

**A funded proposal
 is a successful 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 ← Describes what you've done → Conclusions supported by data and rigorous analysis <i>Nuanced, equivocal</i>	Looks forwards → Describes what you're going to do → Outcomes supported by feasibility and competence 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?"



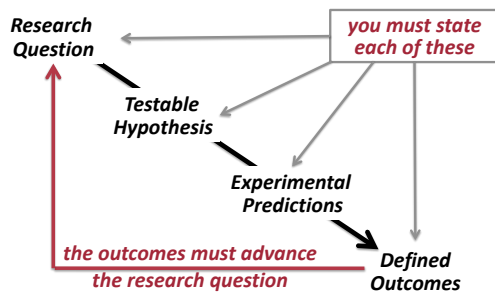
Floyd Bloom, MD

Your proposal must address the review criteria

For example, the review criteria for NIH career development awards:

- Candidate:** do you have potential?
Career Plan: will you learn new skills?
Research Strategy: is it feasible? . . important?
Mentors: do they have experience?
Environment: are there support & resources?

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



The power of narrative . . .

Who is more persuasive?



U.S. Preventive Services Task Force
Guidelines for Prostate Cancer Screening



Rudy Giuliani
"The report does not make sense."

http://commons.wikimedia.org/wiki/File:Rudy_Giuliani.jpg

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

A good narrative is essential for a career development or training proposal

The story is about you!



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
(http://wikilivres.ca/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 “wobble” 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!

1. 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 axon-axon interactions during the initial stages of myelination. In previous studies, supported by MRI scans, we have demonstrated that MAG is an early myelin marker. Using advanced techniques, we have now identified the structure of MAG and we are currently working to determine the mechanism of its regulation during myelination. The studies proposed here will focus on the structure of the MAG gene, the mechanism of its regulation during myelination and remyelination, and attempts to understand the function of MAG in the formation of the myelin sheath. It is the aim of the research studies to:

1. Analyze the mechanism of regulation of the MAG gene.
2. Generate transgenic mice expressing regulatory regions of the MAG gene and to analyze the expression of the MAG gene in vivo.
3. Analyze the expression of the MAG gene in the central nervous system following 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 axon and the myelin sheath. The MAG gene is a major site in myelination following a demyelinating disease. A detailed understanding of the factors that regulate the expression of MAG will be essential for developing strategies to increase the formation of myelin in disease states in 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

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 axon-axon interactions during the initial stages of myelination. In previous studies, supported by this **Set-Up** MRI scans, we have demonstrated that MAG is an early myelin marker in the central nervous system. The studies proposed here will focus on the structure of the MAG gene, the mechanism of its regulation during myelination and remyelination, and attempts to understand the function of MAG in the formation of the myelin sheath. It is the aim of the research studies to:

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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

Short Writing Worksheet Template for a Specific Aims page March 20, 2012

First Paragraph: Possible Introduction
What is the Topic? Write a sentence, or two sentences introducing the topic of the proposal.

What is the Goal? Describe the gap in knowledge or current need that the proposal will address.

What is the long-term Goal? Our long-term goal is to understand . . .

What are the specific Objectives? Describe the objectives for this proposal.

What is the Hypothesis? Outline your hypothesis without reference to experiments.

What is the Evidence for the Hypothesis? Describe the evidence background & preliminary data.

What is the Rationale / Significance? Describe the significance for the proposal.

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 **Rationale / Significance**?

**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 . . .**

"All happy families are alike; each unhappy family is unhappy in its own way."

Leo Tolstoy *Anna Karenina* (1878)

"It was a bright cold day in April, and the clocks were striking thirteen."

George Orwell *Nineteen Eighty-Four* (1949)

"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* (1972)

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.

Diabetes can be prevented by behavioral change.

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.

There are low success rates, however, in sustaining effective behavioral interventions in at-risk groups.

Your turn:

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

Describe the long-term goal of your research

The long term goal of our laboratory is to understand the biology of develop infectious agents to provide a foundation for effective therapies.

Our laboratory focuses on micro-RNAs (miRNAs) in the detection and treatment of cancers.

Our goal is to design and implement behavioral interventions to prevent the onset of diabetes.

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.

Our studies will evaluate novel behavioral interventions in adolescents.

Your turn:

Describe the specific objectives of your project.

Define the hypothesis underlying your proposal

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

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

We hypothesize that on-line approaches, particularly involving mobile media, will be well-accepted by adolescents and effective in this population.

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.

On-line behavioral interventions ("mHealth") have been used successfully in adult diabetic populations; preliminary studies demonstrate that this approach can be successfully translated to adolescents.

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.

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

This proposal is a comprehensive assessment of the effectiveness of mHealth approaches in adolescents.

Your turn:

Define the rationale for your project.

Your Specific Aims should fit the scope of your effort

Fit the aims to the effort:
for a K Award: one person (you!) over 3–5 years

Typically no more than three 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 determine the amino acid sequence of the IRV knob protein.
2. To characterize the regions of the IRV-knob protein necessary for binding to the host cell CAR protein.
3. 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.
3. To measure the expression of circulating miRNA-179A and miRNA-208D in patients with pancreatic cancer.

First define the scope of your aims

1. To develop a mobile mHealth application designed to promote healthy behaviors in adolescents.
2. To assess the acceptability and behavior changes in adolescents at risk of developing early-onset type II diabetes.

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

Aim 2. To determine the regions of the IRV-knob protein necessary for binding to the host CAR protein.

Our hypothesis predicts that alteration of the env region of the knob protein will decrease binding to the host cell CAR protein. We 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 innovation, impact and outcomes

Innovation:

IRV is a new virus: these studies are the first attempt to define the mechanism of its infection.

This proposal applies a novel approach—miRNAs as biomarkers—to the diagnosis of pancreatic cancer.

This proposal is the first evaluation of a novel mHealth approach for behavioral intervention to prevent diabetes in adolescents.

Your turn:

Describe the novel aspects of your project.

The last paragraph focuses on innovation, impact and outcomes

Outcomes & Impact :

These 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 provide a new, cost-effective approach to controlling the early onset of diabetes.

Your turn:

Describe the outcomes & impact of your project.

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

Checkpoint*

- ❑ My reviewers would see my aims as tackling an important problem in a significant field.
- ❑ They would view my aims as being innovative, but not too innovative
- ❑ My Specific Aims can test my hypothesis (or hypotheses)
- ❑ They are doable within the grant period I am requesting
- ❑ The aims and hypothesis (or hypotheses) are concrete and well-focused.
- ❑ I can define endpoints my peer reviewers will be able to assess.

*NIAID Grants Tutorials:

<https://www.niaid.nih.gov/grants-contracts/apply-grant>

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

Questions?