

Principles of Grant Writing*

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Objective: Inform about the communication skills and strategies necessary for success in obtaining research \$\$

* Winning!

Getting Started - Storyboard



The storyboard for 'Taxi Driver' (1976) sketched by Martin Scorsese

"The storyboard for me is the way to visualize the entire movie in advance. Storyboards express what I want to communicate, they show how I would imagine a scene and how it should move to the next" Martin Scorsese

Communicating Your Story

- Have a compelling narrative
- NIH doesn't fund ideas. Translate your idea to measurable outcomes
- Tell it in an engaging manner
- Know your audience. Use NIH resources, <http://projectreporter.nih.gov/reporter.cfm>



<http://public.csr.nih.gov/StudySections/Pages/default.aspx>

Winning

- It's about not making mistakes
- What got you here won't get you there

Start at the End - John Irving

- **I usually begin with endings, with a sense of aftermath, of dust settling, of epilogue.**
- **How can you plot a novel if you don't know the ending first? How do you know how to introduce a character if you don't know how he ends up?**
- **If you start at beginning you can end up 80% into the manuscript only to discover that it isn't really working.**



First Impressions - Paul Argenti

- **“Most employers make a decision in the first minutes of meeting you and then spend the rest of the interview gathering information to support their gut feeling.”**
- **The same holds with grant proposals.**
- **The first paragraph is critical. Write it last.**
- **Think of this as selling a pilot to a TV network. You’ve got to get them hooked right from the start.**



Write the Critique for the Reviewer

- When writing the grant, **embed** the review.
- Use phrases that you want used in the review.
- Have summaries in each section.
- Highlight overall impact in final summary paragraph.

This is some of the most important advice we give you

Key Writing Principles

- Write in simple declarative sentences
- Avoid passive voice, personal pronouns
- Use strong nouns and active verbs
 - **The house was on fire. (passive, boring)**
 - **Flames erupted from the house. (active, strong)**

Key Writing Principles

- Put statements in positive form
- Write in a way that is easy for reviewers to understand
 - Simple declarative sentences
- Define all non-standard abbreviations
- Use grammar and spelling checker!

Presentation

- Use simple, helpful figures with legends
- Leave large margins, plenty of white space
- Tell the story as a linear narrative. Don't make the reviewer return to a previous page to find relevant information or results.

Hypothesis

- A simple declarative sentence with an experimentally testable dependent variable
- Not tentative: “the hypothesis is that a loss of osteocalcin signaling in β -cells could contribute to the decrease in proliferation following the perinatal peak”
- We hypothesize that osteocalcin regulates post-perinatal β -cell proliferation.
- **Avoid waffle words!**

Innovation

- Innovation is used to assess how much a project can 1) shift the current research paradigm or 2) refine, improve, or propose a new application of an existing concept, method, instrumentation, or clinical intervention.
- A new idea is novel, not innovative. Innovation is a new way of testing your hypothesis.

Value

- If you are asking for \$1M in support, make each page contain \$100,000 in value.
- If you spend 80 hr effort writing a 5 yr \$250,000/yr R01, you make ~\$25,000/hr.

Join The Culture of Science

- Become an active and recognized member of your intended research community
- Attend and present at meetings
- Publish in scientific society journals
- Seek society fellowships and grants
- Get involved in peer review

Persuasive Communication

- **The Importance of Being Urgent.** The secret ingredient!
- **Make It Easy to Read.** Have your readers breezing happily through.
- **Grammar for Fundraisers.** Rules you should and shouldn't follow.
- **Persuade with Story, Not Statistics.** One way motivates, the other demotivates them.
- **Keep It Simple.** Complexity kills!
- **Design for Older Eyes.** Design for bifocals-wearing readers.
- **Don't Skimp on Emphasis.** It makes a difference.
- **Make Images Work for You.** The right picture can boost results, but the wrong one can turn them away.*

*5 Philanthropic Blogs that Fundraisers Need to Read (The Atlantic): <http://bit.ly/Vz52yk>
The Fundraiser's Guide to Irresistible Communications. Jeff Brooks: <http://amzn.to/XMaCBB>

Play to Win The Game



Let's Write a Grant!

- When to start? Why? How to get going?

First

- Discuss objectives with mentor, colleagues
- Anticipate and resolve “personal issues” including visa status, team building
- Begin to organize your grant toolbox – experiments, key reagents, coinvestigators, internal and external consultants



Second

- **Formulate your hypothesis and Specific Aims (2-5 in number, we like 2-3)**
- **Perform due diligence. Very, very important.**
- **Where?**

At the bench – do key preliminary studies

Read Literature – scour scientific, clinical and patent resources

Discuss with expert colleagues, potential consultants

Investigate NIH – RePORTER, CSR, Study Sections

Amazing resource: <http://www.niaid.nih.gov/Pages/default.aspx>



NIAID Funding Newsletter and Blog

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[October 24, 2012](#)—read our latest issue.

Feature Articles

Back Issues

- [2012](#)
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Highlights

- [NIAID Funding Newsletter, October 24, 2012](#)
- [All About Grants](#)
- [Strategy for NIH Funding](#)
- [Samples and Examples](#)
- [Sample Applications](#)

Third

- **Set submission timeline** with mentor/colleagues (scientific and administrative)
- **Draft Specific Aims ASAP, seek feedback**
- **Begin active writing 4 months before deadline.**
Allow 1 month for “diligence”, 1.5 for writing, 1.5 for *peer input* and revisions
- **Every time application doc opened, edit Specific Aims**
- **Superb local resource:** <http://www.oorhs.pitt.edu/>
There are several expert grant writers in this office
- This presentation: <http://pharmacology.medicine.pitt.edu/Links>

Fourth

F²'s Etiquette Guide

- **Draft letters for non-Co-Investigator collaborators and consultants, and send to them 6 weeks before deadline so they can “buff”.**
- **When requesting input from colleagues and it is “critical”, *be open-minded and don't argue!***
- **Continue to eat, work in lab, exercise, socialize, be normal**
- **Give colleagues a pdf of the final submitted grant with thanks.**
- **Meet or beat your departmental and school submission timelines.**
- **Thank or do something nice for the administrative staff that spent *hours-to-days* organizing your budget, allied docs and uploading**

Basic Elements of an NIH Grant

The Research Strategy is where you will write your own critique for the review committee

- **Specific Aims**
- **Research Strategy**
 - **Significance**
 - **Innovation**
 - **Approach**

A. Specific Aims

This is the most important page and must be perfect

- **ONE PAGE ONLY! No need to cite references**
- **Define the problem and key issues first.**
- **Briefly state the background and scientific rationale (can be based on your preliminary data) for the hypothesis.**
- **State a clear, succinct, focused and testable hypothesis stemming from the first 1-2 paragraphs (put in bold font).**
- **List one-sentence Specific Aims that will test the hypothesis (in bold font). Brief experimental approaches can be included below each aim (not bold).**
- **Finish with a significance statement, *i.e.*, what the new information will do for science/health if completed.**
- **Here and throughout, avoid excess use (annoying) of bold font, colored letters, italics and underlined words. Your words are ALL important and you only need these tools to help organize and identify key elements of the story you are telling.**

Specific Aims.

A team with significant basic science and clinical expertise in redox-dependent cell signaling, cardiovascular biology and diabetes has devised a research plan that can be rapidly deployed to address a novel therapeutic strategy for treating Type 2 diabetes (T2D). This disease is epidemic in westernized populations, as lifestyle changes lead to obesity. Insulin resistance, an early event predicting and contributing to the onset of diabetes, stems in part from diet-induced initiation and propagation of inflammatory reactions and a state of "oxidative stress" centered in mitochondria. Several classes of drugs are currently prescribed to enhance insulin sensitivity, with the use of some hindered by an increased propensity for adverse cardiovascular events (heart failure, infarction). There thus remains a pressing need for more effective therapeutic strategies. Our research plan will identify specific reactions and dietary factors that modulate insulin sensitivity.

Diets rich in leafy green vegetables and fish, such as the Mediterranean diet, are associated with a striking reduction in obesity, diabetes and overall cardiovascular risk. While "active ingredients" in this diet remain uncertain, recent studies support the hypothesis that the simple salt nitrate (NO_3^-), upon metabolism to nitrite (NO_2^-), supports the generation of signaling mediators including nitric oxide (NO) and nitro-fatty acids ($\text{NO}_2\text{-FA}$). Preliminary data shows that the mitochondrion acts as a "bioreactor" to catalyze the modification of proteins and lipids by NO_2^- , yielding salutary cell signaling species including S-nitrosated proteins and nitrated lipids. Current data reveal that these species regulate fundamental physiological events. This includes mitochondrial function and the expression of inflammatory-related genes via post-translational protein modification and activation of the nuclear lipid receptor PPAR_γ , thereby enhancing insulin sensitivity. These data lead to the hypothesis that **nitrate is a bioactive dietary nutrient that is converted to species that modulate oxidative inflammatory reactions and metabolism, thereby increasing insulin sensitivity (Figure 1)**. This hypothesis will be tested by pursuing the following Specific Aims:

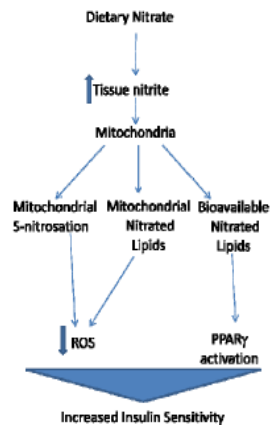


Figure 1: Hypothesized mechanism of nitrate-dependent increase in insulin sensitivity.

sampled intravenous glucose tolerance tests and hyperinsulinemic euglycemic clamps will be performed in conscious, unhandled, mice and the expression of key diabetes-related genes in skeletal muscle and adipose tissue will be measured.

Nitrate, a major constituent of the Mediterranean diet but previously considered to metabolically inert in humans, is now appreciated to serve as a precursor of vasoactive signaling mediators. This proposed research plan addresses a novel concept that is reinforced by solid preliminary studies related to the formation and actions of the various nitrogen oxides that can be derived from dietary NO_3^- . Detailed mechanistic understanding will be obtained regarding how dietary NO_3^- and NO_2^- can influence insulin secretion and sensitivity via mitochondrial redox reactions. This foundation of knowledge will now be extended to new understanding of mechanisms underlying insulin sensitivity and a novel pharmacologic strategy for treating type 2 diabetes. Characterization of the signaling reactions of this dietary molecule abundant in "heart-healthy" foods introduces a new paradigm in the redox regulation of metabolism and is likely to yield profound benefit for managing and preventing insulin sensitivity through simple dietary lifestyle changes. Finally, the research plan will also capitalize on the diversified expertise of a strong team of researchers and the new investigators that they hire and train.

This Specific Aims page meets F² grant prep standards

- Includes summary figure
- Bold hypothesis, aims
- Provides background info
- Addresses significance

Specific Aim 1. Determine the dietary nitrate and nitrite-dependent reactions yielding the nitrosylated and nitrated species that regulate mitochondrial function and activate PPAR_γ -dependent gene expression. Specifically, the entero-salivary conversion of dietary NO_3^- to NO_2^- , and distribution to organs, will be studied in C57Bl6 mice. The mitochondrial generation of S-nitrosothiols and $\text{NO}_2\text{-FA}$, and the factors that influence these reactions, will be determined in vitro and in vivo. Then, the effect of these signaling mediators on mitochondrial reactive oxygen species generation and PPAR_γ activation will be quantified.

Specific Aim 2. Define the impact of nitrate administration on insulin sensitivity. Lean and genetically obese mice will be utilized to evaluate the impact of dietary NO_3^- , and intravenous administration of nitrites and $\text{NO}_2\text{-FA}$ on PPAR_γ -mediated changes in insulin sensitivity of peripheral tissues and insulin secretion from pancreatic beta cells. State-of-the-art frequently

B. Research Plan

1. Significance

- **Identify importance of the problem**
- **Note critical barriers to progress**
- **State what your research will do to improve knowledge in the area**
- **Convey how your results will significantly evolve the development of the field**

Suggest 1 page (no >2) use graphics, summarize at end with bullet points

(Dr. Friedman said – “write your own review”)

B. Research Plan

2. Innovation

- **How will your work shift current research paradigms**
- **ID the novel concepts, approaches, or interventions to be used**
- **State what will be the useful application of your innovation and results**

Suggest 1 page, can use graphics, and remember the F² Principle ... summarize at end with bullet points

B. Research Plan

2. Approach

For a 3-Specific Aim app, this is what BAF does in 9-10 pages

(a) Restate Specific Aim

- 1. General approach and rationale (1 paragraph to 1 page)**
- 2. Preliminary data – include key data/legends (1 page)**
- 3. Specific experimental approach - global methods are grouped, include data and impress with cool experimental approaches, give some exp detail (1-2 pages)**
- 4. Anticipated results and potential pitfalls (1-2 paragraphs)**

Important! Save room at very end for Statistical Analysis (3-6 lines), a Timetable of what will get done when (3-6 lines) and

Overall Summary

Insert this at the end to hopefully be cut and pasted by reviewer as the “Overall Impact” of your critique

Overall summary. The research plan is devised by a unique team of basic- and physician-scientists that share expertise in cardiovascular cell signaling, pharmacology, drug discovery and pathobiology of hypertension and heart failure. Motivated by the consensus view of the 2009 NHLBI Workshop on Heart Failure, that “nitric oxide insufficiency is a central feature in the pathogenesis of heart failure”, an innovative drug discovery strategy will be tested in a murine model of hypertension-induced heart failure. A kinetically superior, clinically-approved, specific inhibitor of XOR (febuxostat) will be tested for its ability to inhibit cardiac and vascular generation of NO-inactivating reactive oxygen species. The investigators have also discovered and characterized nitro and keto derivatives of unsaturated fatty acids, one of which (nitro-oleic acid) is also a potent non-competitive inhibitor of XOR. These electrophilic fatty acids are byproducts of redox reactions and act as potent anti-inflammatory signaling mediators. The species modulate multiple transcriptional regulatory mechanisms (PPAR γ , NF κ B, Keap1/Nrf2, HSF) in a manner that limits inflammatory cell activation, ischemia-reperfusion injury and adverse remodeling events. These signaling actions of electrophilic fatty acid byproducts may also explain a significant component of omega-3 unsaturated fatty acid-mediated cardioprotective actions. While the research plan does not dissect this latter issue, this research endeavor holds a strong likelihood, based on initial observations in cell and animal model studies, that new insights and drug strategies for treating heart failure will be obtained.

Review of an NIH Grant

Study Section IDs the Strengths and Weaknesses of:

Significance, Innovation, Approach – Each is crucial!

Investigators, Environment – If weak, this can hurt

The above are integrated to give:

Overall impact - the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved

Make sure in your diligence process that you found a Study Section with the correct expertise to do review, and that you provided a cover letter with the submission to CSR asking for this review committee. Then, no whining!

NIH Scoring System

Need 1's and 2's ... 3's are toxic
50% of apps not verbally discussed

Impact	Score	Descriptor	Additional Guidance on Strengths and Weaknesses
High	1	Exceptional	Exceptionally strong with essentially no weaknesses
	2	Outstanding	Extremely strong with negligible weaknesses
	3	Excellent	Very strong with only some minor weaknesses
Medium	4	Very Good	Strong but with numerous minor weaknesses
	5	Good	Strong but with at least one moderate weakness
	6	Satisfactory	Some strengths but also some moderate weaknesses
Low	7	Fair	Some strengths but with at least one major weakness
	8	Marginal	A few strengths and a few major weaknesses
	9	Poor	Very few strengths a numerous major weaknesses

Minor Weakness: An addressable weakness, does not substantially lessen impact

Moderate Weakness: A weakness that lessens impact

Major Weakness: A weakness that severely limits impact

The Seven Wonders of a Competitive Application

- Hypothesis-driven experimental aims
- Overall novel, innovative, exciting goals.
- Goals challenge existing views – transformational.
- Technically feasible and not overambitious, dangerous.
- Founded on 2-3 of your related publications.
- Addresses a recognized and important topic.
- Produces relevant information – must significantly advance knowledge for the NIH this is *disease-relevance* and *potential for translational studies*.

These points, and how solidly you achieve them, reveal to the reviewers your passion and scientific intellect

“Doing science is like making love - it may do some good, but that’s not why we do it.” - Richard Feynman