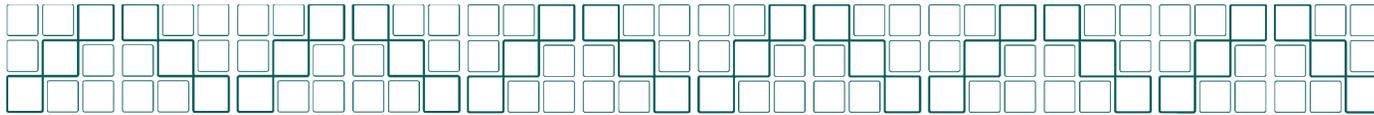
Some Parting Thoughts

- Be careful of over-extending during this process
- If you PI is busy and not engaged, seek help from other mentors
- Be careful which students you get advice from
- If writing is an issue, deal with that now
- This is not the time to "make your mark"

Questions?