

RESEARCH PROPOSAL

The research proposal is similar to a Thesis Proposal, a Predoctoral or a Postdoctoral Fellowship Application. Your research proposal for class is due **Monday May 1 at 12:00**. Each student will then receive two proposals on **Tuesday May 2 (1:30, in Rm 5001 McKinley)** for review in the Study Sections on the afternoons of **May 8, 9, or 10**. You must attend one of the Study Section days. (There will be more information on the Study Section at a later date.)

The proposal is for "your research as a postdoctoral fellow" and is for a period of three years. There must be a substantial genetics component to the proposal. Almost any topic can be undertaken and almost any organism can be used. However, the proposal should not be on the same topic in the same organism as your current or previous laboratory research, although it could be on a related topic in a different organism or a different topic in the same organism. For ideas about topics, you may wish to examine journals (e.g. *Genetics*, *Development*, *Trends in Genetics*, *Current Biology*, etc.) as well as attend Seminars (e.g. Dept. of Genetics, Developmental Biology, etc.). When contemplating possible topics, while it is useful to start more broadly, it is important to focus down to a small research area where there are both remaining unanswered questions as well as discrete experimental approaches that can be applied to address the questions. To ensure that the topic is reasonable and well focused, it should be cleared with Tim Schedl, Jim Skeath or Susan Dutcher (by appointment; a tentative outline of your proposal will be most useful for our discussion). An Abstract and Specific Aims of your proposal (no more than 1 page single-spaced or equivalent) is due **Monday March 20** (send it to advancedgenetics@genetics.wustl.edu). The Abstract should include the basic question or issue that you are addressing, in the context of a paragraph of background material, and the aims (usually two to three) of your proposal. How each of the aims will be executed can be indicated in a few sentences.

You will receive comments back from a faculty reviewer about a week later. You will have a chance to make revisions based on the comments and then present your Aims at your Discussion section in the week of April 10.

From the NIH grant format, only the research section will be used:

RESEARCH PLAN. Organize Sections A-C of the Research Plan to answer the following questions. 1) What do you intend to do? 2) What is known or has already been done? 3) Why is the work important? 4) How are you going to do the work? Do not exceed 20 double-spaced typed pages for sections A-C, which does not include Title pages, Figures, and References. You are limited to 4 pages for Figures / Tables (which can be incorporated into the text), and all references must include the titles of the articles. You may use any page distribution within this overall limitation; however, a typical format and distribution is indicated below:

A. Specific Aims. State the broad, long-term objectives and describe concisely and realistically what the specific research detailed in this application is intended to accomplish and any hypotheses to be tested. Two pages are recommended.

B. Background and Significance. Briefly sketch the background to the present proposal, critically evaluating existing knowledge, and specifically identifying the gaps that the project is intended to fill. State concisely the importance of the research described in this proposal by relating the specific aims to the broad, long-term objectives. Eight pages are recommended.

C. Experimental Design and Methods. Outline the experimental design and the procedures to be used to accomplish the specific aims of the project. Include the means by which the data will be collected, analyzed, and interpreted. Describe any new methodology and their advantage over existing methodologies. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims. Experiments should be organized in a logical progression and you should provide some indication of the relative importance of the different experiments to your overall goals. Provide a tentative sequence or timetable for the investigation. Although no specific number of pages is recommended for this section of the application, the total for Sections A-C may not exceed 20 pages (please number the pages).

The proposals should be converted to PDF format and emailed to me at <advancedgenetics@genetics.wustl.edu> by noon on Monday May 1st. To ensure that the review process is anonymous, on the title page put your student ID number, instead of your name, as well as the proposal title. However, for grading purposes, the file name of your proposal PDF needs to have your last name, first name and student ID number. Proposals that fellow students read will not have the name, only the student ID. To limit possible hard feelings between class members, all discussions in the Study Section are privileged and cannot leave the room. Please also send me a PDF that contains just your title page and your Specific Aims page. This will be given to the non-reviewer students in the Study Section, which is evaluating your proposal, so that they can follow along the discussion.

IT IS NEVER TOO EARLY TO START PLANNING AND THEN WRITING YOUR PROPOSAL!!

You should feel free to consult fellow graduate students, postdocs and faculty about your proposal, on any aspect; however, the writing must be your own. You should have someone proofread your proposal, particularly if English is not your first language.

Below are some helpful hints.

- 1) Don't write the Experimental Design and Methods section last. Since this section depends on knowing the details of techniques that you may not be familiar with and that are not always well explained in the literature, it's good to get your ideas down early. Show it to critical people in labs that have some familiarity with the research area/methods. Their input is useful.
- 2) The Experimental Design section should be organized around questions that you are posing.
- 3) When writing about a strategy/technique (e.g. enhancer screens, two-hybrid etc.), prior successes of the technique can be very persuasive. It is important to cite references for successful uses of such strategies and techniques. Some 'hot' techniques look great on paper but have terrible track records. Have an in depth knowledge of the approach and make sure your use of it is appropriate.
- 4) Know the feasibility of the techniques that you propose. If you propose a screen, what are the assumptions, and how much work will it be? (How long will it take? How many animals

need to be screened? etc.) If you are using a human pedigree, are there a sufficient number of meioses for the analysis?

5) Complete your thoughts. If you plan a screen, hypothesize about what may come out of it. Make it clear that you have thought through the outcomes and what they may tell you.

6) Clear summary charts and figures are highly appreciated by reviewers; even if they don't end up in the final version, they will help to organize your thoughts and facilitate the writing.

7) Your proposal is evaluated on what is stated. If you have an idea, don't assume it will be obvious to everyone. You need to support and defend your ideas. Additionally, your reviewers may know a lot of biology, but may not know the specifics of your area.

8) For this class, your proposal is basically genetic. However, spend time thinking about your proposal from a molecular, cell biological and/or biochemical perspective. Sometimes, a new idea or shortcoming will appear from this different view.

9) Use Correct genetic nomenclature so that the reviewer knows what you are talking about specifically (e.g. *phop-1::GFP*, which is GFP driven from the *hop-1* promoter vs *HOP-1::GFP*, which is GFP fused to the HOP-1 protein expressed from the *hop-1* promoter). Nomenclature is organism specific; details can be found on the model organism databases. We also expect that the reviewers of the class proposals will know what the author means, if the correct nomenclature is used.

10) Before you describe any experiment within the experimental design section, explain the logic/rationale as to why it is important to do this experiment. That is what will you learn and why is this important.

For example, in place of: To generate an eve-GFP fusion construct I will fuse in frame....

The principal objective of this aim is to identify genes that control the formation of the RP2 motor neuron in the *Drosophila* CNS via a classical saturation mutagenesis. Therefore, I need to identify easily and rapidly RP2 motoneurons in homozygous mutant embryos to see if these mutations alter RP2 development. To do this, I will construct a reporter gene that expresses GFP in RP2. I will make use of a defined regulatory region of the *eve* gene known to drive gene expression only in RP2. To generate a eve-GFP fusion construct I will fuse in frame....

11) If multiple methods can be used to achieve a goal (e.g.: yeast two hybrid/immunopurification). State the different ways that can be used, their advantages and disadvantages, and the logic behind your choice. For example:

III) To identify proteins that physically associate with Sanpodo or Numb during CNS development.

Multiprotein complexes carry out most cellular functions. Thus, Spdo and Numb function likely requires their association with many proteins. To understand how Spdo and Numb control cell-fate decisions it is important to identify these proteins and to elucidate their functions. Other labs are examining whether Spdo interacts with Numb or members of the Notch pathway. We will identify additional proteins that interact with Spdo or Numb via immunopurification means. We have chosen this approach over others, such as the yeast two hybrid system, because (i) it should identify proteins that associate *in vivo* with Spdo or Numb

and (ii) it should identify proteins that associate with but do not contact directly the Spdo or Numb proteins.

12) At the end of experimental sections it is helpful to state briefly what type of information you expect to gain from the proposed experiments (this keeps everything in context for the reader and helps them step thru your logic more easily). For example:

Given a detailed knowledge of the dynamics and subcellular distribution of Spdo, Numb, and various forms of the Notch proteins we will then determine if the absence of any of these genes alters the expression profile of the proteins encoded by the others. The results of the epistasis tests will guide our choice of which experiments to perform first. For example, if *spdo* is epistatic to *Notch[intra]*, we will first determine the subcellular localization of the Notch[intra] protein in *spdo* embryos. Notch[intra] normally localizes to the nucleus and nuclear localization is required for its function. Does lack of Spdo block this nuclear translocation? Epistasis tests can fail to detect genetic regulatory loops. Furthermore, protein expression analyses buttress and often refine results obtained from epistasis tests. Thus, we will follow the expression of each protein in each possible mutant background. These analyses should begin to illuminate the molecular pathway through which *sanpodo*, *numb* and *Notch* control asymmetric cell divisions.