Brief Critique

- Pick a partner
- Swap papers
- Read your partners Aim
- 1 min …

Survey …

- Do you understand what your partner is proposing?
- Keywords
  - “The Goal …
  - “The hypothesis is …
  - “To test this hypothesis …” (some sort of method)
  - “The rationale for this experiment is …”
  - “The expected results/significance is …”

Before you write –

- Develop a solid hypothesis
  - What is the overall goal of your research?
  - What specific hypotheses will you address?
  - Why is it significant?
  - What is new, exciting, or creative?
    - Does it “advance the field”?
- Discuss the hypothesis with colleagues

The “Specific Aims” Section

The key word is SPECIFIC – explain what you are going to do and how it will change the world (in one page)

- Hypothesis for each aim.
- Experimental Approach of each aim, i.e., how the hypothesis will be tested
- Expected Results for each aim
- Significance of each aim.

Make Everything Obvious in your Grant Writing

- Tell them what you’re going to tell them
- Tell them
- Tell them what you told them

Tell Them What You’re Going to Tell Them

- One paragraph succinct introduction to the problem:
  - Water is a crucial need for agriculture. The goal of this project is to test the hypothesis that the rain in Spain falls mainly on the plain. This is the widely known Higgins/Doolittle hypothesis (Shaw, B. *Pygmalion.* 1916. Since the first statement of this hypothesis, it has become clear that rain alone is not an appropriate way to evaluate the total corpus of precipitation events, and that there is significant interaction between the type of precipitation and the local geography of peninsulas. Thus, to test this hypothesis we have 3 specific aims. The first two aims will evaluate a different aspect of precipitation in the various geographical subdivisions of the Hibernian Peninsula. In the third Specific Aim we will develop a mathematical model in order to generalize these findings to other peninsulae.

Tell them: Aim 1 – the key to the proposal

- Aim 1 is key – it sets the stage, usually both conceptually and methodologically
  - Specific Aim 1: The hypothesis of Specific Aim 1 is that in the Hibernian Peninsula there is significantly more rainful in the Piedmont areas than in the Plains. To test this hypothesis we will exploit a new rain gauge technology developed in this laboratory (see PRELIMINARY RESULTS) that provides nanosecond resolution of rainfall events. We expect to find that more precipitation per unit time actually falls on the Piedmont areas than on the Plain and that each rainfall event lasts longer in the Piedmont but that the Plain has vastly more surface area. The overall effect heavily tips the balance of the total amount of precipitation with respect to geographical location. If we are correct, it would mean that the often cited Higgins/Doolittle hypothesis is only partially correct. However, the findings will be significant even if we are incorrect in the terms of developing a plan for allocating resources for agricultural development in the Piedmont vs the irrigation needs of the Plain."

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Tell Them: The additional aims must follow logically

- Build on the other aims –
  - Specific Aim 2: The hypothesis of Specific Aim 2 is that snow in Spain falls mainly in the Mountains. This hypothesis will be tested using the same methodology that will use for Specific Aim 1 except that the geographical placement of the collection sites will be altered and power will need to be supplied in order to convert the snow into water. This Aim is necessary in order to understand completely the precipitation pattern in Spain. This is because the Spring runoff snowmelt provides a potential irrigation source for the needs of Plains (as determined from Specific Aim 1). ...
  - Specific Aim 3: For Specific Aim 3 the hypothesis is that other peninsula have similar precipitation patterns to Spain. This is necessary because the experiments of Specific Aims 1 and 2 will provide a conceptual framework for understanding the distribution of precipitation events only in a single peninsula. A global resource expenditure priority requires a general logic for peninsular precipitation. Thus, to test this hypothesis we will use the results of Specific Aims 1 and 2 to build a mathematical model of the effects of peninsular geography on precipitation. The mathematical model will then be modified and then tested in 3 peninsulae selected from the list maintained by the Higgins/Doolittle Society for the Study of Peninsular Precipitation (www.hdsociety.org/myfairlady). The selection will be based on the ..."

Tell Them What You Told Them!

- Give the reviewers some words to use in the review
  - If successful, the 3 Aims of this proposal will provide, for the first time, a global perspective on peninsular precipitation. This perspective will provide for a method to distribute irrigation and other agricultural investments in a rational manner. We estimate that this would increase agricultural efficiency by ~25%. In the US alone this could save taxpayers over $1,000,000,000,000 per year.

Attempt 2: The Specific Aims: Audience with Brain-engaged

- Think about an experiment that you are doing or that you want to do
- Write down a few sentences about that experiment as if you were writing a Specific Aim for a grant
- 5 minutes ....

Brief Critique – Again!

- Pick a partner
- Swap papers
- Read your partner's Aim
- 1 min ...

Survey …

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- Keywords
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  - “The hypothesis is …
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What to write when?

1. Specific Aims
   - These need to be done first
     - They provide a road map for the research
     - Common fatal flaw – A grant with Aim 1 as the key; if it fails then the whole grant collapses → low priority.
   - Get feedback and revise before proceeding

How do I “Get Feedback and Revise”???

1. Get an experienced colleague to read and comment
   - Almost everyone is willing to read the one page Specific Aims sections is easy
2. Ask Robert Reiser to organize a “mock” Study Section
   - Simulation of what happens at a real study section
   - You get to hear what a diverse group of reviewers really think about your ideas
   - If done right you’ll get a good idea of where your project stands in the field.
3. Revise and Repeat – 15-25 drafts to get it right!!!!!

How are grants reviewed and funded?

- NIH has a two step system
  - Study Section rates science
  - Council decides on funding
- NSF has one step system
- Private foundations vary

NIH Funding System

Two Step System

- Grants are first <u>reviewed</u> by a Study Section (“Initial Review Group” or IRG) and assigned a scientific priority. Study Sections evaluate the science against a “gold-standard” perfect grant.
  - The priority score is an absolute number but it is converted to a percentile rank to facilitate comparison among the various IRGs.
  - In Study Section “funding” is the “f-word”, i.e., not spoken
- Grants are <u>funded</u> by Council, an Institute level group of scientists and lay people that funds grants based on a balance of programmatic and national needs.
  - Funding is generally based on percentile rank.
  - “Special” circumstances can result in a lower priority grant getting funded if it would support, for example, a unique field or resource.

What is the IRG? Who is the SRA?

- Initial Review Group, also known as “Study Section”
- Comprised of members, i.e., scientists, who are active and usually funded researchers
- Run by a Scientific Review Administrator (SRA)
  - Chooses the membership and coordinates the meeting
  - Assigns proposals to members for review
  - Relays messages from the reviewer to you and vice versa during the review process
  - Takes notes during the meeting
  - Compiles reviews for the Summary Statement (“Pink Sheet”)
- The SRA is non-partial and should be your only contact with the review process.
- Do NOT call, contact or discuss your grant with IRG members.

What happens before the meeting?

- IRG members can be full members of the panel or recruited (ad hoc) for just that meeting
  - Typically they read 10-12 grants
    - each grant is read completely and multiple times
  - Each grant is reviewed by at least 2 and usually 3 reviewers
  - The reviewers may not be “experts” in <u>your</u> subfield
  - They read the grants before the meeting
  - They write a critique before the study section meeting and submit it electronically
  - Reviewers assign either
    - A tentative priority score if in upper half
    - The designation “Lower Half” if it is judged to be in the lower 50% of all grants that the reviewer has ever seen (“triage”).
  - All reviewers can see the other critiques before the meeting begins – (similarity or differences in opinion can be discerned).

The IRG Member

- Is assigned to read your grant – not voluntary
- May choose an interesting grant that is not assigned (but this happens rarely)
- Must recuse himself if there is a conflict of interest
  - Same institution
  - Collaborator
  - Any appearance of a conflict of interest
  - Leaves room and does not participate in the discussion or vote
- Reads your grant in addition to running a lab, teaching, etc.
  - Often at home after dinner or on weekends, i.e., in their "spare time".
  - Doesn't have time to read anything other than the grant application itself
  - Appendix material is often unread, references to web sites are usually ignored, etc.
- Doesn't have a long attention span
- You can never underestimate your reviewer! – treat them like a student – teach

During the IRG Meeting …

- ALL FELLOWSHIP Applications are discussed
  - for R01's, etc. Lower half proposals are not discussed but must be agreed on unanimously
- Proposals that are discussed are presented by 3 reviewers and voted on by **all** members
- Reviewers present preliminary scores
  - If consistent, then discussion is abbreviated
  - If inconsistent, then discussion can be prolonged
- Primary reviewer then summarizes your proposal to the members and presents a critique including strengths and weaknesses
- Secondary reviewer then presents their critique and score
- Other assigned "readers" then present critique
- Other reviewers then make comments
- All members then vote secretly – score is from 1 (best) to 9 (worst) – usually 5 is goal for 50th percentile
- ALL discussion, etc. is CONFIDENTIAL.

A Real Study Section

- All proceedings are confidential
- Who is **allowed** to be in the room?
  - SRA (Scientific Review Administrator)
  - Reviewers (Members plus Chair)
  - Administrative Assistant
  - NIH Program Officers

A Real Study Section (note windowless room!)

During the IRG Meeting …

- The Discussion is crucial -- while the critiques are presented and the discussion is ongoing:
  - Reviewers have originals with color pages, supplements, etc.
  - Other members are listening and possibly browsing through your proposal
    - Every member has the complete text of every proposal on a CD. Illustrations are usually in B&W.
  - Members will likely only have time to read:
    - Specific Aims
    - Your C. V.
    - A figure or two.
  - Members *might* look at figures of preliminary data or experimental design if the discussion goes long enough and it seems worthwhile especially if the reviewers suggest that they do.
- Translation: The simpler to understand, the more likely you are to get a good priority score.

Formal Review Criteria

- Significance (Is the problem important?)
- Approach (Are the design and methods appropriate to the address the aims?)
- Innovation (Does the project employ novel concepts, approaches, or methods?)
  - High risk/high reward can be considered a good point.
  - High risk/low reward is not good.
- Investigator (Is the investigator appropriately trained to carry out the study?)
  - Collaborators – appropriate and qualified
- Environment (Will the scientific environment contribute to the probability of success?)

What to write when?

1. Specific Aims
   - These need to be done first
     - They provide a road map for the research
     - Common fatal flaw – A grant with Aim 1 as the key; if it fails then the whole grant collapses → low priority.
   - Get feedback and revise before proceeding
2. Experimental Design
   - This is an extension/explanation of the Specific Aims
     - This section should be written to be parallel in structure to the Specific Aims
3. Background and Significance
   - Give the intellectual basis for doing these experiments.
4. Preliminary Data
   - Your <u>relevant</u> preliminary work
5. Abstract/Budget
   - Abstract is for lay people (reviewers don't rely on it)

Who is the Audience?

- For a paper your audience is 10's to 100's of readers
- For a grant your audience is 1 to 20 (probably 3) readers – the REVIEWERS
  - NIH typically has primary, secondary and tertiary reviewers

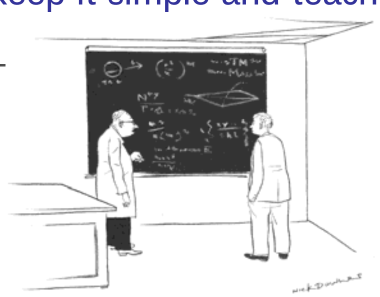
The Audience?

- Who are these #%#$^& reviewers?
  - If you understand the reviewers' perspective, it's easier to write a PROPOSAL that will be reviewed favorably!
  - Grants are "peer" reviewed
  - Peers = "experts in the field", i.e., people who have written funded grants in the past

Address Your Audience

- Don't underestimate the reviewer.
  - The less a reader has to read, the more likely it is you can hold their attention span
  - Leave lots of white space
    - Enumerate
    - Use graphs, figures and tables
  - Don't try to write to the page limit
    - Figure out what to say first
    - Edit to shorten later
  - Use appropriate font type – smaller type is harder to read

Keep it simple and teach



"In layman's terms? I'm afraid I don't know any layman's terms."

TEACH: Make <u>Everything</u> Obvious in your Grant Writing

- YOU (the applicant are the World's expert on your topic)
- Iterative Structure
  - Tell them what you're going to tell them
  - Tell them
  - Tell them what you told them
- Use Explicit guide words:
  - "In this section, the background and justification for Aim 1 is provided."
- Use Lists
  - "There are 3 lines of evidence that support this hypothesis:"

Background and Significance

- Your chance to show that
  - your proposed work addresses an important question
  - your work fits into the larger picture
  - it is timely to address the question
  - you have a novel approach
  - you are intellectually capable of making a contribution to the field
- Focus explaining your hypotheses and how they fit in and/or will change the field

Background and Significance

- Not a review of the literature! It is a sales pitch for YOUR project.
- Demonstrate knowledge of relevant published literature and a critical assessment of open questions. Include your own published work here.
- State explicitly what scientific questions other scientists have not yet answered and how your hypothesis fits with these questions.
- In each paragraph, point out to the reader how your proposed experiments will help resolve important issues in the field (refer to your Aims).
- Some reviewers skip this section on the first read, and only go back if you have forced them.
- Significance should be integrated into your presentation.
  - Explain the importance of your proposed research.
  - Reviewers are looking for the impact of your research on the disease or health issue in question.
  - Relate the hypothesis and research aims to longer-term scientific objectives.

Preliminary Data ...

- Convince the reviewers:
  - That you have excellent and relevant training.
  - That you can communicate and interpret your results.
  - That you already have experimental evidence supporting your hypotheses and indicating the need for further experimentation.
  - That you have command of all the techniques that you propose to use or a plan to acquire that command.

Preliminary Data ...

- Present relevant and pertinent preliminary data. *Show the actual data and explain how you interpreted it.* This will help establish your experience, competence and credibility.
- Present your results (even if they are preliminary) in as professional a manner as possible, with clear and complete figure/table legends, calibrations, statistical analysis, etc.
- This is especially important in a new application in order to document that the applicant can do the work
- *Do not ask reviewers to look at figures in your publications.* Put published data into the B&S section, if it's necessary.
- List your publications and manuscripts submitted or accepted

Experimental Design and Methods

- The sections of the experimental design and methods should be identical to the sections of the Specific Aims.
  - If you have 3 Aims, you should have 3 subsections.
  - Label each subsection clearly – e.g., Specific Aim 1, Specific Aim 2, etc.
  - For each Specific Aim, describe in detail the experiments that you need to fulfill the Aims.

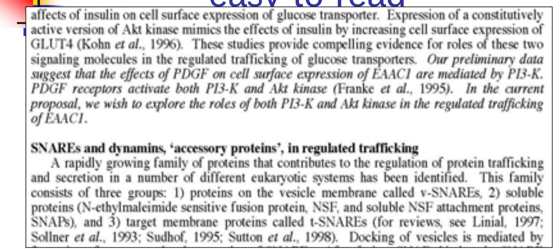
Experimental Design and Methods

- For each aim or subaim (use subheaders to make it easy to follow):
  - Hypothesis and rationale
  - Experimental design (be clear)
    - Relevant control experiments
    - Animal details, source of cells, number of replicates, statistical methods used, etc.
  - Results and expected outcomes
    - What do I expect, and what will it mean?
    - What if the results are different? Explain alternative paths for the alternative results.
    - A graph of hypothetical results might clarify the presentation
  - Potential pitfalls: Discuss potential difficulties and limitations of the proposed procedures and give alternative procedures to achieve the aims.
  - Significance
- Propose only experiments that are directly relevant to testing your hypotheses
- Make sure that that you have the expertise to execute each experiment successfully – recruit a collaborator if necessary.
- Present methods with enough detail to be clear. Avoid excess details unless they are specialized and/or unique or unlikely to be known to reviewers.
- Refer to other Aims and to other sections of the grant – make the grant read like an integrated whole.
  - "As discussed in the Background and Significance Section, ..."
  - "Using the methods described for Figure 4 in the Preliminary Results, ..."
  - "... as will be tested in Specific Aim 2, ..."

Literature Cited

- Demonstrates your familiarity with the field
- Reviewers need complete citations including titles
- Put citations in alphabetical order of authors
- Use a computer program for managing citations

Use Text Formatting to make it easy to read



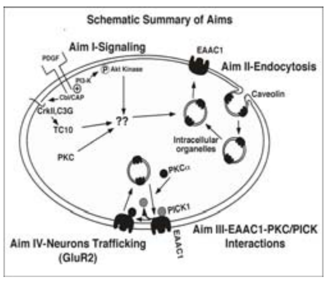
affects of insulin on cell surface expression of glucose transporter. Expression of a constitutively active version of Akt kinase mimics the effects of insulin by increasing cell surface expression of GLUT4 (Kohn *et al.*, 1996). These studies provide compelling evidence for roles of these two signaling molecules in the regulated trafficking of glucose transporters. *Our preliminary data suggest that the effects of PDGF on cell surface expression of EAAC1 are mediated by PI3-K. PDGF receptors activate both PI3-K and Akt kinase* (Franke *et al.*, 1995). *In the current proposal, we wish to explore the roles of both PI3-K and Akt kinase in the regulated trafficking of EAAC1.*

SNAREs and dynamins, 'accessory proteins', in regulated trafficking

A rapidly growing family of proteins that contributes to the regulation of protein trafficking and secretion in a number of different eukaryotic systems has been identified. This family consists of three groups: 1) proteins on the vesicle membrane called v-SNAREs, 2) soluble proteins (N-ethylmaleimide sensitive fusion protein, NSF, and soluble NSF attachment proteins, SNAPs), and 3) target membrane proteins called t-SNAREs (for reviews, see Linial, 1997; Sollner *et al.*, 1993; Sudhof, 1995; Sutton *et al.*, 1998). Docking of vesicles is mediated by

- Most reviewers believe scientists need to be able to pay attention to detail
- Most reviewers will assume that a person who submits a disorganized proposal with typographical errors will conduct sloppy science!

Use Schematics – specifically developed and labeled for the grant



After you have a draft

- Find readers to critique the proposal
  - They need enough time to be helpful!
- Who should read your application?
  - *Non-specialists* (preferably funded scientists with study section experience) to be certain that the proposal is understandable and logical to a non-specialist.
  - *Specialists* (someone from your field) to be certain that the goals are interesting, that the experimental plan is efficient and compelling, that the best available techniques to answer the questions are used, etc.
  - *Proofreader* – get someone to read your application for style, grammar, spelling, etc.

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What to do if you're not funded?

- <u>Read</u> the critique – all 3 reviews count.
  - Reviews are edited after the meeting to comport with the discussion
- Read between the lines
  - Reviewers don't like to say your ideas are no good, look for the <u>absence of positive statements</u> regarding significance
- Don't take it personally and don't get angry!
  - If the reviewer didn't understand, then it wasn't written clearly.
  - Remember: The reviewer is always right (even when he/she is wrong).
- Get feedback
  - Find a colleague to read the critique
  - Find an experienced reviewer who can read the critique
  - If something isn't clear, call the SRA (probably only useful if the review was scored).
- Change the proposal – dramatically if necessary
- Most common error for a first proposal is excess ambition.
  - If a reviewer suggests that the work is "unfocused"
    - cut the off topic aims and expand the details on the remaining
    - sometimes this can be drastic, e.g., cut 2 aims and expand the remaining one into a new grant.
- Next most common error is trying to edit when the need is to delete and redesign.

Be Persistent ...

- *If at first you don't succeed, try, try again"*
  - *Teacher's Manual' (1840) by American educator Thomas H. Palmer*