RESEARCH! LOUISVILLE

THE ART OF GRANTSMANSHIP

Presented by
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Topics

- What do reviewers want?
- How do we accomplish this?
- Guts and Glory of Multidisciplinary and Translational Research
- Writing Goals, Hypotheses, and Specific Aims for the reviewer
- Writing Summaries that do not embarrass you later
What Makes the Reviewer Happy?

App. # 99-036
App. # 99-047

Who reviews my project?
• What does the reviewer judge?
• What is the process?
• How can I make the reviewer understand my project better?
What is Peer Review?

• Judging of an investigator’s grant application by colleagues who are scientific peers

• Peer reviewer must not have any significant prior connections to the applicant (mentor, employee, collaborator, former student, etc.)

• Anonymous (maybe, maybe not)
Characteristics of Reviewers

• Good research skills; well-respected
• Good marketing skills
• Good communication skills
• Ingenuity and flexibility
• Administrative skills
• Current in National Priorities
• Persistence, patience
• Integrity
Reviewers Understand:

- Grantsmanship
- National Priorities
- The Review Process
- Writing for the Reviewer
- Use of Good Expository Writing
- Art of Responding to a Set of Instructions
What do Reviewers Want?

The TOTAL Package

Q—Qualifications of PI/Team
U—Understand the Budget
E—Evaluation Plan
S—Significance, Innovation, and Importance
T—Truthful and Realistic
Scientific/Professional Credit Card

- Review Paper of a Concept
- Internal grant funding, small foundation
- Small project--student training, presentation of results at meeting
- Write up of project for publication in peer-reviewed journal
- Interact with peers and colleagues through partnerships or collaborations
Archaeology

- Distribution of Ceramics as a Function of Economic Trade in Mexico--looked at materials and patterns
- Collaborations with places that could do work that she could not
- National Geographic Society
- THECB grant
  - Werner-Gren
  - Heinz
- State of Texas Funding
Historian

- Aerospace and Aviation Historian struggling after the Challenger disaster
- Impact of Airports on Economic Development--Advisory Position at Dallas Love Field
  - $25K--1 sem.--no fringe award--foundation
  - Year at the Air and Space Museum
Bilingual Education

- Hispanic
- Education-Curriculum Doctorate
- Teachers of Hispanic children were having problems
- Development of small capsules of curriculum
- Published results: presentations
- Office of Education funding
Cell Biologist

- Movement of chemicals through membranes
- Signal Transduction
- 2 unfunded applications

- Pink Sheets
- Aims ???
- Ctr. For Biomedical Engineering
- Statistics group
- 2 funded R01s by the next year
Why are they successful?

- Worked closely with the administration--chair, dean, vice chancellor for research
- Developed credit cards of expertise, willingness to help, dependability
- Persistent and patient
- Pieced together small parts into a whole
Use Web sites !!

• Lists of NIH Reviewers/Review Panels
• Summaries of Funded Investigators/Projects on PHS CRISP
• Guidelines and Application Forms
• Review Criteria
• Publications of Reviewers
Positive Appearance

• Well-designed Diagrams
• Figures, especially in preliminary data section
• Type in 11 font, 15cpi, <6 lines/inch
• Font, such as Arial, Helvetica, Palatino Linotype, or Georgia, not condensed
• Brief Sentences
• Budget that matches the project
When do we get funded?

Application carries the optimism of success

Promotes:

- Importance, innovativeness
- Familiarity with science
- Literature/hypothesis
- Relevance in field
- Rationale for experiments
Understand the Budget

- Budget Errors
  - Budget too large for research plan
  - Budget too small for research plan
  - Poor estimation of time required to do project
  - Capped budgets do not match plan
  - Budget not completed early enough to make changes to the research plan
    - “This is an ambitious project…”
Evaluation of the Proposed Project

- Why?
- What?
- How?
Facets of Scientific Development

- Discovery
- Characterize the Discovery
- Model Development
- Characterize the Model
- Mechanistic Studies
Progress of Knowledge

- Observation
- Mechanisms
- Enhancement
  - Suppression
  - Suppression
## Assessing the Need for Evaluation

<table>
<thead>
<tr>
<th>New Knowledge</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discovery of mutations (observation)</td>
<td>Presence or absence of mutation</td>
</tr>
<tr>
<td>Discovery of polymerase presence during DNA replication (observation)</td>
<td>Presence or absence of polymerase</td>
</tr>
<tr>
<td>Quantification of polymerase activity during DNA replication</td>
<td>Comparison of quantity of polymerase during high and low replication phases (t-test)</td>
</tr>
<tr>
<td>Use of chemical X to enhance or chemical y to inhibit production of polymerase</td>
<td>Use of multiple doses of chemical x or y to determine optimum dosage for controlling polymerase activity (ANOVA)</td>
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Measurable Outcomes
Indicate Prior Planning

“The correct statement of an objective is the first step to its attainment.”

--Batten (1965)
Choosing Fundable Projects

- Exciting the Reviewer!!
- Exciting your Team!!!
- Doing “State of the Art--Cutting Edge” Research
Marketing Your Project

- Knowledge of Agency Priorities
- Review Criteria
- Geology of the Body of Knowledge
- PI and Collaborators
- Techniques and Equipment
Agency Priorities

- Identify Funding Sources (Web-sites, funding Databases)
- Identify the Priorities of Each Agency
- Match Your Strengths, Expertise, Resources with the Appropriate Agency
- Analyze Possible “Stretches”
- Select the Best Two or Three Matches
Review Criteria and Process

- Confirm Priorities with Agency Program Director—Don’t be shy!
- Identify Review Criteria
- Identify Review Process
- Develop a Project Protocol Based on Findings
Project Components/Review Criteria

- Interesting/Exciting
- Important/Significant
- Feasible/”Do”able
- Priority
- Cost-effective
- Innovative
Analysis

- Assessment of High vs. Low Interest for Significance and Excitement
- Assessment of High or Low Risk for Significance and “Do”ability
- Is this innovative?
- Self Assessment of Your Own Project Given the Priorities of Your Targeted Agency
Other Aspects - Qualifications of PI

- Are your collaborators qualified to do their portions of the research?
- Do you have mentors?
- What are some of the “Trade-offs”?
- Can you get supporting letters from reviewers who would be conflicts of interest?
Demonstrating Qualifications

- Appropriate Academic Training and Credentials
- Post-doc or Fellowships in Area of Investigation
- Peer Reviewed Publications
- Abstracts/Community Work in Area
- Industrial Collaborations
Other Aspects - Techniques and Equipment

- Document Unique Capabilities of the Institution
  - Centers
  - Research Cores
  - Specialized Personnel
  - Clinical Research Groups
  - Database Capabilities
  - Other Expertise Related to Project
Summary

- Organize!
- Organize!
- Organize!
- Organization indicates to the reviewer that you are truly prepared to conduct the proposed project
TRUTHFUL and REALISTIC

- Skipping over the shortfalls
- Assuming everything will work perfectly
- 4 years of work proposed in a 3 years grant award
- Preliminary data is real and done by you
- Fear that disclosing a potential weakness will lead to non-funding
• Describe research design and methods to be used
• Data to be collected, analyzed and interpreted
• New methodologies--advantages
• Anticipated difficulties and limitations
• Alternative approaches to achieve aims
• Timeline
• Hazardous procedures, situations, or materials (precautions)
Multidisciplinary Research
What is Multidisciplinary Research?

Multidisciplinary--Composed of several specialized branches of learning, as for achieving a common aim
Why Promote Multidisciplinary Research?

SYNERGY

1 + 1 + 1 = 4

“the end result is greater than the sum of the individual components”
Career Implications of Multidisciplinary Research

Increased Scholarly Productivity

- graduate students
- paper presentations
- manuscripts
- teaching of research
- curriculum improvements
Possible Caveats of Multidisciplinary Research

Prior experience of research team as evidenced by collaborative publications:

• New teams have presented seminars, posters, or papers with multiple authors on this topic or related topics

• Older collaborations have published papers that have been peer reviewed

• Not a requirement of all agencies, but NIH does!!
Support for Multidisciplinary Research

Funding Agencies--Funding Opportunities

Congress--Increased $ Allocations to those Funding Agencies
Internal Partnerships to Achieve Multidisciplinary Research

**FACULTY**--establish working relationships across disciplines; across departments; and across institutions

**ADMINISTRATION**--sponsored programs office support for grant awards; academic policy to promote academic success; strategic planning to focus the university; allocation of resources

**FUNDING AGENCY**--determine funding priorities; allocate resources, establish appropriate review; award mechanisms
Roles to Prepare for Multidisciplinary Research

FACULTY--Identification of multidisciplinary strengths of institution; begin collaborative activities; SHARE

ADMINISTRATION --”Big Hairy Goals”; other Aspects of Strategic Planning process

AGENCY--RFP’s published; National Priorities
How can Faculty Help?

FACULTY PROFILES--tied to Web Page, vitas

IDENTIFY RESEARCH STRENGTHS--categorize

REACH OUT TO OTHER FACULTY AND OTHER INSTITUTIONS--make visits, talk at meetings

HELP YOUR ADMINISTRATION UNDERSTAND WHAT YOU NEED--use a quality improvement approach to design research infrastructure

*Ask not what your institution can do for you, but what can you do for your institution***!!
Translational Research

Concept

Product or Service
Scope of Translational Research

- Basic
- Clinical

- Cause
- Prevention
- Diagnosis
- Treatment
SBIR/STTR Programs

- SBIR originated in early 1980’s
- Originally designed to help entrepreneurs gain seed funds to develop new products that would create JOBS for America
- Phases I-III have always been in place, with Phase III being funded by a large corporation or investment group.
Addressing the NIH Mission

- Conduct innovative research and development that results in products, processes or services that:
  - Improve patient health
  - Speed process of discovery
  - Reduce cost of medical care/cost of research
  - Improve research and communication tools
University Partnerships

- Provide analytical or other service support
  - Consultant on an SBIR/STTR
  - Subcontract to do work
  - Senior Personnel
  - Principal Investigator (with permission from the university)
  - Own small firms (assign someone else to be the PI)
Who is the Applicant? PI?

- Applicant is the small business, regardless of SBIR or STTR, organized for profit and 51% US owned. Business located in the US and with less than 500 employees.
- SBIR PI must have primary employment with small business during project (>50%).
- STTR PI must spend 10% of time on project.
What’s the University’s Cut?

- SBIR—optional 33% to research institution partners (Phase I) (Phase II = 50%)
- SBIR—required 30% to research institution partners (Phase I)

- Intellectual Property Agreement—Allocation of rights in IP and rights to carry out follow-on R & D and commercialization.
Caveats

- **Phase I**
  - Agreement to establish a consortium
  - STTR budget page for collaborator
  - Application must be from small business
  - Modular budget not acceptable even though the award is usually about $100,000
  - Narrative limited to 15 pages, certain restrictions apply to other enclosures
  - NO Appendices
Phase II
- SBIR—at least 50% of work carried out by small business concern
- STTR—at least 40% of work by small business; 30%, by research partner
- Phase I Final Report
- Commercialization Plan, limited to 15 pages
- Model agreement signed
- Identification of possible business partners for Phase III funding
- May receive competing continuation
Phase III
- Requires outside partners with funding, usually no funding from federal government

Rule of 10
- Phase I = $100,000
- Phase II = $1,000,000 (only $750,000 allotted)
- Phase III = $10,000,000 - $1,000,000,000
What is Needed?

- Angel investors
- Takes technology and marketing
- So out of the scientist’s control!
- Bar raises every year
Be Prepared

- Patent Application
- Concept of Prototype
- Trials to proof patent
- Placebo trials—follow up
- Adverse effects
- Time-sensitive schedule to get investment return
- Safety and Efficacy
What Does the Investor Want?

- What is the Market Potential?
- What are the Benefits?
- What are the Features?
- How Safe is This?
- How Effective is This?
- The TRUTH
The Total Package
- Qualified PI
- Understand the Budget
- Evaluation Plan
- Significance, Importance, Innovativeness
- Truthful and Realistic
Proposal Components

- GOALS
- HYPOTHESIS
- SPECIFIC AIMS
- Background and Significance
- Preliminary Data
- Research Design
- SUMMARY
Why are we doing This?

- The statement of the goals, hypotheses, and specific aims is the most important component of the grant application. More than 50% of applications are rejected because the inter-relationship among these three scientific descriptions is incorrectly or poorly stated. This inter-relationship is the cornerstone of the application. Without it, the research plan is baseless, sound and fury, but no storm. The research plan is reduced to a description of techniques. Goals demonstrate that there is a master plan for, not only this project, but for others to come. Hypotheses, while not necessary in all applications, are the basis for scientific discovery and the documentation to prove or disprove a theory. The specific aims or objectives tell us what work is going to be done in support of a hypothesis and the benchmark for achieving that aim or objective.
Goals

- Long-range plans, often continuous
- Often exceed the scope of the application
- Usually does not have terminal end points that can be measured
- “Fuzzy” verbs
  - Understand
  - Contribute to the knowledge of...
The overall goal of this research is to establish simple and applicable methods for quantifying drug sensitivity in leukemia patients.

The long-term vision is to contribute to the development of a multivariate screening process to assess the cumulative risk of patients vulnerable to cardiac failure.
The long term goals of my research program are to find novel functions for both estrogens and estrogen response proteins, and then to identify the molecular mechanisms mediating these functions. Our long range goal is to clarify cellular events during vascular injury by toxic chemicals.
The long-term goal of this research is to understand the molecular events that result in female reproductive development and egg formation.
NASA Research Goals

- **Vision**
  - To improve life here
  - To extend life to there
  - To find life beyond

- **Mission**
  - To understand and protect our home planet
  - To explore the Universe and search for life
  - To inspire the next generation of explorers

...as only NASA can
Activity

- Are these goals?
  - Our goal will be to induce vasculogenesis in engineered tissue constructs grown on three dimensional polymer scaffolds.
  - The main focus of the proposed research will be to use these cell lines to evaluate well established non-mutagenic environmental carcinogens for kinetotoxicity.
Hypothesis

- State question, problem, need, etc. as a hypothesis.
  - We will test the hypothesis that “x” selectively destroys “y” in the presence of “abc”.
  - There is selective involvement in the relationship of “x”, “y”, and “abc”
- Should be directional, not null hypothesis
- Should be proved or disproved by the end of the study
- Doesn’t include techniques
NOTE: OMISSION OF THE HYPOTHESIS MAY CAUSE THE REVIEWER TO CRITICIZE YOU FOR GOING ON A “FISHING EXPEDITION.”

NIH does not fund fishing expeditions—only those studies with hypotheses based on the results of pilot studies.
Are these hypotheses?

- Hypothesis 1. HSP 70 plays a critical role in targeting the nascent apoB for secretion.
- Hypothesis 2. MTP-PDI plays an essential role in apoB secretion by facilitating the completion of apoB translocation across the ER membrane.

What would be a better way to state these hypotheses?
Specific Aims

- Specific aims are tests of the Hypothesis grouped by experiments
- Omit aims that are dependent upon the success of the aim(s) preceding
- Compare to “objectives”
- Three or four must do the job for regular projects
Specific Aims/Objectives

- Behavioral
- Performance
- Product
- Process
- Research
Specific Aims/Objectives

- **Sample Behavioral Objective**
  - During an inservice workshop, physicians will demonstrate their comprehension of diagnostic and prescriptive techniques as measured on an AMA-developed test.

- **Components**--objective, activity, those affected, expected change, evaluation
Specific Aims/Objectives

- Sample Performance Objective:
  - At the end of the third week of the residency program, doctors will demonstrate their comprehension of diagnostic and prescriptive techniques as measured by a minimum gain of ten raw score points on a staff-developed pre-and post-test.

- Components--subjects, activity, testing instrument, evaluation criteria
Specific Aims/Objectives

- **Sample Product Objective**
  - Within 6 months of the receipt of the signed contract, university investigators will furnish 5 different designs and prototypes of a laser-tip designed to minimize prostate tissue damage

- **Components--Activity, who is working?, what is product?, evaluation of product.**
Specific Aims/Objective

Sample Process Objective:
- Physicians and medical researchers will participate actively as council members in the planning and operational phases of the general practitioner program curriculum revision.

Components--who is doing the work? what is being done? what is the activity? end-product of process?
Specific Aims/Objectives

**Most Common Errors**
- Aims/Objectives are confused with the methods/procedure
- Aims/Objectives are confused with the overall goals
- Proposal doesn’t use term correctly or consistently
- Use of cascading aims
Differences between educational/social sciences objectives and those of scientists

- Scientists tend not to use the activities or measurements in their objectives. It is also assumed that the scientist or his team will be the group completing the project.

Similarities

- Use of “to” followed by a verb
Activity

- Weak verbs for aims--characterize, determine, understand, identify
- Stronger verbs for aims--assess, analyze, develop, define, create, compare
- Too many aims indicates that you do not know what is involved in scientific investigation
Aims are specific—concise and to the point.

Aims are experiments done to test your hypothesis.

Aims are written so that there should be a measurable outcome to each one.

Do not confuse the aims with the techniques that you are using.
Writing the Abstract or Summary
The first place to use the goals, hypotheses and specific aims is in the summary statement. The summary statement includes not only the aforementioned, but also tells the reviewer how the work is to be accomplished, how the project will be evaluated, and why this project is important. Once the summary statement is completed, the investigator has the roadmap for writing the application (and the basis for developing a budget).
Abstract or Summary?

- **Abstract**--A summary of a statement, document, or speech. Tends to be more the “essence” of something or an idea.

- **Summary**--A comprehensive and usually brief abstract, recapitulation, or compendium of previously stated facts or statements.
Rationale

- Often the last section written by the investigator
- Should probably be one of the first sections to be constructed
- May be the only section read by a reviewer
- If project is funded, it becomes public material and may be circulated electronically (peers, industry, competition)
- Must present an overall view of proposed project in layman’s terms.
NSF--Project Summary

Suitable for publication

Not an abstract of proposal, but a self-contained description

Written in third person

Must include a statement of objectives, methods to be employed, and the potential impact on advancing knowledge....

Understandable to a scientifically or technically literate person
NIH--Description

Note instructions on the form page. If funded, description becomes public information.

State application’s broad, long-term objectives and specific aims.

Reference health-relatedness.

Describe concisely research design and methods to achieve these goals.

Avoid summaries of past work.

Avoid use of first person.
Include the objectives of the study, including any hypotheses

Include the experimental approach to be used (provides an accurate description of work to be accomplished)

Include the expected results, how it addresses the research needs identified in the research solicitation, and any risk assessment or management that will result from the completion of the project
Summarizing Summaries

- Relevance/Long Term Prospects--Why?
- Contains Aim/Objectives/Hypotheses--What?
- Description of Design and Methods--How?
- You and Colleagues--Who?
- Institution--Where?
- Budget--How Much?

This information is often contained in forms.
Good Practices for Summaries

No first person statements

No summaries of past accomplishments

No bragging on the PI

No begging and pleading

Focus on innovation, creativity, relevance, well-designed research plan, etc.!!!
Analyze an Abstract
The overall goal of this grant is to identify new genes involved in antigen processing and presentation. The specific aims are: 1) to search for genes that affect the processing and presentation of HLA class II restricted antigens; 2) to search for these genes in the MHC, in unstudied flanking regions of chromosome 6p, and in the rest of the genome; 3) to identify new genes that affect the processing and presentation of class I restricted antigens; 4) to investigate whether the MCH-linked heat shock genes have a role in antigen processing and presentation; and 5) to investigate the basis for the alteration in recognition of antigen processing/presentation mutants as targets for alloreactive T cell clones. The basic approach to new gene identification will be to isolate mutants affected for processing/presentation, using selective schemes designed to distinguish between antigen processing-competent and -incompetent cells…It is anticipated that these studies will lead to the discovery of genes involved in class I and class II restricted antigens processing. In a more general way, the project should enhance our understanding of the mechanisms involved in antigen presentation to T cells, mechanisms that are critical in host defenses against microbial pathogens and that may play a role in the pathogenesis of autoimmune diseases.
Wrap-up

- Reread YOUR summary
- Does the summary match your current goals, hypotheses, and specific aims/objectives?
- Rewrite the abstract to match the refined grant application
- Revisit the abstract after the methods section has been designed and written.
SKELETON OF A SUMMARY

SIGNIFICANCE

RELEVANCE

GOAL

HYPOTHESIS

AIM 1

AIM 2

AIM 3

TECHNIQUES

PRODUCT
To be economically viable in the trade market, our country needs to reduce the costs of importing goods from the Far East. Factors that increase these costs include the payments of tariffs, land caravans for portage, and associated personnel expenditures. The goal of this project is to establish the feasibility of a new trade route to the Far East that, once established, would reduce import costs and increase trade profits. The hypothesis is that the shortest, most economical route to the Far East can be obtained by sailing westward. Our objectives will be to: 1) determine the best route for the sailing ships; 2) embark on a westward sailing track to find the Far East; 3) explore the surrounding area for new crops or products, precious metals, and potential trading ports. To accomplish this, we will utilize 3 small sailing ships with experienced crews to sail westward out of Lisbon. A daily journal will be kept with latitude and longitude readings taken 24 times/day. The journal will record not only the position, but the types of wind and weather affecting the journey. Additionally, any new ports or civilizations discovered will be described physically, ethnically, and economically. We will secure samples of crops, metals, and other items for trade consideration in the future. Funding has been leveraged by a 50% match from private investors. This projected results of this journey will enhance Spain’s current economic status in the European world.
What do Reviewers Want?

- A Total, Organized Package that Reads Well
  - Q  Qualified PI/Team
  - U  Understandable Budget
  - E  Evaluation Plan
  - S  Significance, Innovation, Importance
  - T  Truthful and Realistic