First, writing a grant is different from writing a paper

<table>
<thead>
<tr>
<th>Paper</th>
<th>Grant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Looks backwards</td>
<td>Looks forwards</td>
</tr>
<tr>
<td>Describes what you've done</td>
<td>Describes what you're going to do</td>
</tr>
<tr>
<td>-&gt; Conclusions supported by data and rigorous analysis</td>
<td>-&gt; Outcomes supported by feasibility and competence</td>
</tr>
<tr>
<td>Nuanced, equivocal</td>
<td>Confident, direct</td>
</tr>
</tbody>
</table>

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!

It is essential to start with a good question

What is the mechanism of X?

Is this drug a better treatment?

Does this change in clinical practice improve outcomes?

For NIH research proposals high impact is determined by . . .
the likelihood for the project to exert a sustained, powerful influence on the research field

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

- Research Question
- Testable Hypothesis
- Experimental Predictions
- the outcomes must advance the research question
- Defined Outcomes

you must state each of these

©2016 Robert J. Milner, Ph.D. & Joan M. Lakoski, Ph.D.
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.”

So, 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.
Never use the passive where you can use the active.

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

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

There are good resources to help you write well

Writing Science in Plain English, Anne E. Greene (2013)
Houston, We Have a Narrative, Randy Olson (2015)
The Sense of Style, Steven Pinker (Penguin, 2014)
Why Academic Writing Stinks, Steven Pinker (Chronicle of Higher Education)
Plain Language — US Government
Written Communication — CLIMB (Northwestern)
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 good format for a Specific Aims Page is a sandwich

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

Set-Up
- Specific Aims
- objectives, description

Action

Last paragraph
- impact, outcomes

Resolution

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!

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!

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

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 the fourth most common cause of death from cancer in the USA.

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.

Diagnosis and treatment, however, is challenged by a lack of biomarkers for early stage detection.

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 develop effective therapies against infectious agents through understanding their basic biology.

Our laboratory focuses on the function of miRNA (miRNAs) in the detection and treatment of cancers.

Our long-term goal is to understand how behavioral modification can prevent the early onset of diabetes.

Your turn: Describe the long term goal of your project.

Describe the specific objectives of your project

This proposal will focus on understanding IRV infection through defining the mechanism of virus binding to its host cells.

I will focus this proposal on the expression of miRNAs in pancreatic cancer with the goal of developing biomarkers for early detection.

This proposal will focus on testing behavioral interventions in adolescents.

Your turn: Describe the specific objectives of your project.

Define the hypothesis underlying your proposal

By homology with other respiratory adenoviruses, we hypothesize that IRV initiates infection by binding of the IRV-knob protein to the CAR protein.

Our hypothesis is that tumorigenesis results in dysregulation of both cellular and secreted miRNAs.

On-line approaches, particularly involving mobile media, are well-accepted by adolescents. Therefore, our hypothesis is that these approaches will be most effective in this population.

Your turn: Define the hypothesis for your project.

Describe the evidence for the hypothesis

In preliminary studies using an in vitro system IRV is able to infect CAR positive host cells but not CAR-negative cells.

In preliminary studies I 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.
Describe the rationale for the proposal

This proposal will enable me to apply the expertise of our laboratory with adenoviruses to understand the pathogenesis of a novel virus.

This proposal will apply our extensive experience with miRNAs to an important and common 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

<table>
<thead>
<tr>
<th>Aim</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 recently discovered 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.

To our knowledge, this proposal is the first attempt to use mHealth approaches for behavioral intervention in adolescents.

**Outcomes & Impact:**
The proposed studies will define the mechanism of IRV infection and provide a foundation for immune therapy.

Development of biomarkers for early detection has the potential for 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.

### 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.


### You can also use your specific aims to . . .

Talk with a Program Officer
Test your thinking by getting feedback on your ideas in a safe and constructive manner
Open new opportunities as you develop your ideas and look for potential research collaborators.