

**A successful proposal
is an effective act of
communication**

The key to good communication is knowing your audience and putting yourself in their place



“The Reviewer at Work”

The audience for your research proposal . . .



Your goal is to excite and persuade your reviewers

How do you want the reviewers
to react to your proposal?



First, writing a grant is different from writing a paper

Paper	Grant
Looks backwards	Looks forwards
Describes what you've done	Describes what you're going to do
—> Conclusions supported by data and rigorous analysis	—> Outcomes supported by feasibility and competence
Nuanced, equivocal	Confident, direct

There are key elements to writing a successful proposal

Your proposal must have a high likelihood of producing results that will have an impact:

— **Emphasize Significance, Innovation!**

Your proposal must be easy to understand:

— **Keep it simple, concise & logical!**

You must know what is required for the proposal:

— **Read the Instructions!**

You must know how the proposal will be reviewed:

— **Write to the Review Criteria!**

Research questions must have significance and impact

Does the project address an important problem?
A gap in knowledge or treatment?

If the goals of the project are achieved,

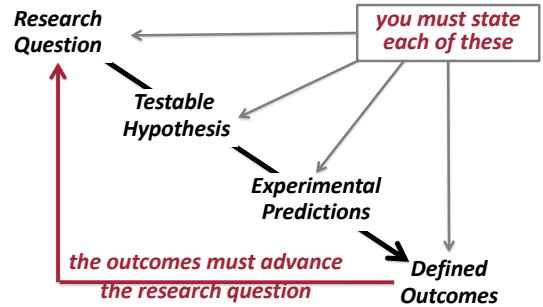
- how will scientific knowledge or clinical practice be improved?
- will the results **exert a sustained, powerful influence on the research field?**

"Now you know that, what do you know?"

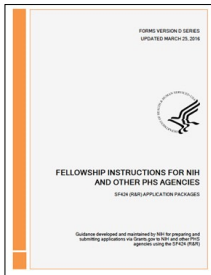


Floyd Bloom, MD

Your proposal must have a logical framework and tell a coherent story



Understand the instructions and write to the review criteria



Candidate's Preparedness and Potential



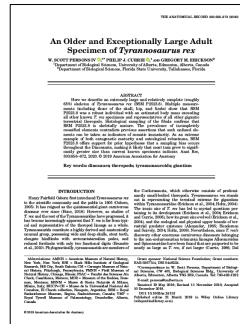
Research Training Plan



Commitment to Candidate

The power of narrative . . .

Which is more persuasive?



<https://www.flickr.com/photos/vipnyc/2620302548>

Tell a good story . . .

Your audience will be convinced by your evidence but excited by your narrative . . .

Narratives have three parts:

1. **Set-Up** (exposition)
— the problem or question
2. **Conflict/Action**
— how you will solve that problem
3. **Resolution**
— the outcome you expect

The Specific Aims page defines your narrative

PAR Statement

Problem

Action

Result

Write simply, clearly, and logically

Apply George Orwell's rules for writing well . . .



Never use a long word where a short one will do.

If it is possible to cut a word out, always cut it out.

Never use the passive where you can use the active.

Break any of these rules sooner than say anything outright barbarous.

Politics and the English Language, Orwell, 1945
(https://biblio.wiki/wiki/Politics_and_the_English_Language)
Image: George Orwell's press card: <http://www.netcharles.com/orwell/>

If it is possible to cut a word out, always cut it out

Most **adjectives** and **adverbs** are unnecessary
— **cut them out!**

Delete the “**wiggle**” words:
— a number of (some, several)
— in order to (to)
— is able to (can)

Remove **excess modifiers**:
— quite, totally, completely, absolutely

Avoid **redundancies**:
— (knowledgeable) experts
— (new) innovation



The Specific Aims page is the most important part of your proposal . . .

Describes concisely the goals, objectives & outcomes of the proposed studies

Is a useful summary for obtaining early feedback on your proposal (*reality check!*)

Is the hardest part of the proposal to write

You must devote time to draft & polish your Specific Aims!

A. SPECIFIC AIMS
Myelin associated glycoprotein (MAG) is a 100,000 dalton component of the myelin membrane. The molecule is similar in structure to neural cell adhesion molecules and it has been proposed that MAG may mediate the initial stages of myelination. In previous studies, supported by this grant, we have demonstrated that it is likely that MAG plays a critical role in the early stages of myelination. The studies proposed here will focus on the structure of the MAG gene, the mechanisms of its regulation during myelination and remyelination, and attempts to understand the function of MAG in disrupting its expression. It is the aim of the proposed studies to:

1. Analyse the mechanism of regulation of the MAG gene.
2. Generate transgenic mice expressing regulatory regions of the MAG gene and to analyse the expression of the MAG gene in vivo.
3. Analyse the expression of the MAG gene following a demyelinating viral infection of the central nervous system.
4. Disrupt the expression of the MAG gene in order to assess the functional consequences of decreased or absent MAG expression on myelination.
5. Investigate the genetic defects in the mouse mutant quivering and the relationship of this mutation to the MAG gene.

MAG appears to play a critical role in the early stages of myelination by mediating the initial contact between the myelinating cell and the axon and it is likely that MAG plays a similar role in remyelination following a myelinating injury. A better understanding of the ways that regulate the expression of MAG will be essential for designing strategies to encourage the formation of new myelin in diseases such as multiple sclerosis.

A good format for a Specific Aims Page is a sandwich

First paragraph — topic, goals, objectives, hypothesis, rationale

Specific Aims — objectives, description

Last paragraph — impact, outcomes

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The Specific Aims page should address the reviewer's three major questions

Is the study based on good science & worth doing?

Are the methods sound & feasible?

Will the outcomes change science & human health?

Using the Template for a Specific Aims Page . . .

The Template lists the essential elements of a Specific Aims page
— complete each element as a sentence
— combine the sentences into a narrative
— polish
— review
— polish again
— ask for feedback
— polish again

ATC Neuroscience Institute **NSF Grant Reviewer** **September 10, 2005**
Template for a Specific Aims page
First Paragraph / Introduction
What is the topic? Write a concise, active sentence describing the topic of the proposal.
What is the gap? Describe the gap in knowledge or current need that the proposal will address.
What is the long-term goal? Try to state the goal to be understood . . .
What are the specific objectives? Describe the objectives for this proposal.
What is the hypothesis? Define your hypothesis without reference to experiments.
What is the rationale for the hypothesis? Describe literature background & preliminary data.
What is the Summary (Outcome / Significance)? Provide a sentence summarizing the project.
Specific Aims (The Goal)
Write a short descriptive title.
Write a short descriptive sentence to be performed. Hypothesis to be tested. A clear outcome predicted by hypothesis (this should have clear, measurable outcomes).
Aim 1.
Aim 2.
Second Paragraph / Concluding Comments
What are the long-term outcomes / impact? Describe how the research combined with the training plan will enable you to become a productive independent researcher.

The first paragraph provides the rationale for the proposed studies

What is the **Topic**?

What is the **Gap** in knowledge?

What is the long-term **Goal** of your research?

What are the specific **Objectives** for the proposal?

What is the **Hypothesis**?

What is the **Evidence** for the hypothesis?

What is the **Summary**?

You have a half page or less (~300 words) to set the stage for the proposal & excite the reviewer!

**You must grab the reviewer's attention at the start
—consider opening lines in fiction . . .**

"It is a truth universally acknowledged, that a single man in possession of a good fortune, must be in want of a wife." Jane Austin *Pride and Prejudice*

"It was a bright cold day in April, and the clocks were striking thirteen." George Orwell *Nineteen Eighty-Four*

"We were somewhere around Barstow on the edge of the desert when the drugs began to take hold." Hunter Thompson *Fear and Loathing in Las Vegas*

"124 was spiteful." Toni Morrison *Beloved*

Compare with . . .

"It was a dark and stormy night; the rain fell in torrents, except at occasional intervals, when it was checked by a violent gust of wind which swept up the streets (for it is in London that our scene lies), rattling along the house-tops, and fiercely agitating the scanty flame of the lamps that struggled against the darkness."

Edward George Bulwer-Lytton, *Paul Clifford* (1830)

Start the Specific Aims with a concise, active statement introducing the topic of the proposal

Infantile Respiratory Virus (IRV) is a new agent that causes rapid inflammation of the lungs in young children.

Pancreatic cancer is commonly diagnosed only at an advanced stage.

Dysfunction of small vessels of the brain is associated with early cognitive impairment in dementias.

Your turn:

Compose a topic sentence for your proposal.

Next describe the gap in knowledge or unmet need that your proposal will address

But the exact mechanism of its pathogenesis is unknown, providing little guidance for treatment.

The lack of biomarkers for early-stage detection challenges effective treatment of this deadly cancer.

Vascular damage is usually ascribed to accumulation of amyloid- β but recent evidence implicates early changes in the blood brain barrier (BBB).

Your turn:

Describe the gap in knowledge or unmet need that your proposal addresses.

Describe the long-term goal of your research

My goal is to understand the biology of infectious agents to provide a foundation for effective therapies.

My goal is to develop novel methods for the detection and treatment of cancers.

My goal is to study the function and dysfunction of the brain in dementias.

Your turn:

Describe the long term goal of your project.

Describe the specific objectives of your project

This proposal will define the mechanism of virus binding to its host cells in order to understand the pathogenesis of IRV.

The goal of this proposal is to develop biomarkers for early detection of pancreatic cancer by investigating the expression of miRNAs.

In this proposal I will investigate the action of a novel factor — AFF1 — secreted by astrocytes on the BBB.

Your turn:

Describe the specific objectives of your project.

Define the hypothesis underlying your proposal

I will test the hypothesis that IRV initiates infection by binding of the IRV-knob protein to the CAR protein.

My hypothesis is that tumorigenesis changes the expression of cellular and secreted miRNAs.

I hypothesize that inflammation of astrocytes stimulates release of AFF1 from astrocytic endfeet resulting in breakdown of the BBB.

Your turn:

Define the hypothesis for your project.

Describe the evidence for the hypothesis

Preliminary studies have shown that IRV can infect CAR-positive host cells but not CAR-negative cells.

We have shown that miRNA-179A and miRNA-208D are increased in expression in pancreatic tumor cells compared to normal tissue.

AFF1 was identified in a screen for genes upregulated in astrocytes following inflammation; knockout mice for AFF1 showed a decrease in BBB breakdown after an inflammatory stimulus.

Your turn:

Define the evidence for your hypothesis.

Provide a Summary for the proposal

The expertise of our laboratory on adenoviruses will be applied to the pathogenesis of a novel virus.

I will apply our extensive experience with miRNAs to the diagnosis of a common and highly lethal cancer.

This proposal will investigate the mechanism of action of AFF1 in vitro.

Your turn:

Define the rationale for your project.

Your Specific Aims should fit the scope of your effort

Fit the aims to the effort:

- Fund award one person (you!) over 3–5 years
— typically, 2–3 aims

Avoid contingent aims (the “fatal flaw”)

Provide a timeline for your aims in the proposal

Aim	Year 1	Year 2	Year 3
1	→		
2	→		
3	→		

First define the scope of your aims

1. To characterize the regions of the IRV-knob protein necessary for binding to the host cell CAR protein.
2. To develop monoclonal antibodies against regions of the IRV-knob protein that inhibit binding to CAR.

First define the scope of your aims

1. To characterize the expression of miRNA-179A and miRNA-208D in pancreatic tumor cells.
2. To determine the relationship between expression of miRNA-179A and miRNA-208D and pancreatic tumorigenesis.

First define the scope of your aims

1. To characterize the release of AFF1 from astrocytes in vitro.
2. To determine the action of AFF1 in astrocyte-capillary co-cultures.

Expand each specific aim to provide a short descriptive title & brief description

Aim 1. To determine the regions of the IRV-knob protein necessary for binding to the host CAR protein.

My hypothesis predicts that alteration of the env region of the knob protein will decrease binding to the host cell CAR protein. I will test this prediction by

- a) Generating variants of the knob protein with structural alterations in env.
- b) Assessing binding to the CAR protein in vitro.

Your turn:

Write a title & description for a specific aim.

The last paragraph focuses on impact and outcomes

Outcomes & Impact :

This project will define the mechanism of IRV infection and provide a foundation for immune therapy.

Development of biomarkers for early detection will result in dramatic improvement in the survival rate for pancreatic cancer.

These studies will characterize the function of a new factor with implications for the pathogenesis of dementias.

Your turn:

Describe the outcomes & impact of your project.

The last sentence should be a statement about the training potential of the proposal

"This project and the associated training and mentoring will enable me to advance my goal of becoming an independent investigator in the field of [INSERT FIELD]."

Next steps: put the elements into a coherent & logical narrative, polish, and get feedback

Checklist *

[Print](#)

Iterative Approach to Application Planning Checklist

Staying in your niche, propose a project that

- Addresses a highly significant problem.
- Is innovative—can create new knowledge.
- Is unique.

Outline three Specific Aims and one or more testable hypotheses.

- Create (usually) three Specific Aims you can achieve in four or five years.
- Make sure they have clear endpoints reviewers can readily assess.
- Create a hypothesis (or hypotheses) that is well focused and testable by the aims and experiments.
- Identify a potential funding institute and a study section that would likely embrace your research.
- Outline experiments.
- Assess feasibility.
- See whether you have access to all needed resources and expertise.
- Make sure the project is not growing too big for your targeted time and budget.
- If you hit a roadblock, go back to the failure point and revise your plans.

***NIAID Grants Tutorials — Specific Aims:**
<https://www.niaid.nih.gov/grants-contracts/draft-specific-aims>

Well written specific aims help you . . .

Sort out the logic of your proposal:

- how many aims
- dependence of aims on each other
- feasibility and scope

Get **early** feedback on your proposal

Talk with a Program Officer