Writing your Specific Aims

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Note that some of the material in this presentation was taken from the online document below.

The Specific Aims are:

• A concise explanation of your proposal’s goals
• The **heart** of your proposal
• Your chance to grab the attention of the reviewers and convince them that the work is important and that you are the person or team to do it
• The section you should write first. Once you have good Aims, the research plan will fall into place.
Today

- What are specific aims?
- What is their importance?
- Components of the Specific Aims section
- What to address
- Strategy
- Review sample specific aims
- If time- try writing
Why so much emphasis on Specific Aims?

Reviewers will often only read

1. The Title (so it better be good)
2. The Abstract
3. The Specific Aims- you need to convince them in this section or they will stop reading.
Is this the response you want from your reviewer?

OMG! I don’t understand a word! Get me a Tylenol.
Or this??
This is what you are going for. Right?
How to write a compelling Specific Aims section
The specific aims section is usually **one page** in length for most grant proposals (including the ASCEND Pilot Research Program)

- State concisely the goals of the project
  - Test a stated hypothesis
  - Create a novel design
  - Solve a specific problem
  - Challenge an existing paradigm or practice
  - Address a critical barrier
  - Develop a new technology
- Summarize the expected outcomes
- State the impact the findings will have on the field
Is there a formula that can be used to write specific aims?

Yes

But...the science needs to be good
Many Specific Aims sections have introductory paragraphs

Use the introductory paragraph to:
1. introduce your topic and grab attention
2. describe a gap in knowledge in your area of study that *directly relates to the mission of the funding agency*

**Format:**
1. First sentence is the attention grabber. What is the topic and why is it important
2. Next 3-5 sentences: State what is known about your topic.
3. State the gap in knowledge that you are addressing
4. How does filling this gap address a critical need in the field

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.
Second Introductory Paragraph

May not be necessary

What does this paragraph do?
1. Introduces the solution that fills the gap mentioned in paragraph 1.
2. Convinces the reviewers that you have the solution and the expertise.

Include the following components:
1. State the long term goal and align it with the mission of the funding agency
2. State the proposal hypothesis and the objectives
3. Discuss the rationale. How did you arrive at the hypothesis? Past studies, preliminary data?
4. Briefly state qualifications and/or essential, innovative technology available
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.
Now What?

The aims themselves of course

How many aims?
• Large, multi-year grants will have 2-4 aims, usually 3.
• Smaller grants (e.g. the ASCEND pilot grant) will have 1 or 2.

Important!
• The aims should be related to one another, but not dependent on one another. Why?
• Use the active voice and strong verbs.
• Use bold font or bullets to separate aims from one another. The separation and distinction makes for easy reading.
Structure of the Specific Aim

In 2-4 sentences, describe the experimental approach and how it will answer part of your larger hypothesis.

• First sentence or title: Each aim should have an active, to the point first sentence that clearly states the objective and how it relates to the hypothesis
• Brief summary of the experimental approach and anticipated outcome
• Pay-off for each aim indicates its value and independence
Sample Specific Aims

**Aim 1** 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** 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-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.
Other sample specific aims

**Introduction**

Does the intro grab your attention?
Do you know what the topic is and why it's important?
Is there info on what is known?
Is a gap in knowledge addressed?
What need is addressed?
Relevance to mission of funding agency

**Further along**

Has the solution to the gap been presented?
Is a long term goal presented?
Is a hypothesis presented?
Rationale? How did they arrive at the hypothesis?
Is it clear?
Are you convinced that the investigators know what they are talking about and can do the work?
Summary Paragraph

Not always included, but it can reinforce the impact of your proposed work

Address the following:

• Innovation: What is new? What’s added to the body of knowledge in the field?
• Expected outcomes: For each aim. Can be included in each aim instead of in summary.
• Impact/Pay-off: How will the outcomes impact the important need addressed in introduction?
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.
Practical Considerations

1. Be practical. Can you do the work proposed in the allotted time (e.g. 1 year)? Really.
2. Is the budget appropriate for the work described?
3. Always be thinking of the next step.

Think it through. Get help. Create a timeline.

Edit, edit, edit!
Writing excellent specific aims is not easy. It takes a lot of practice. Work with others. Ask successful grant recipients to work with you and critique your efforts. Consult the many available online resources.

The End