

Grant Writing Series

Office for Postdoctoral Scholars
Mahley Auditorium, Gladstone Institutes

Writing a Clear & Compelling Specific Aims Section

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How do the Specific Aims fit into the proposal?

For All Funding Agencies, the Proposal Provides Answers...

1. What do you intend to do?
2. Why is this worth doing? How is it innovative?
3. What has already been done in this field?
4. What will this new work add to the field of knowledge and to public health?
5. What have you (and your mentor/collaborators) done to establish the feasibility of what you are proposing to do?
6. How will the research be accomplished?

The Research Plan for Most Agencies

Each section describes an important aspect of the proposed research:

Specific Aims: research steps for testing your hypothesis or accomplishing your objective

Background and Significance: concise description outlining the important need addressed by your research, its scientific merit, and the impact of the research to the field of science and to public health (tailored to your research focus)

Preliminary Studies: data showing the viability of your proposal

Research Design and Methods: detailed description of your planned experiments or intervention (including statistical analyses & sample size calculations); expected outcomes; anticipated problems & alternative approaches

The Research Plan for NIH NRSA and K Awards

SPECIFIC AIMS (1 page)

RESEARCH STRATEGY (6 pages), includes:

Significance

Innovation (K awards)

Approach

For each aim:

Rationale

Research design

Methods (including statistical)

Expected outcomes

Potential problems and alternative strategies

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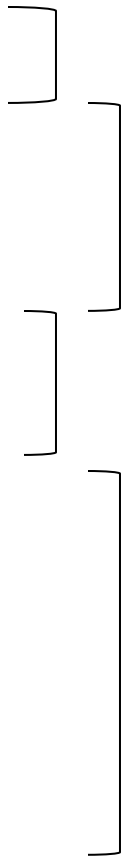
The Components of the Aims Section

- introduces **the problem** you are addressing; indicates if your research has contributed
- identifies the **specific gap** in knowledge that the proposed research will fill.
- introduces the **aims or objectives** of project and the specific hypotheses to be tested; describes the basis for the hypothesis.
- briefly **describes the main techniques** you will use to answer questions;
- highlights your qualifications to do the research
- describes **the advance** your study represents.

Review of Specific Aims Sections
(Exercise 1 in Supplemental Handout)

Eukaryotic innate immune systems act as effective barriers to infection by microorganisms. Understanding the mechanisms that bacterial pathogens employ to circumvent innate immune systems will improve our ability to control disease. Plants and animals use specific pattern recognition receptors (PRRs) to recognize conserved molecules of microorganisms (known as PAMPs). Plants have numerous PRRs that can recognize specific virulence proteins specifically present in pathogens (known as Avr proteins). Many Gram-negative bacteria use type III protein secretion systems to inject effector proteins into host eukaryotic cells. We have shown that a primary role for many *Pseudomonas syringae* type III effectors is to suppress innate immunity. However, the enzymatic activities and the mechanisms that type III effectors use to suppress innate immunity are not well understood. Identifying the enzymatic activities of type III effectors and their substrates is essential to identify important components of innate immunity and to improve strategies to control bacterial diseases.

Our long-term goal is to elucidate the molecular basis for suppression of innate immunity by type III effectors. The objective of this application is to identify targets of the P. syringae type III effector HopU1, a mono-ADP-ribosyltransferases (ADP-RTs), and to determine its roles in bacterial pathogenesis. The central hypothesis of the proposed experiments is that the targets of the HopU1 ADP-RT type III effector will be components of innate immunity. We formulated this hypothesis based on the literature and on our research on other type III effectors as well as our preliminary data showing that HopU1 suppresses outputs of innate immunity. Based on our preliminary data, one of these proteins, AtGRP7, plays a role in innate immunity.



We are prepared to undertake the proposed research because we have extensive experience in manipulating type III systems, and we were among the first to report that certain type III effectors suppress innate immunity. In addition, our preliminary identification of HopU1's substrates has positioned us well to perform the experiments described in this application. Our research team includes experts in the following areas: type III secretion systems, proteomics and mass spectrometry, Affymetrix microarrays, plant glycine-rich RNA-binding proteins, and animal pathogen ADP-RTs. This qualified group of investigators will insure that our discoveries are linked to basic concepts of pathogenesis and immunity in both plants and animals.

The Specific Aims of this application are as follows:

- 1. Determine the molecular consequence of ADP-ribosylation on the function of AtGRP7 and elucidate the role this protein plays in innate immunity.** *Our working hypothesis* of this aim is that AtGRP7 binds to immunity-related RNAs to enhance the innate immune response and that ADP-ribosylation by HopU1 disrupts its function.
- 2. Identify additional substrates of HopU1 and verify their involvement in innate immunity.** *Our working hypothesis is* that the plant targets for the HopU1 ADP-RTs will be important components of plant innate immunity.
- 3. Analyze the affect that HopU1 has on host-microbe interactions.** *Our working hypothesis of this aim is* that HopU1 type III effector suppresses innate immunity. This is based on our preliminary data and in this aim we will determine to what extent this occurs with HopU1.

The proposed research is innovative because, to date, ADP-RTs have not been implicated in the suppression of innate immune surveillance systems. Moreover, RNA-binding proteins have not been described as substrates for ADP-RTs and, therefore, represent novel substrates for this important group of bacterial toxins. Collectively, we expect the outcomes of these experiments will greatly add to our understanding of the activities and roles of type III effectors, particularly in how they suppress innate immunity in eukaryotes.

Overview/construction of typical Specific Aims page

Specific Aims

Succinct statement regarding the overall research area in relation to human health and disease. For example: Cardiovascular disease is the leading cause of death and disability in developed countries and is highly associated with numerous risk factors. These factors include genetics, diet, obesity, cigarette smoking, hypertension, blah blah blah.

What's known (this section should include references!)

Gap in knowledge (*i.e.*, what's missing). For example: Despite advances in the diagnosis and treatment of occlusive cardiovascular disease, the mechanisms involved in _____ remain to be established.

The proposed studies will address this gap by _____. The combined results of these investigations will _____.

The long-term goal of these research efforts will examine the hypothesis that _____. The following Specific Aims will address this hypothesis as follows:

Specific Aim #1: To verb (define, establish, elucidate etc)

Hypothesis:

Rationale and/or Approach:

Specific Aim #2: To verb (define, establish, elucidate etc)

Hypothesis:

Rationale and/or Approach:

Specific Aim #3: To verb (define, establish, elucidate etc)

Hypothesis:

Rationale and/or Approach:

Summary paragraph with restatement of the problem to be addressed and the area/approach of study. For example: In summary, the proposed studies will _____. The proposed studies are *significant* because _____. The planned approach is *innovative* because _____. As a result, these studies will have a significant *impact* on our understanding/approach to _____, and will lead to improved treatments for _____ to reduce the death and disability associated with these devastating disorders. Completion of the proposed studies will also insure the comprehensive research training of the applicant and contribute to the development of a successful career as an independent (clinician) investigator.

40,000 foot view

~3/8 page

~3/8 page

~1/4 page

Specific Aims: NIH Template

Source: *NIH F-Award (NRSA) Handbook, UT Austin*

ANOTHER EXAMPLE – Mentored NIH K proposal

Paragraph 1

3. SPECIFIC AIMS AND HYPOTHESES Community-acquired pneumonia causes substantial morbidity and mortality worldwide.¹⁴ In the U.S., CAP is among the most common and costly causes of hospitalization in young children.¹⁵ Clinical examination and chest radiography do not differentiate between viral and bacterial CAP.^{16,17} Conventional diagnostic tests (e.g., sputum cultures) used in adults are not feasible in young children and high yield tests (e.g., lung tap)¹⁸ are too invasive to be routine. Other bacterial diagnostics infrequently identify the causative pathogen (e.g., <7% for blood cultures) limiting their diagnostic utility. Viral tests, while often positive, do not exclude the possibility of bacterial co-infection.^{19,20} Therefore, patients with CAP receive empiric antibiotic therapy, which confers no benefit for children with non-bacterial infections, but places children at risk for adverse drug reactions, treatment-related complications (e.g., *Clostridium difficile* colitis) and antibiotic resistance.²¹ There is a pressing and unmet need for *non-invasive diagnostic tests that permit accurate and timely clinical decision-making in children with CAP.*²²

Paragraph 2

The interaction between pathogen and host results in a unique metabolic profile that is detectable in the host's urine.⁷ Quantitative metabolomics can simultaneously detect and quantify metabolites (small molecules, < 1 kDa) in a biological sample using ¹H- NMR.^{23,24} Quantitative metabolomics testing of the urine is *simple, noninvasive and rapid* (< 1 hour, as opposed to >24 hours for conventional blood culture techniques).²⁵ We developed a prospective cohort study in our Emergency Department to examine approaches to investigate the etiology of pediatric CAP. Using this cohort, I began investigating the potential for metabolomics to distinguish pathogens in CAP. Over the past 3 years, we enrolled 169 children between 3 months and 11 years of age with CAP. Our preliminary data suggest that distinct urine metabolite profiles cluster by class of pathogen. Evaluating the change in these metabolite profiles in response to antimicrobial therapy also offers a tremendous opportunity to non-invasively gauge appropriateness of initial antibiotic choice. *Urine metabolite profiles may provide a fast, accurate and non-invasive approach for pathogen identification of CAP in children representing a critical innovation in the severely limited current practice.*

Paragraph 3

My long-term goal is to become an independent investigator in infectious diseases epidemiology with a focus on translating bench science research to bedside application. The overall objective of this application is to combine robust clinical data (e.g. smoking exposure, antibiotic receipt) with metabolomics data using advanced statistical and metabolomics methodologies to inform pathogen-detection in childhood CAP. I will use a clinical database and specimen biorepository from an established, funded, and fully-operational prospective cohort study of children with CAP. I will acquire knowledge and skills in systems biology sciences and their application to clinically challenging infections such as CAP. To accomplish this objective, I will pursue the following specific aims:

Paragraph 4

- 1. To characterize the sources of variability in the urine metabolite profiles of healthy children.** The *primary hypothesis* is that between subject variability will be larger than within subject variability in the metabolites in the urine of healthy children and the highest proportion of variance will be attributable to age and sex.
- 2. To determine and compare the urine metabolite profiles of children with viral or bacterial CAP with those of healthy children.** The *primary hypothesis* is that urine metabolite profiles of children who have viral pneumonia will be uniquely different from those of healthy children. In addition, urine metabolite profiles of children who have *Streptococcus pneumoniae* (the most common bacterial pathogen) or *Mycoplasma pneumoniae* (the most common atypical bacterial pathogen) will be distinct from those of healthy children.
- 3. To evaluate longitudinal changes in the urine metabolite profile of children with CAP compared with healthy children.** The *primary hypothesis* is the magnitude of change in the metabolome of a child with viral or bacterial CAP will be greater than the diurnal fluctuation of the metabolome in a healthy child. A *secondary hypothesis* is that longitudinal changes in metabolite patterns of children with CAP will differentiate response from non-response to antibiotics.

Paragraph 5

Successful completion of these aims will generate preliminary data on distinct metabolite profiles associated with bacterial and viral pneumonia. These findings will inform an R01 application for a large scale, multi-center, validation study that includes more diverse microbial causes of CAP to advance the development of point-of-care diagnostic tests. *This study will further the field of CAP by introducing a method to differentiate bacterial and viral pathogens thereby increasing targeted antibiotic therapy for children.*

In the narrative part of the Specific Aims of many outstanding applications, people also used their aims to

- State the technologies they plan to use.
- Note their expertise to do a specific task or that of collaborators.
- Describe past accomplishments related to the project.
- Describe preliminary studies and new and highly relevant findings in the field.
- Explain their area's biology.
- Show how the aims relate to one another.
- Describe expected outcomes for each aim.
- Explain how they plan to interpret data from the aim's efforts.
- Describe how to address potential pitfalls with contingency plans.

Do you know who the reviewers are?



Write to the Audience: Appeal to Everyone and Make Advocates out of Assigned Reviewers

NIH and Many Other Funding Agencies:

Primary and secondary reviewers, plus at least one reader

Make those reviewers your advocates - write and organize the application so the primary reviewer can readily grasp what you are proposing and be well poised to explain it to the others.

For many other funding agencies, the “audience” is similar – but be aware when there are “lay members” of a review committee (Disease Foundations).

Write to the Audience

“During the roughly 15-minute discussion, members of the group will ask the assigned reviewers questions and skim parts of the application—most likely, the following:

- Abstract
- Specific Aims
- Significance section of your Research Strategy

So you'll write those sections to meet the needs of those reviewers who are experts in other fields... be sure to use a level at which an intelligent reader can understand your work, as in a *Scientific American* article.”

<https://www.niaid.nih.gov/grants-contracts/draft-specific-aims>

Template for ½ Page Aims Section (Foundation & Society Grants)

Succinct statement regarding the unmet need and/or gaps in our knowledge and why this is an important topic of study. Our overall goal is to understand _____. The specific objective of this proposal is to _____. The central hypothesis is that _____. We formulated this hypothesis, in part, based upon our strong preliminary data, which shows that _____. The rationale for the proposed research is that once it is known how _____ we can _____. We will pursue these studies in three Specific Aims:

Aim 1. To verb (define, establish, determine, etc).

Our working hypothesis for this Aim is that _____.

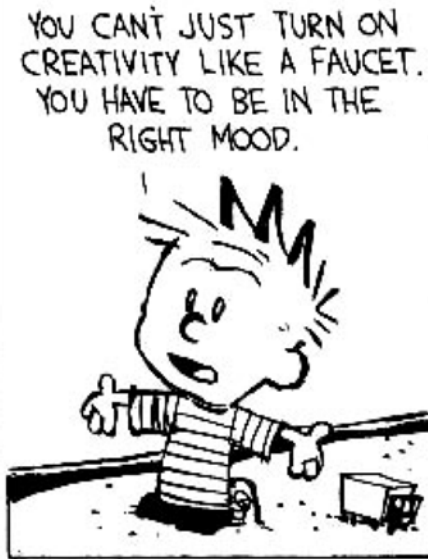
Aim 2. To verb (define, establish, determine, etc).

Our working hypothesis for this Aim is that _____.

Aim 3. To verb (define, establish, determine, etc).

In these studies, we will examine the *prediction* that _____. The proposed work is significant because it _____, and is innovative because it capitalizes on _____. We expect that the combined work proposed will establish _____. By conducting this study, I will gain hands-on experience in _____, _____, and _____, as well as _____, all of which will provide a valuable foundation for my development as a surgeon' scientist.

How do I get started?



Step 1

✓ Develop Your Research Goal:

The theme of your research/ long range plan that extends
beyond a single grant

OR

The overall project goal to be achieved in this proposal

BUT

NOT a hypothesis or specific aim!

Which Long-Term Goal Statement is Unambiguous?

1. Our long-term goal is to determine the diagnostic and prognostic utility of genetic markers of thyroid cancer.
2. We aim to analyze the structural and molecular composition of SFG rickettsial antigens and to determine which components stimulate protective immunity.
3. Our objectives are to define mechanisms of transcriptional regulation in metazoans, to understand how a regulatory factor specifies programs of gene expression as a function of developmental, cellular or physiological cues, and to decipher gene regulatory circuits.

Step 2

✓ Develop Your Proposal's Hypothesis or Objective

A focused objective or hypothesis must be

- Logical / Relevant to a gap in recent scholarship and/or assessed needs
- Feasible
- Stated precisely

From Description to Hypothesis-Basic Science

1. **We hope to observe how** tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.
2. **We propose to determine how** tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.
3. **We propose to determine the mechanisms by which** tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.
4. **We will test the hypothesis that x or y is the mechanism by which** tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.

From Description to Hypothesis: Clinical or Epidemiological

1. **We hope to observe that** HPV infection is a risk factor for heterosexual HIV infection among women in Zimbabwe.
2. **We propose to establish a relationship between** HPV-mediated cervical lesions and the incidence of HIV infection among women in Zimbabwe.
3. **We will test the hypothesis that HPV-mediated cervical lesions are not only more prevalent but enhance** the acquisition of HIV in HIV+ women.

*based on Sarah Averbach, MD, “the effect of cervical HPV infection on HIV acquisition among women in Zimbabwe (UCSF Pathways to Discovery Program, 2009)

Exercise 2: The Logical, Testable, Feasible Hypothesis

What are the problems with the following hypothesis statements? Can you revise?

1. We hypothesize that analogs to chemokine receptors can be biologically useful in HIV.
 2. Our hypothesis is that a wide range of molecules can inhibit HIV infection.
- or-***
3. Write or revise **your own hypothesis statement**, so that the language is very precise and the hypothesis is clearly testable.

Step 3

✓ Develop your Specific Aims

A specific aim should *describe concisely and realistically what the proposed research is intended to accomplish*:

test a stated hypothesis

create a novel design

solve a specific problem

challenge an existing paradigm or clinical practice

address a critical barrier to progress in a field

develop a new technology

*For proposals that are not “hypothesis-driven” see examples:
<https://www.niaid.nih.gov/grants-contracts/sample-applications>*

Develop Your Specific Aims

A general (or long-term) goal is not the same thing as a specific aim:

General goal: To improve the quality of alcoholism treatment

Specific aim: To determine the relative efficacy of Treatment A vs. Treatment B for increasing abstinence among alcohol-dependent patients

Develop Your Specific Aims

A general (or long term) goal is not the same thing as a specific aim:

General Goal: Our *long-term goal* is to elucidate the molecular basis for suppression of innate immunity by type III effectors.

Specific Aims:

1. Determine the molecular consequence of ADP-ribosylation on the function of *AtGRP7* and elucidate the role this protein plays in innate immunity.
2. Identify additional substrates of HopU1 and verify their involvement in innate immunity.
3. Analyze the effect that HopU1 has on host-microbe interactions.

Source: NIAID

Develop Your Specific Aims

A common type of Specific Aim might ask a question like “Does A cause B?”

However, your project could come to an end if A doesn't turn out to cause B.

We will test the hypothesis that x or y is the mechanism by which tumor cells respond to TGF-beta and if the responses promote angiogenesis and tumor growth.

Source: NIAID

Develop Your Specific Aims

Another common type of Specific Aim is descriptive. For example, “We will measure levels of X in 1,000 samples of Y to characterize the pattern of expression of X.”

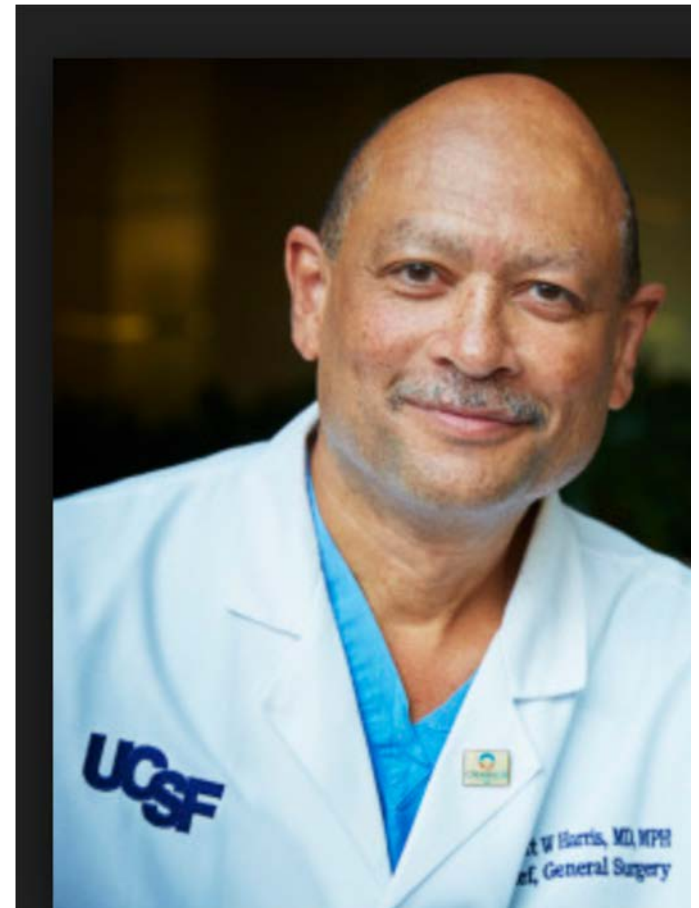
Source: NIAID

Develop Your Specific Aims

Write Aims Early and Not in a Vacuum. Incorporate feedback from your mentor and others. Essential to leave enough time to get other perspectives!



“If you only share ideas with others who have drunk the same ideological Koolaid, you may come away with a false sense of security”.



Develop Your Specific Aims

How Many Aims? Probably 3.

How Much Preliminary Data? Depends on where you are in your career (for early independent investigator: usually have it for Aim 1). Seek input on this from mentors and those willing to review your proposal.

Specific Aims Section: Remember...

YOUR GOAL: Convince every reviewer that the problem or need that you identify is relevant to the mission of the funding agency.

Provide an overview that frames the problem or need and establishes its significance.

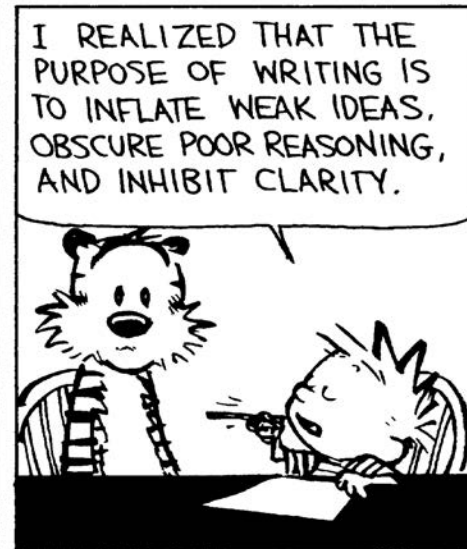
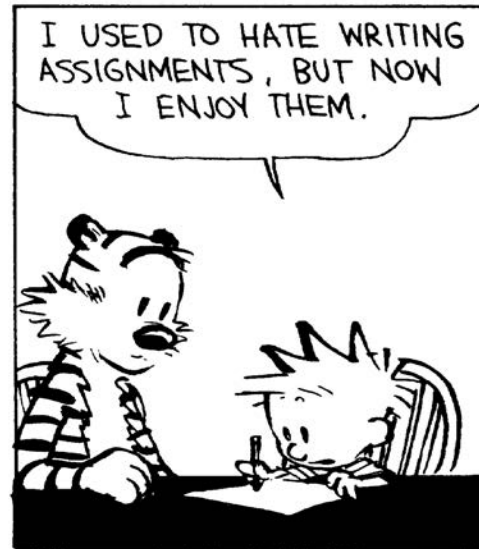
Make sure to make it clear what is *known* and what is *unknown*.

Make it clear that your aims are focused, clearly conceptualized, and feasible, (and in many cases, will test a hypothesis).

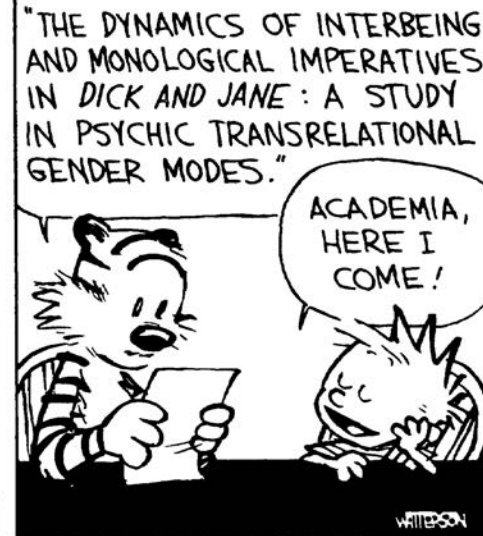
Write your Aims and plan to rewrite them. Send them to whoever is willing to review them. Allow enough time for this iterative process.

Organization, clarity, and brevity are critical.

How do I achieve clarity and readability?



WITH A LITTLE PRACTICE, WRITING CAN BE AN INTIMIDATING AND IMPENETRABLE FOG! WANT TO SEE MY BOOK REPORT?



Writing Clearly: Start with Your Words

Words *in scientific writing should be:*

1. Precise (increase/decrease NOT change; dog, mouse, NOT animal)

2. Simple (prior to→before, following→after, initiate→begin)

3. Necessary (fewer words = less “noise” and more message)

4. Familiar

Do not invent words (endorphinized→injected endorphins)

Avoid jargon

Limit use of abbreviations

5. Humane (*patients do not fail therapy*)

Use Precise Words

The underlined words are imprecise. Can you revise?

The cells were exposed to lipoprotein-deficient serum for 48 h.

In all animals, the reaction was inhibited.

Infusion of serotonin was related to an increase in microvascular pressure.

Use Precise Words

The cells were incubated in lipoprotein-deficient serum for 48 h.

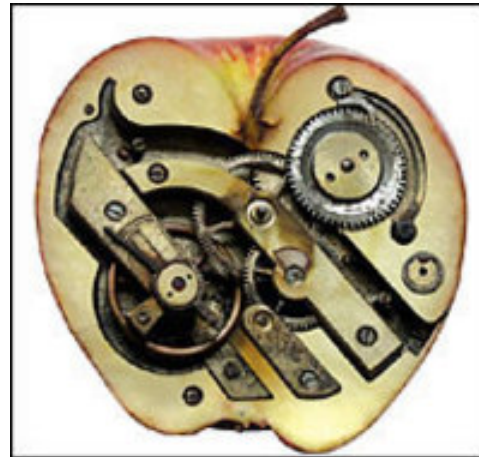
In all mice, the reaction was inhibited.

Infusion of serotonin increased microvascular pressure.

Use Simple Words

Example

The superiority of this technique has not previously been demonstrated.



Use Simple Words

Revisions

Whether this technique is better is not known.

We are the first to show that this technique is better.



Revising: Use Simple Words

Most Common:

- *administer* for *give*
- *demonstrate* for *show*
- *employ or utilize* for *use*
- *encountered* for *found*
- *following* for *after*

Find a simple word for...

constitutes

represents

exists

serves as

initiate

initial

methodology

modify

optimum

Use Necessary Words

Find a 1-2 word equivalent:

has the capability to = **can**

is of the opinion that = **we think**

was unable to = ?

as a consequence of

accounted for by the fact that

at the present moment

despite the fact that

Use Necessary Words

Find a 1-2 word equivalent:

due to the fact that

during the course of

during the time that

if conditions are such that

in all cases

in a satisfactory manner

lacked the ability to

Use Necessary Words

Replace Empty “Numerical” Phrases:

one of the = **one**

a small number of = ?

a limited number of

a proportion of

a sufficient number of

a number of

a majority of

fewer in number

Use Necessary Words

Omit Entire Phrases:

It is important to acknowledge that

It is interesting to note that

It is not impossible that

A not unlikely cause could be that

It may be said that

It is not a large theoretical leap to consider that

Use Familiar Words

- Minimize the Abbreviations

If you are creating “alphabet soup” because you are worried about space, remember:



- ✓ Many words and whole phrases can be cut!
- ✓ Clarity is the goal!
- ✓ Abbreviations definitely detract from clarity.

Use Familiar Words

“Rules” for Abbreviations:

- Avoid them as much as possible in the Specific Aims and Abstract.
- Use them often enough in the proposal so that the reader does not forget the meaning (> 10 X).
- Readers can handle 2-3 abbreviations per paragraph.
- Readers won't notice that you write terms out—they'll just have an easier time reading and getting the message.

Use Familiar Words

“Rules” for Abbreviations:

– OK to use:

- Units of measurement (g, mol, mL)
- Standard abbreviations
 - Chemicals: DNA, ATP, Tris, HEPES
 - Methods: ELISA, MRI, PCR
 - Diseases: HIV, HPV
- Very long terms no one can pronounce
 - Tetradecanoylphorbol acetate (TPA)

Use Familiar Words





LANGUAGE

YOU'VE BEEN VERBED

Friending, trending, even evidencing and statementing...plenty of nouns are turning into verbs. What's going on?

Use Humane Words

Example

Patients who fail radiation therapy will be placed on a chemotherapy regimen.

Patients should not be blamed if therapy fails.

Use Humane Words

Revisions

Patients for whom radiation therapy fails will undergo chemotherapy.

When radiation therapy fails, patients will undergo chemotherapy.

Use Passive Voice Selectively, Not Exclusively



“We wish to suggest a structure for the salt of the deoxyribose nucleic acid (D.N.A.).”

JD Watson & FHC Crick (1953)

If Watson & Crick Wrote in the Passive Voice...

In this communication, a suggestion is made as to the structure for the salt of deoxyribose nucleic acid (D.N.A.).

Use Passive Voice Selectively

Use active voice when you are talking about your aims, hypotheses, inferences, or assumptions, and when you need to distinguish that previous findings or studies or models are *yours*:

- ✓ Our hypothesis is that co-transplantation of donor-specific Tregs and donor cells will improve host engraftment.
- ✓ We have established the previously described fetal mouse model in our laboratory.

Use passive voice to describe methods when you just want to emphasize what was done, rather than highlighting *who did it*:

- ✓ DNA was extracted from the sample.

Simple passive voice is fine when you want to emphasize what will be done in your proposal:

'the ions from the plasma will be sampled by...'

'the coating will be removed with alcohol'

'the burners will be inspected regularly'.

But it is tempting to take a further step and expand these statements to:

'ion sampling from the plasma will be achieved by...'

'removal of the coating will be effected by the application of alcohol'

'regular inspections of the burners will not be carried out'.

In taking this extra step we not only change the verb forms from active to passive, but also introduce colorless 'general purpose' verbs 'carrying' abstract nouns. We no longer sample, remove and inspect; we achieve, effect and carry out.

-J Kirkman, That Pernicious Passive Voice, 1975

Put the Action in the Verb

Verbs express action in English.

If the action of a sentence is expressed by the main verb, the sentence is natural and direct and easy to understand.

Genomic DNA was eliminated.

As opposed to this:

Elimination of genomic DNA was performed.

Liberate Imprisoned Verbs!

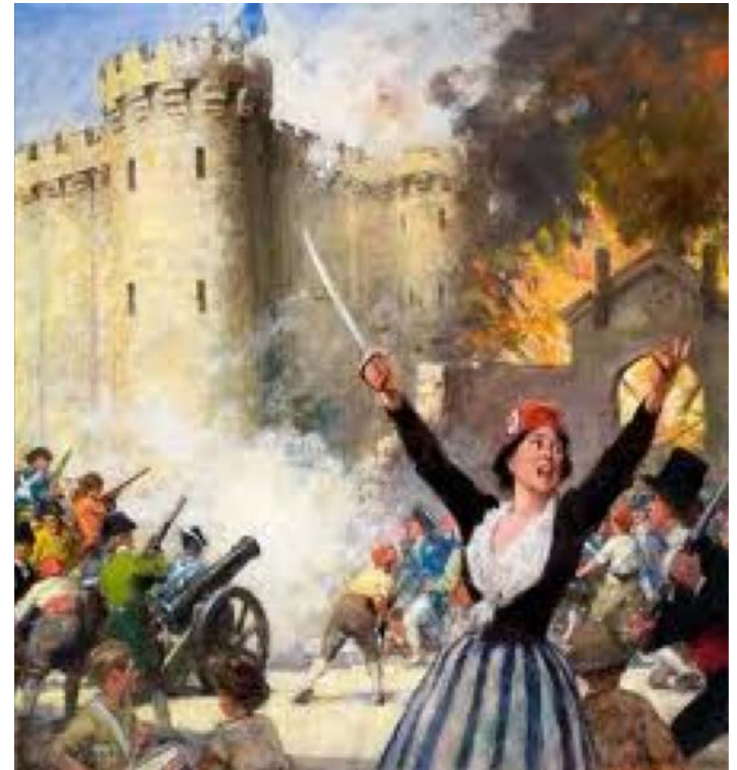
Look for "increase" and "decrease" as nouns.

Look for weak verbs, such as...

occurred
was achieved
was observed
was noted
was seen

Look for nouns made from verbs:

-tion	prolongation, formation
-ment	measurement, assessment
-ence	occurrence, existence
-al	removal, disposal



Use Clear Pronouns

Pronouns: words that replace and refer to a noun:

it, he, she, they, those, these, them

this, that, which...

Use Clear Pronouns

If the noun that a pronoun refers to is unclear, the reader may have trouble understanding the sentence. *In the Aims section, clear logical relationships between sentences is critical.*

Example

Patients with a latent infection may need to be monitored for several months because they are at risk of developing the active form of the disease. This diminishes over time.

What does “this ” refer to?

Use Clear Pronouns

Revision 1: Patients with a latent infection may need to be monitored for several months because they are at risk of developing the active form of the disease. **This risk** diminishes over time.

Revision 2: Patients with a latent infection may need to be monitored for several months because they are at risk of developing the active form of the disease. **The need to monitor these patients** diminishes over time.

Providing Background Information: Synthesize, don't Rehash

Example: Topic sentence first, then details:

Currently, the standard treatment for congenital hematopoietic stem cell disorders is postnatal bone marrow transplantation. The treatment efficacy using this approach is often limited by transplantation complications, such as graft versus host disease and graft rejection, by the availability of few HLA-matched donors, and by the morbidity of host myeloablation preceding transplantation (reviewed in ²). The induction of donor-specific tolerance to transplanted allogeneic stem cells without long-term immunosuppression would therefore have important clinical applications.

Background: It's about synthesis

- ✓ **Focus on the ideas, not the names & dates**

Example

Numerous studies have shown that inflammation increases SQ RBC adhesion (5, 30, 34, 40) but few have provided direct evidence linking inflammation to vaso-occlusion. **In the most convincing study to demonstrate this link (30)**, platelet activating factor increased SQ RBC-endothelial adhesion and vaso-occlusion in the artificially perfused rat mesentery, and blockade of the pro-adhesive integrin $\alpha_5\beta_3$ attenuated these events.

Background: It's about synthesis

Example: Tying it all together (paragraph with **topic sentence**, supporting sentences, **transition words/phrases**), **explicit link to the proposed work**. NOTE: No names & dates!

Regulatory T cells (Tregs) have been implicated as critical regulators of the immune system, responsible for maintaining immune self tolerance⁹. Through the production of inhibitory cytokines and/or direct inhibition with cell to cell interactions, Tregs function to inhibit immune activity and thereby maintain self tolerance. **Furthermore**, recent evidence has demonstrated the ability of Tregs to promote tolerance following allogeneic postnatal bone marrow transplantation¹⁰. **Little is known, however**, regarding their involvement in allogeneic IUHSCTx and **this proposal will address the application of Tregs to improve host engraftment after IUHSCTx**.

Source: Amar Nijigal MD, UCSF Department of Surgery

Specific Aims: Reviewer-Friendly Writing

Help reviewers make the connections you want to make *by telling them using **explicit language***:

Our long term goal is/ What is not known is/

The overall objective of this proposal is/ Our central hypothesis is/

The rationale behind the proposed research is/

With respect to outcomes, we expect the work proposed in Aim 1 to....

Specific Aims: Reviewer-Friendly Format

From the example in Exercise 1:

Our long-term goal is to elucidate the molecular basis for suppression of innate immunity by type III effectors. *The objective of this application* is to identify targets of the *P. syringae* type III effector HopU1, a mono-ADP-ribosyltransferases (ADP-RTs), and to determine its roles in bacterial pathogenesis. *The central hypothesis of the proposed experiments* is that the targets of the HopU1 ADP-RT type III effector will be components of innate immunity. We formulated this hypothesis based on...

Writing Clearly: Learn More!

Faculty & Postdocs: Take the Writing Course offered by the UCSF Department of Surgery <http://sciencepubs.surgery.ucsf.edu/scientific-writing-course.aspx>:

- 8 weeks, usually offered in Fall & Spring
- In-depth writing and revising skills, reports of original research, grant proposals, journal submission, peer review & authorship
- Lots of writing and revising in class and outside of class.

Everyone: Read more about how to write clearly.

Derish PA and Eastwood S. *A Clarity Clinic for Surgical Writing*. J Surg Res 2008, 147:50-58. Learn several techniques for achieving clarity in your writing, including choosing words carefully, designing well-constructed sentences, building structured paragraphs, and displaying your thinking clearly by using topic sentences and transitions <http://www.ncbi.nlm.nih.gov/pubmed/17655864>

Zeiger M. *Essentials of Writing Biomedical Research Papers* (second edition). New York: McGraw-Hill, 1999. Indispensable and authoritative. Available at Amazon.com.

Resources

Specific Aims templates and tips:

https://iims.uthscsa.edu/sites/iims/files/Education/F-troop/F_Handbook.pdf

www.northwestern.edu/climb/resources/written-communication/index.html

<https://www.niaid.nih.gov/grants-contracts/prepare-your-application>

<http://www.biosciencewriters.com/NIH-Grant-Applications-The-Anatomy-of-a-Specific-Aims-Page.aspx>

