

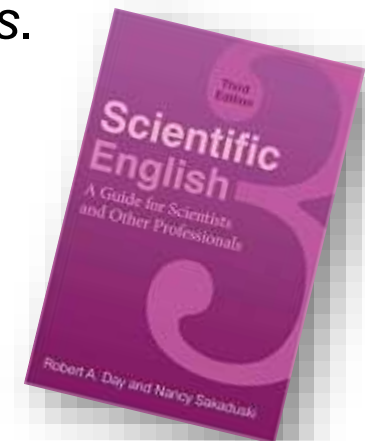
Hypothesis Development

ENGR 361: Scientific Research Communication

<https://www.csulb.edu>

References

- Alred, G. J., Brusaw, C. T., & Oliu, W. E. (2009). *Handbook of technical writing*. Macmillan.
- Day, R. A., Sakaduski, N., & Day, N. (2011). *Scientific English: A guide for scientists and other professionals*. ABC-CLIO.



Hypothesis Development

- **Grant Applications**

- Questions to ask before you submit
 - Is the work novel, exciting and necessary?
 - Are you repeating experiments already done by others?
 - Do you have preliminary data or evidence to support the feasibility of the proposed studies?
 - Are the experiments that you are proposing appropriate?

Hypothesis Development

- **Problem Statement**

- A clearly stated problem should permit clear description of overall goals and specific aims
- All hypotheses should be testable

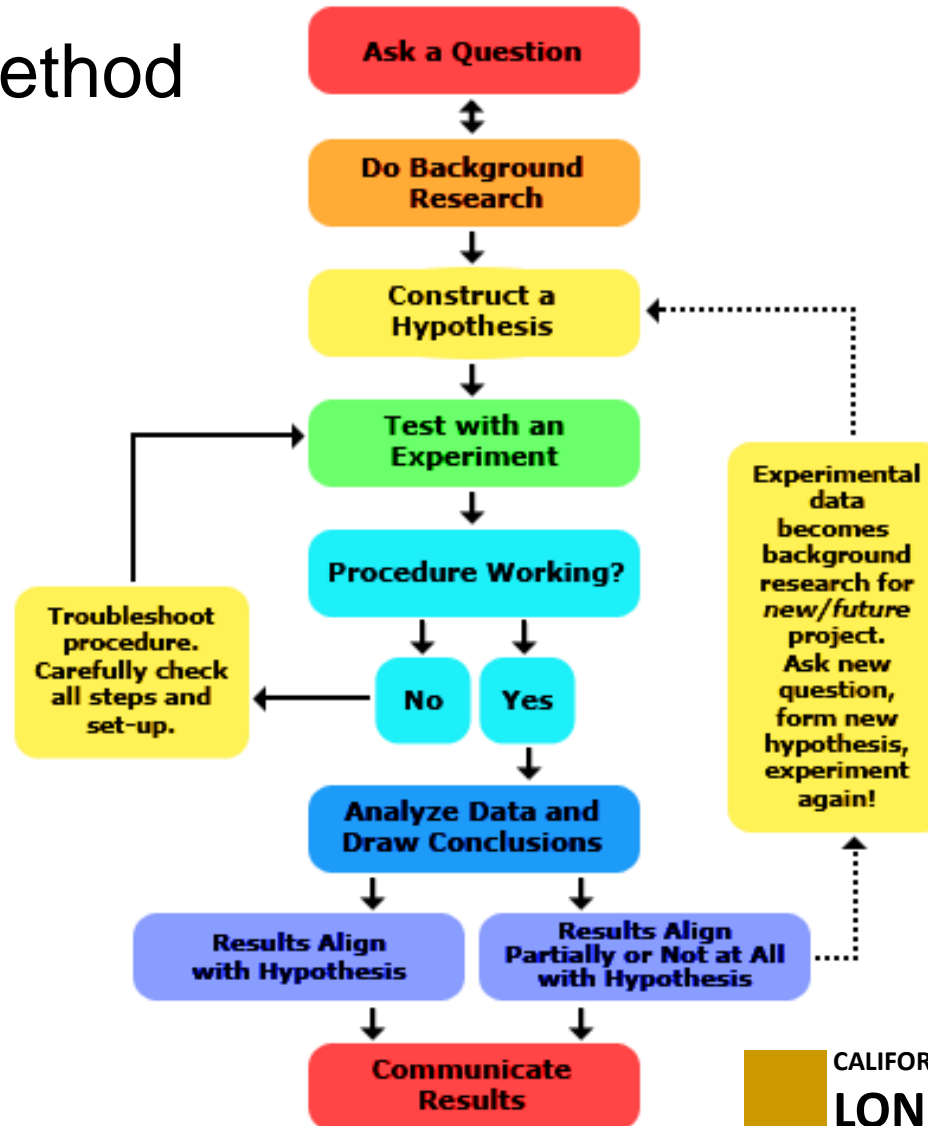
Hypothesis Development

- **Goal, Objective, Specific Aims**

- Goals reflect a vision of what the research seeks to accomplish in the long run
- Objectives are the more immediate outcomes of studies
- Specific aims serve as practical guide posts for daily, weekly and monthly research efforts

Hypothesis Development

- Scientific Method



Hypothesis Development

■ Construct a Hypothesis

- A hypothesis is an educated guess or proposition that attempts to explain a set of facts or natural phenomenon
- A hypothesis is declarative sentence that asserts a desired, expected, or possible conclusion of a goal



Hypothesis Development

■ Hypothesis

- Tentative answer to a research problem that is advanced so it can be tested
- Developing a hypothesis requires the researcher to identify one character, variable, or descriptor of a sampling unit (*independent variable*) that relates (*causes, affects, or influences*) to another character, variable, or descriptor of the same or other sampling units (*dependent variable*)

Hypothesis Development

- **Formulating a Hypothesis**

- Important to narrow a question down so that it can be reasonably studied in a research project
 - Qualitative
 - Quantitative

Hypothesis Development

■ Qualitative Research

- Kleining presents 4 rules for scientific & qualitative processes
 1. (Refers to the subject/researcher) *“Prior to understandings of the phenomenon to be researched should be seen as provisional and should be transcended with the discovery of new information with which they are not consistent.”*
 2. (Refers to the object of study) *“The object is provisional; it is only fully known after the successful completion of the process of discovery.”*

Hypothesis Development

- **Qualitative Research**

- Kleining presents 4 rules for scientific & qualitative processes

3. (Refers to the action in relation to the subject of research, hence to data collection) *“The object should be approached from ‘all’ side; rule of the maximum variation of perspectives.”*
4. (Refers to the evaluation of the information gathered) *“Analysis of the data for common elements.”*

Hypothesis Development

- **Quantitative Approach**
 - Comparison and relationship between variables
 - Independent & Dependent variables to be separated and measured separately
 - Descriptive, Exploratory, & Experimental Studies

Hypothesis Development

- **Hypothesis: A Case Study**
 - **Case Study:** Salmon in fish farm
 - **Observation:** Fish have more fungus in summer, when water levels are low
 - **Background Research:** Fish that are oxygen stressed (low water levels) get more fungus



Hypothesis Development

- **Hypothesis: A Case Study**

- **Hypothesis #1:**

- Water levels affect the amount of fungus in fish

- **Hypothesis #2:**

- Salmon suffer more fungus in low water levels



Hypothesis Development

■ Hypothesis: A Case Study

— Hypothesis #3:

- Salmon have more fungus in low water conditions as there is less oxygen present

— Null Hypothesis:

- Low water conditions do not cause higher fungus levels in salmon
- Established variables, so now testable
- Test by eliminating other variables



Hypothesis Development

- **Good Hypothesis?**

- ***Ladybugs are a good natural pesticide for treating aphid infected plants.***
- Whether or not something is a '*good natural pesticide*' is too vague for a science fair project
- There is no indication of what will be measured to evaluate the prediction

Hypothesis Development

- **In-Class Activity**

- Refine your Hypothesis, Specific Aims, and Research Plan for your Grant Proposal

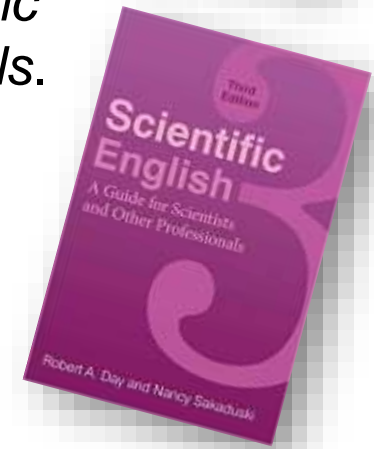
Writing Grant Proposals: Specific Aims Page, & Background

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Additional References

- Porter, R. (2007). Why Academics Have a Hard Time Writing Good Grant Proposals. *Journal of Research Administration*, 38(2), 37-43.
- Zlowodzki, M., Jönsson, A., Kregor, P. J., & Bhandari, M. (2007). How to write a grant proposal. *Indian journal of orthopaedics*, 41(1), 23.

Grant Proposals

■ Checklist

1. What is the problem to be addressed?
 - *Define the Question*
2. Is the Question Answered?
 - *Literature Research*
3. Formulate Hypothesis
4. Choose appropriate study design
5. Identify team & collaborators
6. Determine environmental & financial needs
7. Write study protocol

Grant Proposals

■ Elements of a Study Proposal

- I. Title Page
 - i. Table of Contents & Table of Figures
- II. Abstract
- III. Research Plan
 - i. Hypothesis & Specific aims
 - ii. Background & Significance
 - iii. Preliminary Results (if applicable)
 - iv. Research Design & Methods
 - v. Expected Outcomes & Impact
- IV. Budget & Justification
- V. Resources & Environment
- VI. Timeline
- VII. References

Zlowodzki *et al.* 2007

Writing Grant Proposals

Hypothesis & Specific Aims

- After Title Page, Table of Contents, & Abstract, the proposal has a one-page Specific Aims Page
 - Specific Aims page typically contains:
 - Introductory Paragraph
 - Second Paragraph
 - The Aims
 - Final Summary Paragraph

Writing Grant Proposals

Hypothesis & Specific Aims

- **Introductory Paragraph**

- First Sentence/*Hook*

- Briefly describe your proposal's main idea
 - Convey a sense of importance or urgency to your research
 - Explain quickly WHAT your research topic is and WHY it is critical that you conduct the research (i.e. saving lives, preventing cancer, etc.)

Writing Grant Proposals

Hypothesis & Specific Aims

- **Introductory Paragraph**

- What is *Known*

- State what is currently known
 - Not be very long (3-5 sentences) but it should ground the reader in the subject of your research
 - Provide the reader with only the necessary details to understand why you are proposing the work
 - Be concise and focused on only the key points

Writing Grant Proposals

Hypothesis & Specific Aims

- **Introductory Paragraph**

- *Gap in Knowledge*

- Information that is not known
 - Clearly state the gap in knowledge that needs to be addressed
 - Convey that your research will fill this gap using the funding that you are requesting

Writing Grant Proposals

Hypothesis & Specific Aims

- **Introductory Paragraph**

- The *Critical Need*

- Knowledge (hypothesis-driven), technique, new compound, or treatment that you propose to develop
 - This need is important to increase medically relevant knowledge or improve health care or other mechanical or bio-technology
 - The reason your proposal should be funded
 - Emphasize the significance of the problem you are trying to address

First Paragraph Example

Viruses are thought to be involved in 15% to 20% of human cancers worldwide, thus providing critical tools to reveal common mechanisms involved in human malignancies. As the etiologic agent of adult T cell leukemia/lymphoma (ATLL), human T cell leukemia virus type I (HTLV-1) is just such a virus. HTLV-1 encodes a potent oncoprotein, Tax, which regulates important cellular pathways including gene expression, proliferation, apoptosis, and polarity. Over the years, Tax has proven to be a valuable model system in which to interrogate cellular processes, revealing pathways and mechanisms that play important roles in cellular transformation. Although the Tax oncoprotein has been shown to transform cells in culture and to induce tumors in a variety of transgenic mouse models, the mechanism by which Tax transforms cells is not well understood. A large number of Tax mutants have been generated and their biological activities have been thoroughly characterized, primarily in cell culture systems. Currently, a major obstacle in the field is that the transforming activity of Tax mutants cannot be compared using available transgenic models due to random transgene integration sites, variable transgene copy number, and inconsistent transgene expression levels, making it difficult to link the biological activities of Tax mutants with their transforming potential.

- Color Key: Hook Known Information Gap in Knowledge Critical Need

Writing Grant Proposals

Hypothesis & Specific Aims

- **Second Paragraph**

- Introduce your solution that fills the gap in knowledge
 - What do you want to do?
 - Why are you doing it?
 - How do you want to do it?

Writing Grant Proposals

Hypothesis & Specific Aims

- **Second Paragraph**

- *Long-Term Goal*

- Overarching research goal
 - Since requesting support from a particular funding entity, important to ensure that your long-term goals align with their mission
 - Keep your wording general in this sentence—you are stating your long-term plans, and the reviewers understand that the specifics may be subject to change

Writing Grant Proposals

Hypothesis & Specific Aims

- **Second Paragraph**

- *Hypothesis* and *Proposal Objectives*

- State central hypothesis clearly, specifically, and with simple language
 - Demonstrate to the reviewers that you have a hypothesis-driven proposal that is testable
 - Describe how your project addresses the critical need, and clearly state the proposed solution
 - Avoid vague hypotheses because it will be unclear to the reviewers what you expect to determine with the proposed research

Writing Grant Proposals

Hypothesis & Specific Aims

- **Second Paragraph**

- *Rationale*

- Explain how you arrived at your central hypothesis (for example, using past studies and published literature)
 - State what your project's completion would make possible (e.g., new therapeutics), and tie it to the funding entity's mission

Writing Grant Proposals

Hypothesis & Specific Aims

- **Second Paragraph**

- *Qualifications*

- Briefly state your experimental design and why your team are the best to accomplish the research goals
 - Mention factors such as your preliminary data, personnel qualifications, laboratory equipment, etc., but keep it concise

Second Paragraph Example

To solve this problem we will develop an innovative mouse model system in which to study Tax tumorigenesis using targeting vectors containing wild-type or mutant Tax genes that are silenced by a preceding floxed stop cassette. These vectors will be knocked in to the Rosa26 locus of recipient mice by recombination. After crossing these mice with Lck-CRE mice, the stop cassette will be specifically excised in developing thymocytes where the Lck promoter is active, allowing conditional expression of wild-type or mutant Tax proteins in T cells, the natural target of HTLV-1 infection. The feasibility of our proposed mouse model is supported by the fact that Lck-Tax transgenic mice have been developed and produce a leukemia that closely resembles ATLL. Thus, targeting of Tax expression in cells in which the Lck promoter is active is expected to produce a similar disease in our model. In our improved model system, insertion into the Rosa26 locus will eliminate random integration sites and standardize gene copy number resulting in consistent levels of wild-type and mutant Tax protein expression.

- Color Key: Long-term Goal Proposal Objective Rationale Hypothesis Pay-off

Writing Grant Proposals

Hypothesis & Specific Aims

■ The Aims

- Briefly describe the Aim(s) that you will use to test your hypothesis
- Typical NIH R01 grants will have between 2 and 4 Aims
 - 2 to 4 sentences per Aim
 - Describe the experimental approach
 - How each aim will help answer your larger hypothesis
- You may have only 1 or 2 AIMS

Writing Grant Proposals

Hypothesis & Specific Aims

■ The Aims

- Tips that may help you to formulate aims:
 - Give your aim an active title that clearly states the objective in relationship to the hypothesis
 - Include a brief summary of the experimental approach and anticipated outcomes for each aim
 - If you have room, you may wish to include a sub-hypothesis and a short description of the *impact* of each aim
 - Sub-hypotheses are helpful to create the impression that each aim is valuable, testable, and independent of the others
- Plan to describe each aim in more detail in the methodology section of grant

Aims Example

Aim 1: The authors will establish an innovative mouse model for HTLV-1 Tax tumorigenesis.

Targeting vectors containing silenced wild-type or mutant Tax genes will be knocked in to the Rosa26 locus of C57BL/6 mice. These mice will then be crossed with homozygous Lck-CRE mice, thereby excising the stop cassette and generating mice that express wild-type or mutant Tax proteins specifically in T cells.

Aim 2: The authors will examine the effect of mutations that disable specific biological functions of Tax on Tax-mediated tumorigenesis.

Tax can bind to and regulate the activity of members of the SRF, CREB, NF-kB and PBM protein families, each of which has been implicated in oncogenesis. Mice established in Aim 1 will allow us to compare for the first time the tumorigenic potential of wild-type and mutant Tax proteins in an effort to identify pathways that are required for Tax tumorigenesis.

- Color Key: Aim Title Experimental Strategy Outcome or Impact

Writing Grant Proposals

Hypothesis & Specific Aims

■ **Final Summary Paragraph**

- This final paragraph of the Specific Aims is often overlooked, but vital for the impact of your proposal
- Think of your Specific Aims page as an hourglass, where the wide parts represent the general information and global significance, and the narrow parts are the fine details
 - If you end with the Aims Section you will end on fine details and a narrow scope
- Therefore, this final paragraph creates a firm, broad base to support your entire proposal

Writing Grant Proposals

Hypothesis & Specific Aims

■ Final Summary Paragraph

— Innovation

- Plainly state what is innovative about your project
 - What would completion of this proposal bring to the field that is not present currently?

— Expected Outcomes

- State your expected outcomes for this project
 - What do you expect to see at the completion of each aim?

— Impact

- State how your project would help those who need the new development
- Include a broad impact statement about how your proposal will benefit the people or other subjects that you mentioned in the opening paragraph

Final Summary Paragraph Example

The proposed studies will establish a new mouse model that will overcome current limitations and provide greater insight into the mechanism of HTLV-1 Tax tumorigenesis, knowledge that is currently lacking and that promises to yield novel insights into viral and cellular biology. The new and improved mouse model for Tax tumorigenesis will provide a valuable resource for the wider scientific community to pursue a multitude of studies that have not previously been possible due to limitations of existing mouse models of Tax.

- Color Key: Innovation Expected Outcomes Impact/Pay-off

Specific Aims Page

RUNNING HEADER...

Specific Aims

Viruses are thought to be involved in 15% to 20% of human cancers worldwide, thus providing critical tools to reveal common mechanisms involved in human malignancies. As the etiologic agent of adult T cell leukemia/lymphoma (ATLL), human T cell leukemia virus type I (HTLV-1) is just such a virus. HTLV-1 encodes a potent oncoprotein, Tax, which regulates important cellular pathways including gene expression, proliferation, apoptosis, and polarity. Over the years, Tax has proven to be a valuable model system in which to interrogate cellular processes, revealing pathways and mechanisms that play important roles in cellular transformation. Although the Tax oncoprotein has been shown to transform cells in culture and to induce tumors in a variety of transgenic mouse models, the mechanism by which Tax transforms cells is not well understood. A large number of Tax mutants have been generated and their biological activities have been thoroughly characterized, primarily in cell culture systems. Currently, a major obstacle in the field is that the transforming activity of Tax mutants cannot be compared using available transgenic models due to random transgene integration sites, variable transgene copies number, and inconsistent transgene expression levels, making it difficult to link the biological activities of Tax mutants with their transforming potential.

To solve this problem, we will develop an innovative mouse model system in which to study Tax tumorigenesis using targeting vectors containing wild-type or mutant Tax genes that are silenced by a preceding floxed stop cassette. These vectors will be knocked in to the Rosa26 locus of recipient mice by recombination. After crossing these mice with Lck-CRE mice, the stop cassette will be specifically excised in developing thymocytes where the Lck promoter is active, allowing conditional expression of wild-type or mutant Tax proteins in T cells, the natural target of HTLV-1 infection. The feasibility of our proposed mouse model is supported by the fact that Lck-Tax transgenic mice have been developed and produce a leukemia that closely resembles ATLL. Thus, targeting of Tax expression in cells in which the Lck promoter is active is expected to produce a similar disease in our model. In our improved model system, insertion into the Rosa26 locus will eliminate random integration sites and standardize gene copy number resulting in consistent levels of wild-type and mutant Tax protein expression.

- **Aim 1:** The authors will establish an innovative mouse model for HTLV-1 Tax tumorigenesis.
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Tax can bind to and regulate the activity of members of the SRF, CREB, NF-κB and PBM protein families, each of which has been implicated in oncogenesis. Mice established in Aim 1 will allow us to compare for the first time the tumorigenic potential of wild-type and mutant Tax proteins in an effort to identify pathways that are required for Tax tumorigenesis.

The proposed studies will establish a new mouse model that will overcome current limitations and provide greater insight into the mechanism of HTLV-1 Tax tumorigenesis, knowledge that is currently lacking and that promises to yield novel insights into viral and cellular biology. The new and improved mouse model for Tax tumorigenesis will provide a valuable resource for the wider scientific community to pursue a multitude of studies that have not previously been possible due to limitations of existing mouse models of Tax.

- Specific Aims page follows the Abstract
- Typically singled-spaced to fit on one page
- **STRONG 1st sentence**

Writing Grant Proposals

Background

■ **Background & Previous Research**

- This section may be labeled differently depending on the guidelines
- Provide the status quo of the relevant work field and identify a gap in knowledge or activities that must be filled to move the field forward
- Lay out the rationale for the proposed research project & summarize currently available data in the literature relevant to project
- If no systematic review or meta-analysis is in literature, you should do one

Writing Grant Proposals

Background

■ **Background & Previous Research**

- Addresses why proposed work is important in the field, and answers the question, “so what?”
- Show why the previous work needs to be continued
- Describe the magnitude of the problem to be addressed
- What is the population you are targeting?
- What is the incidence of the problem?
- Is the problem likely to increase in the future?
- Provide evidence of your own competence in the field

Writing Grant Proposals

Background

■ **Background & Previous Research**

- Describe the historic management of the problem and whether or not there is any consensus on the current management of the problem
- Are there any uncertainties about the treatment that need to be resolved?
- The purpose of the background & previous research section provides justification for the proposed study
- You need to convince the granting agencies that it is worth their money

Writing Grant Proposals

Background

■ **Background & Previous Research**

- Literature reviews should be selective and critical
 - Reviewers do not want to read through a voluminous working bibliography
 - Review pertinent works and provide your evaluation of them
- Discussions of previous work should therefore lead the reader to a clear impression of how you will be building upon what has already been done and how your work differs from theirs
- Establish what is original in your approach (innovative), what circumstances have changed since related work was done, or what is unique about the time and place of the proposed research

Writing Grant Proposals

Background

■ **Background & Previous Research**

- PI may include their own work (and that of their research team) related or preliminary to the proposed study
- Preliminary data or pilot studies must relate directly to the hypothesis or aims
 - Demonstrate to the reviewer that the aims are feasible and the team has the required experience and skills
 - Data may or may not be published, but published data have more credibility

