Grant Writing 101

"<u>EXAMPLE</u>: The American Heart Association"

Brian R. Wamhoff, Ph.D.
wamhoff@virignia.edu
Dept of Medicine, Cardiovascular Division

Other mechanisms:

- NIH – K99 Award
- JDRF
- ADA
- APS
- NRSA
- ACS

Science Focus
of the AHA

"Research broadly related to cardiovascular function and disease, stroke <u>or</u> related to clinical, **<u>basic</u> <u>science</u>**, bioengineering or biotechnology, and public health problems."

"Optimizing your funding success with the American Heart Association"

1. My personal experiences with the AHA

2. The AHA Mid-Atlantic and National Affiliates

3. How the Review Process Works
   a. Reviewing the Pre- and Post-Doctoral Fellowship and *Grantsmanship Tips*
   b. Reviewing the Scientist Development Grant & the Beginning Grant-in-Aid

4. Concluding remarks

My personal experiences with the AHA

Pre-doctoral Fellowship
1999 – 2001 AHA Heartland Affiliate, "Smooth muscle calcium regulation: Cardioprotective effects of exercise in diabetic swine with coronary artery disease." University of Missouri, PI: Michael Sturek, Ph.D.

Post-doctoral Fellowship (declined for APS fellowship)
2002 – 2004 AHA Mid-Atlantic Affiliate, "Molecular mechanisms of decreased smooth muscle differentiation marker expression associated with the pathophysiology of atherosclerosis." University of Virginia, PI: Gary K Owens, Ph.D.

Scientist Development Grant (accepted), Beginning Grant-in-Aid (rejected)
2005 – 2009 National Affiliate. "Calcium-dependent regulation of smooth muscle phenotype." University of Virginia, PI: Brian R. Wamhoff, PH.D.

Used SDG to generate data for current **NIH RO1** – 07/01/06 – 06/31/11

Study Section
2005 –   AHA National Affiliate BASIC 1 Study Section

Board of Directors
2005 –   AHA Local Affiliate, spokesperson for AHA impact on UVA funded research and training young cardiovascular scientists

The AHA Mid-Atlantic and National Affiliates

http://www.americanheart.org/presenter.jhtml?identifier=10813

Mid-Atlantic Affiliate

Deadline:
Jan, 2007

Offering Programs:
Pre-doctoral (29/115 25% down from 34%)
Post-doctoral (21/99 21% up from 15%)
Beginning Grant-in-Aid (22/74 30% up from 14%)

Grant-in-Aid

National Affiliate also collectively reviews National, Greater Midwest, Heartland and Pacific Mountain Affiliates

Deadline:
July, 2006
Jan, 2007

Offering Programs:

Scientist Development Grant (85/356 24%, $65K, 3-4y)

Fellow-to-Faculty

NIH paylines are dropping at an astounding rate!

Current pay lines are <12% for NHLBI, down from approximately 20-24% in 2004-05

SOLUTION: Start writing good grants early in your career because this is what you will be doing for the rest of your career, in good times and bad!

Post-docs that have funding keep their jobs.

Current AHA Funded Proposals at CVRC

Mid-Atlantic Affiliate

Pre-doctoral fellows ($20K 2+1y):
Jeremy Mauldin
James Thomas
Matt Alexander

Post-doctoral fellows ($35K 2+1y):
Elena Galinka
Tracy Deem
Anthony Ore

Beginning Grant-in-aid ($66K 2y):
Elaine Felecia Etter
Brant Isakson

National Affiliate

Scientist Development Grant ($66K, 4y):
Brian Wamhoff
Tadashi Yoshida

How the Review Process Works "Prior to Study Section"

Proposals are assigned to a study section based on the specific "<u>codes</u>" you select for describing your grant.

Science Focus

"Research broadly related to cardiovascular function and disease, stroke <u>or</u> related to clinical, **<u>basic science</u>**, bioengineering or biotechnology, and public health problems."

Mid-Atlantic Affiliate

The proposal does not need to be related to CVD!

Mid-Atlantic 1A
Integrative Cardiac Biology/Regulation
Radiology & imaging
Surgery

Mid-Atlantic B
Electrophysiology & Arrhythmias/Regulation
Vascular Biology & Blood Pressure/Regulation
Cardiovascular Regulation (autonomic regulation)

Mid-Atlantic 2
Lipoproteins & Lipid Metabolism
Thrombosis
Vascular Wall Biology

Mid-Atlantic 3
Cardiorenal
Lung, Respiration & Resuscitation
Immunology & Microbiology

Mid-Atlantic 4
Cell Transport & Metabolism
Cellular CV Physiology & Pharmacology

Mid-Atlantic 5
Molecular Signaling

Mid-Atlantic 6
Basic Cell & Molecular Biology
CV Development

National Affiliate

Basic Cell & Molecular Biology 1 (25 members)
Basic Cell & Molecular Biology 2
Behavioral Science, Epidemiology & Prevention
Bioengineering & Biotechnology
Brain
Cardiorenal
Cardiovascular Development
Cardiovascular Medical Research and Education Fund
Cell Transport Function & Metabolism/Electrophysiology & Arrhythmias
Immunology & Microbiology
Integrative Cardiac Biology/Regulation
Lipoproteins, Lipid Metabolism & Nutrition
Lung, Resuscitation & Respiration
Molecular Signaling 1
Molecular Signaling 2
Radiology, Imaging & Surgery
Thrombosis
Vascular Biology & Blood Pressure/Regulation
Vascular Wall Biology 1
Vascular Wall Biology 2

How the Review Process Works "Prior to Study Section"

Putting yourself in the mindset of the Reviewer can only help.

Applications are received 1 month prior to study section.

The average time spent reviewing an application is **2.5-4 hrs**.

Each Reviewer receives 12-14 applications: 12 x 3 = **~36 hrs**.

For each application, the Reviewer is assigned as:
Primary Reviewer (R1)
Secondary Reviewer (R2)
Reader (R3)

The Reviewer critiques and scores all applications **collectively** according to AHA guidelines (Scale of 1-5, where 1 is outstanding)

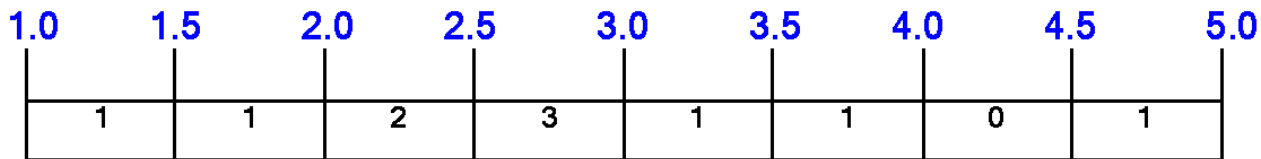33% of all applications are **streamlined**.

All scores are posted online 1 week prior to study section.

OBJECTIVE: Score applications using the full range of scores

SAMPLE:

Reviewer scored 10 applications = (7 primary or secondary assignments with 3 reader assignments)

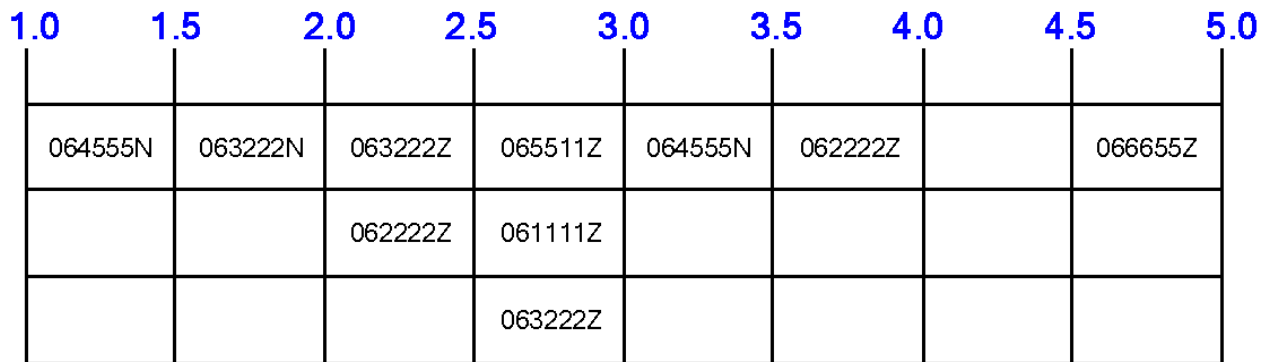PRIORITY SCORE RANGE: (Below is an example of an appropriate distribution of scores)

1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
1	1	2	3	1	1	0	1	

STREAMLINED APPS = 33%

Note: all pre-doc, post-doc, SDG and BGIA are scored collectively

SAMPLE DISTRIBUTION OF APPLICATIONS AMONG PRIORITY SCORE INTERVALS:
(Reviewer should evaluate distribution for use of full range prior to posting critiques and scores on the Electronic Peer Review website)

1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
064555N	063222N	063222Z	065511Z	064555N	062222Z		066655Z	
		062222Z	061111Z					
			063222Z					

STREAMLINED APPS = 33%

Pre-doctoral & Post-doctoral Fellowships

Objective To help students or trainees initiate careers in cardiovascular and stroke research by providing research assistance and training. *Awardees will be expected to devote full time to research or activities directly related to their development into independent researchers.*

CRITIQUE LAYOUT

A. **Name of Applicant & Research Project Title**

B. **Proposal Description:** Briefly describe the project, (approximately one paragraph) including;
- Scientific objectives
- Research design and methods

C. **Critique**: Address the following criteria in this order, listing strengths and weakness include detailed suggestions for enhancements for a future resubmission. **Use the quality of these areas as comparison points for assigning priority scores to applicants in these programs**:

1. Evaluation of Proposal   (1/3rd of score):   Location within application:

▪ Scientific merit of proposed project	**1.3**	Body of 12 page scientific proposal
▪ Probability of achieving scientific objectives		Body of 12 page scientific proposal

2. Evaluation of Investigator: (1/3rd of score):   Location within application:

▪ Evidence of potential for a research career	**1.9**	Page 4 and quality of scientific proposal
▪ Trainee's academic record (academic achievement, GPA)		Pages 4-7-8, biosketch and page 11
▪ Quality of trainee's previous research		Pages 4-7-8, biosketch, other support page and any included reprints from applicant
▪ Trainee's familiarity with literature and work of other investigators in the field of interest		Listed references/ bibliography
▪ Trainee's need for the training experience		Pages 4-7-8 and biosketch
▪ Quality of required 3 reference letters (do not use specific names)		Letters included in application documents, names on page 10

3. Evaluation of the Sponsor/Institution: (1/3rd of score):
A. Qualifications of the sponsor: *Sponsor's reputation as an investigator*   Location within application:

▪ Publications and funding history		Sponsors information pages, other support page
▪ Track record with trainees	**2.5**	Sponsors information pages
▪ Commitment to applicant's training		Sponsors information pages
▪ Quality and comprehensiveness of the Training plan		Body of 12 page scientific proposal, Sponsors information pages – detailed training program
▪ Current funding available to support Fellow's project		Sponsors information pages, other support page

B. Qualification of the Facilities and resources available from institution: Location within application:

▪ Space stated in the sponsor's laboratory	Page 11 & 12
▪ Evidence of exposure to a research training environment.	Page 12, reviewer knowledge of institution

1.9 (1.8-2.0)

1. Evaluation of Proposal	(1/3rd of score):	Location within application:
▪ Scientific merit of proposed project		Body of 12 page scientific proposal
▪ Probability of achieving scientific objectives		Body of 12 page scientific proposal

1. The **SCIENCE** must be **good**!

2. Simple, clear transition of thought process, structure. **Simple, Simple, Simple.**

3. Have a <u>HYPOTHESIS</u>.

4. <u>FOCUSSED</u>, not OVERAMBITUOUS

   #1 comment of reviewers: ***"This is grant is unfocussed and overambitious."***

5. Mechanistic not Descriptive.

   #2 comment of reviewers: ***"This Aim is descriptive."***

6. Clearly state <u>CAVEATS</u> and <u>POTENTIAL PITFALLS</u> for each Aim.

7. Supportive <u>preliminary data</u>, whether it's your data, data from a previous member of your lab or data from another lab.

American Heart Association
Application for Research Award
PROJECT SUMMARY

American Heart
Association.
Fighting Heart Disease and Stroke

1. Applicant:

Brian	R.	Wamhoff		Ph.D.
First	Middle	Last	Jr/Sr/etc	Degree(s)

2. Institution where work will be done: University of Virginia ▼

3. Sponsor (if applicable):

Gary	K.	Owens		Ph.D.
First	Middle	Last	Jr/Sr/etc	Degree(s)

4. Department Head:

Andrew	P.	Somlyo		M.D.
First	Middle	Last	Jr/Sr/etc	Degree(s)

5. Applying to: Mid-Atlantic Affiliate ▼

6. Award program: Postdoctoral Fellowship ▼   Resubmission? ☐ ⑦

7. Dates of proposed award: Start: 07/01/2002 ⑦ End: 6/30/2004
mm/dd/yyyy   mm/dd/yyyy

8. Project title (limit to 120 characters or less): Molecular mechanisms of decreased smooth muscle ⑦
differentiation marker expression associated with atherosclerosis.

9. Project summary (must be completed on this page): ⑦

Atherosclerosis, the principal cause of heart attack and stroke, is a complex inflammatory-fibroproliferative response to various forms of insult to the endothelium resulting in phenotypic modulation of smooth muscle cells (SMC) of the artery wall (FIG 1). A characteristic feature of SMC phenotypic modulation is decreased expression of SMC differentiation marker proteins (i.e. smooth muscle myosin heavy chain (SMMHC) and SM22a), increased proliferation, decreased contractility and increased matrix production - that contribute to lesion formation. The overall aim of this proposal is to determine molecular mechanisms that contribute to the decreased SMC-specific differentiation marker expression associated with vascular injury and atherosclerosis. Recent studies from our lab were the first to show that transcriptional regulation of the SMMHC and SM22a promoter are decreased in transgenic mice following carotid injury (FIG 3). We identified a "novel mechanism" of SM22a gene regulation whereby mutation of the SM22a G/C-rich repressor cis regulatory element attenuated the injury-induced decrease of the SM22a transgene. Further, we showed by electrophoretic mobility shift assays that the transcription factors Sp1 and Sp3 (both of which are increased in SMCs in models of vascular injury) bind to the G/C-rich repressor region (FIG 4). However, it is UNKNOWN whether 1) Sp1/Sp3 or other trans-acting factors contribute to the repressor effect in vivo and 2) how SMMHC and SM22a gene expression are regulated in an animal model of atherosclerosis (TABLE 1). Therefore, my overall hypothesis is that decreased SMMHC and SM22a gene expression associated with atherosclerosis is mediated, in part, by Sp1/Sp3 binding to the G/C repressor region of the SMMHC and SM22a genes. This hypothesis will be tested by addressing the following three specific aims: 1) To determine the role of the G/C repressor in regulating SMMHC and SM22a gene expression in the ApoE -/- mouse model of experimental atherosclerosis with and without vascular injury; 2) To determine trans-acting factors and mechanisms that regulate the activity of the SMMHC and SM22a G/C repressor elements, including the role Sp1 and Sp3; 3) To determine the ability of the factors identified in Aim 2 to modulate injury-induced SMC gene expression in vivo using adenoviral-mediated gene transfer. The experimental design will integrate cellular and molecular biology with animal models to address the overall hypothesis.

10. Amount Requested: ⑦

$30,000	$30,000	$0	$0	$0
Year 1	Year 2	Year 3	Year 4	Year 5

Layout of the proposal

Project Summary (250-300 word Abstract)

Phenomena X or disease X is… A characteristic feature of this process is… Although ABC has been shown to… it is unknown whether… **Preliminary studies** [or **Recent studies** from our lab] show that… However, it is unknown whether… Therefore, the **overall hypothesis** is that… This hypothesis will be tested by the following **specific Aims:** *Aim 1* will determine… *Aim 2* will determine… *Aim 3* will determine…

A. **Specific Aims (1 page)**

B. **Background (3 pages)**

C. **Research Design and Methods (7.5 pages)**

D. **Ethical Aspects of Proposed Research (1/2 page)**

A. **Specific Aims** (1 page)

This Page will "make" or "break" your application. When the reviewer has finished reading this page, they will already have a preconceived notion of the quality of the proposal and a score.

[Restate your original Project Summary and expand on each Aim]

Phenomena X or disease X is… A characteristic feature of this process is… Although ABC has been shown to… it is unknown whether… **Preliminary studies** [or **Recent studies** from our lab] show that… However, it is unknown whether… Therefore, the **overall hypothesis** is that… This hypothesis will be tested by the following **specific Aims:**

Aim 1 will determine… Aim 1 will utilize X and Y methodology to… In Aim 1A we will… In Aim 2A… We hypothesize that…

Aim 2 will determine…

Aim 3 will determine…

The **results of this study** will lead to a better understanding of….

Tips on Aims

1. Your aims should be **interconnected but not dependent** on the successful outcome of another aim.

   EXAMPLE: **Bad** – Aim 2 cannot proceed until the studies in Aim 1 are completed.
             Good – Aim 2 proceeds in parallel with Aim 1 and findings from Aim 1 might direct future studies in Aim 2 or 3.

   In the end, *aims relate back to the overall hypothesis*.

Overall Hypothesis

Aim 1   **Aim 2**   **Aim 3**

time
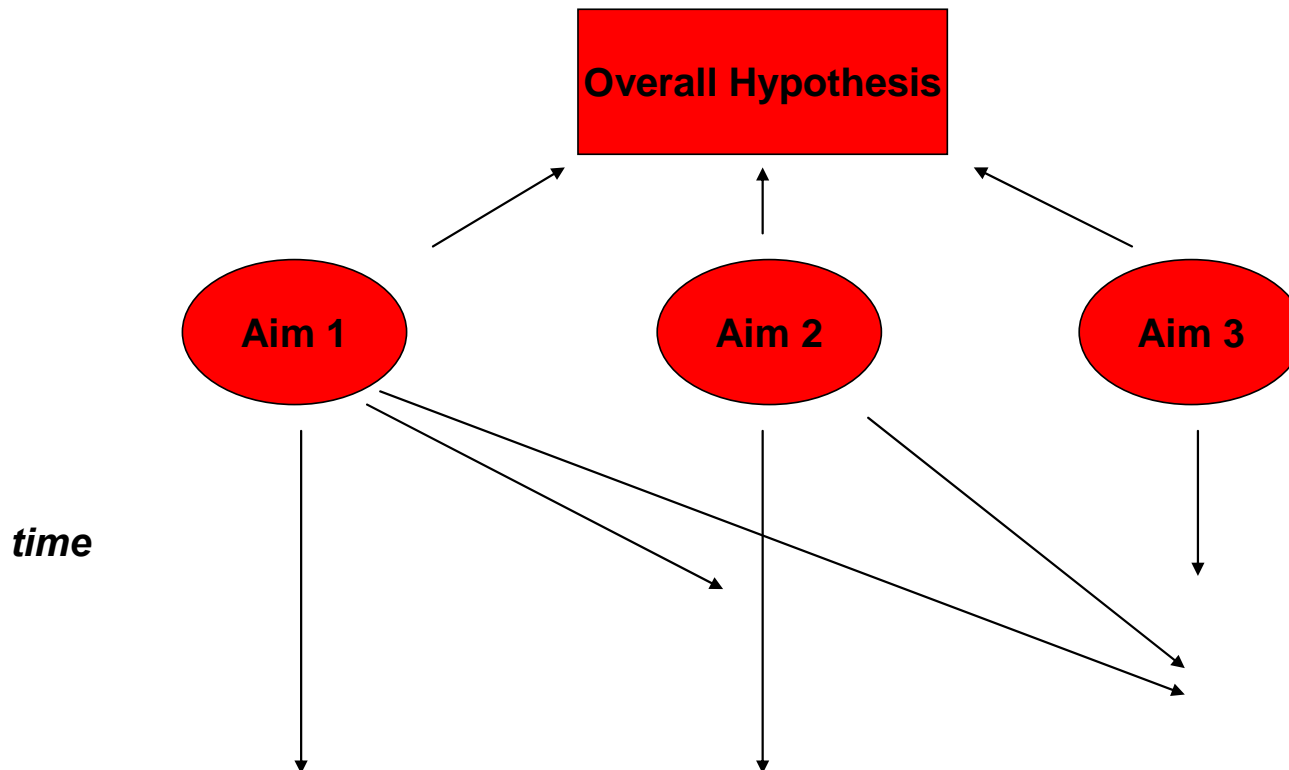
Tips on Aims

2. If the Aims are not interconnected, the project can be perceived as **overambitious and unfocussed** where each Aim is probably a proposal in itself.

3. If you cannot keep you Aims page to 1 -1.5 pages, then you are proposing too much and the grant is probably **overambitious and unfocussed**.

4. If the project is 2 years, then the probability of achieving the Aims should be 2 years. Proof that the applicant has thought this through is usually addressed in Section C, Predicted Results/Interpretation of Results and with a timeline or timeline statement.

5. The standard rule of thumb for a pre/post-doc fellowship is **two Aims**. It is OK to propose three Aims. However, if Aim 3 will not fit into the 2 year timeline, but it is clearly a logical progression of the studies, then simply state:

Aim 3 is to determine the… Although this Aim does not fit the time frame of this proposal, future   studies by the applicant will…

6. **Descriptive Aims:** If the Aim cannot have a stand alone hypothesis, then it is probably **descriptive**, not **mechanistic**, and may be detrimental to the success of the grant. Example: gene arrays (this ties into pt 1).

Tips on Aims

7. **Never propose to make a knockout mouse or transgenic mouse** for a 2 year proposal. If you do not have the mouse in-house, you are not ready to submit a proposal. These proposals are viewed as risky, especially during tight funding periods. If you have the mouse in-house, show preliminary data.

For example, you received or made a mouse null for XYZ. Show a Southern blot with the XYZ deletion or histology images that show a phenotype, etc…
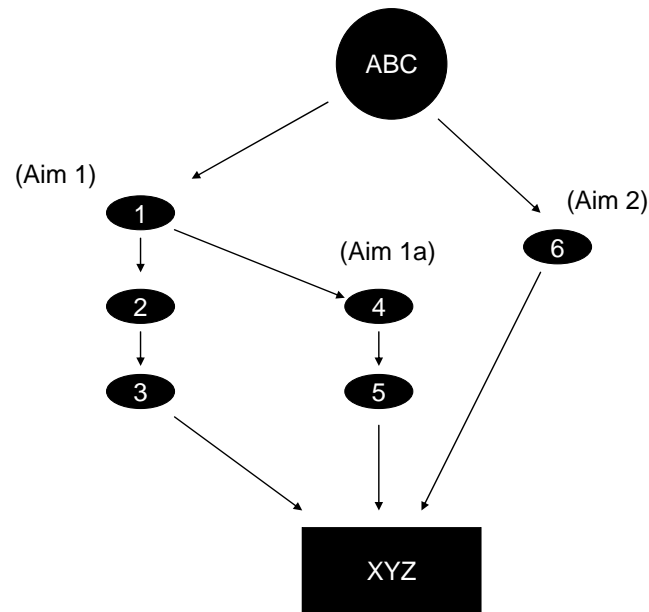
8. **Developing a new technology is risky.** For example, if you are proposing to measure flow patterns in diseased blood vessels but Aim 1 is to complete the technology, this will probably not get funded.

Use tools, models, animals that are readily available to you.

B. **Background** (3 pages)

1. ***Do not assume that the reviewer is an expert in your field!***

2. Expand on the brief background that has already been stated in the Project Summary. ***Use the Project Summary as your outline*** (subsections for Section B).

3. If the mechanisms you are proposing are complex on paper and thus very difficult to visualize in one's mind, make a **Schematic/Cartoon** that you can refer to throughout the proposal, in your aims and in your predicted results.

   For example: ABC regulates XYZ. Although we propose ABC regulates XYZ via 1, 2, and 3 (Aim 1), 1 can also activate 4 and 5 to regulate XYZ (Aim 1a). Moreover, preliminary studies show that ABC can mediate XYZ via 6 (Aim 2).

Schematics can be drawn such that they encompass the entire proposal.

INJURY

↑ platelets
↑ *S1P? (Aim 2a)*
↑ SMC proliferation

Disrupted S1P signaling?
(Aim 2a)

S1P

S1P1   S1P2   S1P3
(Aim 1a)

Signaling?
(Aim 1b)

Ac Me
Myoc
SRF SRF   SRF SRF
H   CArG B   CArG A

→ *SMMHC*
   SM α-actin
   SM22α

Transcriptional
Regulation (Aim 1b/2b)
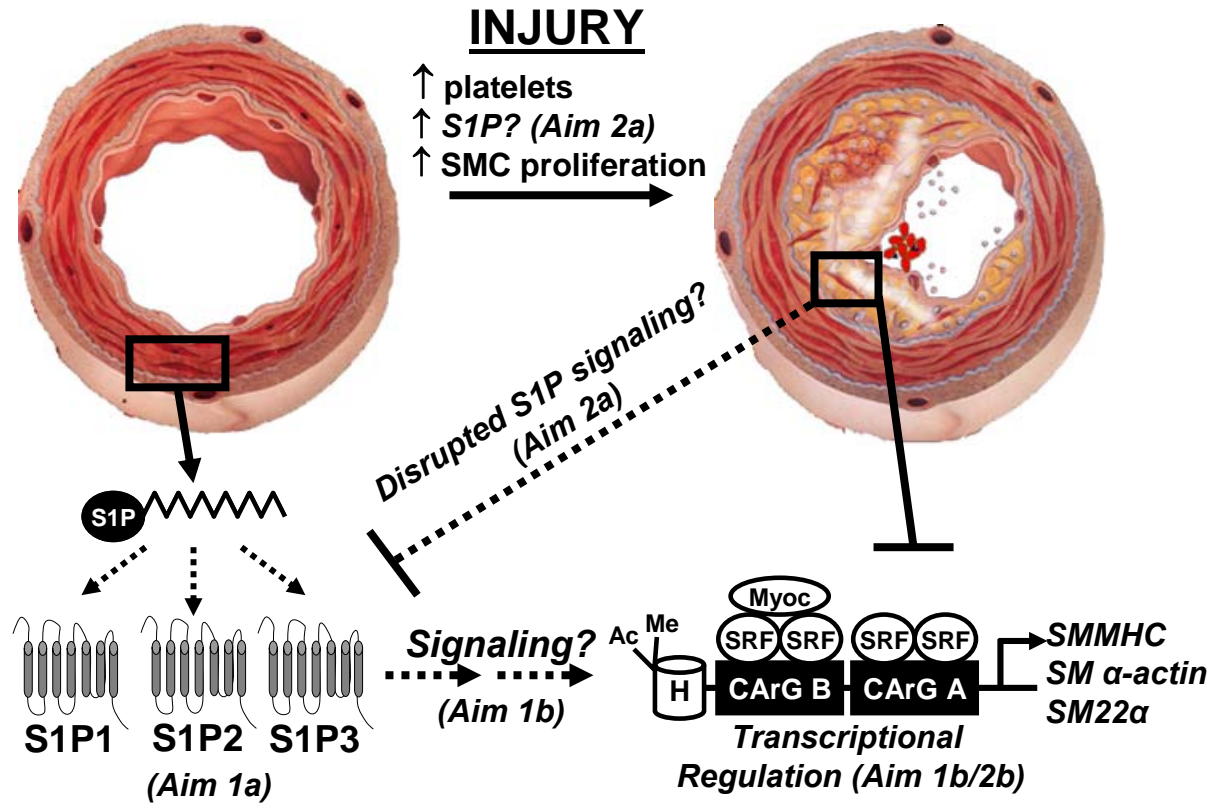
Figure 1. Overall hypothesis for this proposal.

4. Avoid jargon and multiple abbreviations, e.g. _VGCC_ _mediates_ _Ca_ _influx to activate_ _ROK-dependent activation of_ _SMGX_. VGCC = voltage-gated Ca channel, Ca = calcium, ROK = Rho kinase, SMGX = smooth muscle cell gene expression.

Use abbreviations for terms that are used throughout the proposal and are obvious.

5. Preliminary data: Although _preliminary data are not required for a pre-doc_, **show preliminary data**. Preliminary data may simply be proof that you can do the exps your proposing or that a critical exp has been performed by another lab or someone previously in your lab. However, if there is a key piece of data that your overall hypothesis hinges on, you must show that data.

For example, if you are proposing that **ABC** effects **XYZ** by **123**. You should have the preliminary data showing that **ABC** effects **XYZ**. Each Aim will then determine **123**.

ABC → 1 2 3 → XYZ
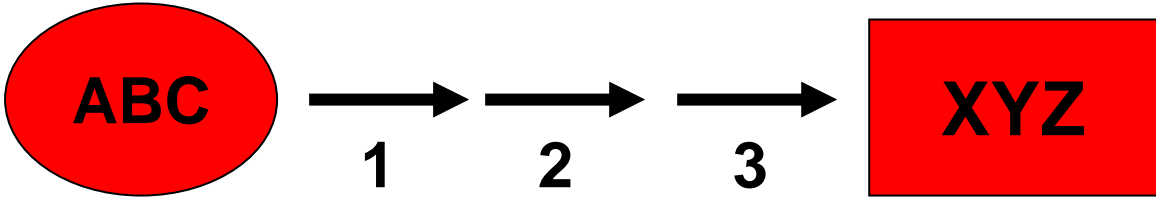
You may only have 1 preliminary Figure that is yours.

***6. Show the reviewer the experiment is feasible even if the data do not address the specific hypothesis – **PROOF OF PRINCIPLE DATA!**

C. **Research Design and Methods** (7.5 pages)

Restate the overall hypothesis. Keep the Reviewer focused.

Specific Aim 1: To determine…

Rationale:
Briefly restate why your doing this aim. The hypothesis for Aim 1 is that…

Experimental Design:
Unless absolutely necessary to the question being asked, you do not need details of the experiment that include pH of solutions, time of transfection, how RNA is isolated, etc.

**Interpretation of Results:
1) State what you predict will happen. 2) State what can go wrong and how you will interpret these findings. This is **critical** and shows the reviewer that you have thought through all of the experimental parameters and outcomes. Have alternative hypotheses.
As your mentor has probably said, *"99% science is failure and the 1% success is learning from failure"* – every reviewer knows this.

Future Directions:
If there are future directions beyond the scope of this proposal/timeframe, briefly state that you are aware of this; a sign that you see beyond the limited scope of this proposal.

Timeline: End Section C with a timeline or course of action for each Aim over 2 years.

D.Ethical Aspects of Proposed Research (1/2 page)

For example, if you are using animals, is it absolutely necessary or can these same questions be addressed *in vitro*?

Modified from Wamhoff, post-doc: Although *in vitro* studies can provide substantial information regarding the molecular mechanisms regulating of X, such data may be confounded by the changes that occur when the cell is not in its native *in vivo* setting. Thus, in addition to detailed *in vitro* studies, it is essential to assess the results of key genetic manipulations in an integrated manner in terms of organ/whole animal phenotype and there is no alternative to studies in animals. The mouse is the mammalian model of choice for studies of genetic manipulation due to its small size, rapid breeding, low costs and the swiftly increasing knowledge of its genome.

Cell culture vs. animals

2. Evaluation of Investigator:	(1/3rd of score):	Location within application:
▪ Evidence of potential for a research career		Page 4 and quality of scientific proposal
▪ Trainee's academic record (academic achievement, GPA)		Pages 4-7-8, biosketch and page 11
▪ Quality of trainee's previous research		Pages 4-7-8, biosketch, other support page and any included reprints from applicant
▪ Trainee's familiarity with literature and work of other investigators in the field of interest		Listed references/ bibliography
▪ Trainee's need for the training experience		Pages 4-7-8 and biosketch
* ▪ Quality of required 3 reference letters (do not use specific names)		Letters included in application documents, names on page 10

This is YOU

Reference letters are CRITICAL!

Get people who *know* you as a *scientist* and *person* to write your letters.

Example, if you tanked a few classes as an undergraduate, have someone write a letter that emphasizes how you've changed since then, if applicable ☺

3. Evaluation of the Sponsor/Institution: **(1/3rd of score):**

A. Qualifications of the sponsor: *Sponsor's reputation as an investigator*   **Location within application:**

▪ Publications and funding history	Sponsors information pages, other support page
▪ Track record with trainees	Sponsors information pages
▪ Commitment to applicant's training	Sponsors information pages
▪ Quality and comprehensiveness of the Training plan	Body of 12 page scientific proposal, Sponsors information pages – detailed training program
▪ Current funding available to support Fellow's project	Sponsors information pages, other support page

B. Qualification of the Facilities and resources available from institution: **Location within application:**

▪ Space stated in the sponsor's laboratory	Page 11 & 12
▪ Evidence of exposure to a research training environment.	Page 12, reviewer knowledge of institution

This is your PI and UVA

The PI's *training plan* is CRITICAL!

Can and how will the PI and the PI's environment turn you into a world-class scientist?

1. Sponsor's research and applicant's connection to this work.
2. Sponsor's plan to develop the applicants research capabilities and a sequence in which the applicant will be given responsibility to conduct the research.
3. Indicate other training or course work required for this proposal.
4. Relationship of the research training plan to your career goals, i.e. does your PI have any clue what you want to be in the future?

Your PI must be able to currently fund your work.
Read your PI's training plan before submitting. Make sure it addresses all 4 points.

Pre-doctoral & Post-doctoral Fellowships

Objective To help students or trainees initiate careers in cardiovascular and stroke research by providing research assistance and training. *Awardees will be expected to devote full time to research or activities directly related to their development into independent researchers.*

CRITIQUE LAYOUT

A.   **Name of Applicant & Research Project Title**

B.   **Proposal Description:** Briefly describe the project, (approximately one paragraph) including;
   - Scientific objectives
   - Research design and methods

C.   **Critique**: Address the following criteria in this order, listing strengths and weakness include detailed suggestions for enhancements for a future resubmission. **Use the quality of these areas as comparison points for assigning priority scores to applicants in these programs**:

1. Evaluation of Proposal   (1/3rd of score):   Location within application:

Criteria				Location within application:
Scientific merit of proposed project	1.3	3.0	3.5	Body of 12 page scientific proposal
Probability of achieving scientific objectives				Body of 12 page scientific proposal

2. Evaluation of Investigator: (1/3rd of score):   Location within application:

Criteria				Location within application:
Evidence of potential for a research career	1.9	1.9	3.5	Page 4 and quality of scientific proposal
Trainee's academic record (academic achievement, GPA)				Pages 4-7-8, biosketch and page 11
Quality of trainee's previous research				Pages 4-7-8, biosketch, other support page and any included reprints from applicant
Trainee's familiarity with literature and work of other investigators in the field of interest				Listed references/ bibliography
Trainee's need for the training experience				Pages 4-7-8 and biosketch
Quality of required 3 reference letters (do not use specific names)				Letters included in application documents, names on page 10

3. Evaluation of the Sponsor/Institution: (1/3rd of score):

A. Qualifications of the sponsor: *Sponsor's reputation as an investigator*   Location within application:

Criteria				Location within application:
Publications and funding history				Sponsors information pages, other support page
Track record with trainees				Sponsors information pages
Commitment to applicant's training				Sponsors information pages
Quality and comprehensiveness of the Training plan	1.6	1.6	2.0	Body of 12 page scientific proposal, Sponsors information pages – detailed training program
Current funding available to support Fellow's project				Sponsors information pages, other support page

B. Qualification of the Facilities and resources available from institution: Location within application:

Criteria				Location within application:
Space stated in the sponsor's laboratory				Page 11 & 12
Evidence of exposure to a research training environment.				Page 12, reviewer knowledge of institution

1.6 2.1 3.0

Scientist Development Grant

Objective - To support highly promising beginning scientists in their progress toward independence by encouraging and adequately funding research projects that can bridge the gap between completion of research training and readiness for successful competition as an independent investigator. At the time of award activation, no more than four years will have elapsed since an applicant's first faculty/staff appointment at the assistant professor level or its equivalent. A pivotal requirement is the *demonstration that the award will promote independent status for the applicant*. An applicant cannot hold, nor have held, any other national award prior to the activation date of the Scientist Development Grant. A sponsor should not be required, although it is important that applicant's Department Head provides assurance that the applicant has the institution's support.

CRITIQUE LAYOUT

A. **Name of Applicant & Research Project Title**

B. **Proposal Description:** Briefly describe the project, (approximately one paragraph) including;
- Scientific objectives;
- Research design and methods.

C. **Critique**: Address the following criteria in this order, listing strengths and weakness include detailed suggestions for enhancements for a future resubmission. **Use the quality of these areas as comparison points for assigning priority scores to applicants in these programs**:

1. Future Independence of Investigator:

	Location within application:
Demonstrated evidence that the award will promote independent status for the applicant by the end of the 3 or 4-year award. Should not serve as enhanced funding for professional personnel working on the research program of an established scientist.	Mentioned in SDG reference letters and department head letters

2. Scientific excellence of the research proposal:

	Location within application:
Originality of ideas	Body of 12 page scientific proposal, mention in reference letters
Projected scientific impact	Body of 12 page scientific proposal, mention in reference letters
Soundness of approach	Body of 12 page scientific proposal
Logical organization	Body of 12 page scientific proposal

3. Investigator - Qualifications of the applicant:

	Location within application:
Appropriate professional career stage	Pages 3, 4, and 7, Biosketch
Relevant experience	Pages 4, 7 and Biosketch
Productivity in previous training and research	Pages 4, 7, 14 and Biosketch
Current relationship to supervisor/mentor	Might be mentioned in Dept. Head Letter, page 15, or in reference letters
Prior awards, if any, and resulting accomplishments	Pages 4, 7, 14 and Biosketch
Number and quality of publications in peer reviewed journals	Biosketch
Quality of required 3 reference letters (do not use specific names)	Page 10 lists names, 3 referent letters

4. Qualification of the Facilities and resources available from institution:

	Location within application:
Adequacy of available resources, including consultative support, and facilities	Pages 11-14
Institutional commitment as demonstrated in Department Head letter	Pages 6, 11 and 15

Beginning Grant-in-Aid

Objective - To promote the independent status of promising beginning scientists. At application, applicant must be an M.D., Ph.D., D.O., D.V.M. or equivalent initiating independent research career. Applicant must have faculty/staff appointment (up to and including assistant professor or equivalent) at activation. A sponsor should not be required, although it is important that applicant's Department Head provides assurance that the applicant has the institution's support.

CRITIQUE LAYOUT

A. **Name of Applicant & Research Project Title**

B. **Proposal Description:** Briefly describe the project, (approximately one paragraph) including;
- Scientific objectives
- Research design and methods

C. **Critique**: Address the following criteria in this order, listing strengths and weakness include detailed suggestions for enhancements for a future resubmission. **Use the quality of these areas as comparison points for assigning priority scores to applicants in these programs**:

1. Future Independence of Investigator:

Location within application:

Demonstrated evidence that the award will promote independent status for the applicant at the completion of first or second award. Should not serve as enhanced funding for professional personnel working on the research program of an established scientist.	Mentioned in department head letter

2. Scientific excellence of the research proposal:

Location within application:

	Location within application:
Originality of ideas	Body of 12 page scientific proposal
Projected scientific impact	Body of 12 page scientific proposal
Soundness of approach	Body of 12 page scientific proposal
Logical organization	Body of 12 page scientific proposal

3. Investigator - Qualifications of the applicant:

Location within application:

Appropriate professional career stage	Pages 3, 4, and 7, Biosketch
Relevant experience	Pages 4, 7 and Biosketch
Productivity in previous training and research	Pages 4, 7, 14 and Biosketch
Current relationship to supervisor/mentor	Might be mentioned in Dept Head Letter
Prior awards, if any, and resulting accomplishments	Pages 4, 7, and Biosketch
Number and quality of publications in peer reviewed journals	Biosketch

4. Qualification of the Facilities and resources available from institution:

Location within application:

Adequacy of available resources, including consultative support, and facilities	Pages 11 - 14
Institutional commitment as demonstrated in Department Head letter	Pages 6, 11 and 15

The SDG and BGA are very similar. What these grants ultimately come down to are *<u>independence issues</u>*:

1. The science must be excellent, good grantmanship, feasibility, etc.

2. Will the award foster independence and National funding?

<u>Classic situation</u>: The applicant still resides at the institute where they trained as a post-doctoral fellow. In fact, the applicant most likely has dedicated lab space within the former PI's lab (at least on paper). Is the work proposed in this application different enough from the former PI that this work will eventually lead to funding on the national level, i.e. NIH RO1?

<u>The #1 Reviewer Comment</u>: *I am not convinced that the applicant is/will be independent from their previous mentor.*

What convinces a reviewer of independence or strive to be independent:

1. Department Chair letter and commitment to space (non-issue for tenure track).
2. **Letter from former mentor clearly stating how this work is different.
3. Prior awards and quality of publications and how they relate to this proposal (not necessarily quantity).

How the Review Process Works
"Day of Study Section"

__LENGTH__: 1 day
__START__: 7:00 AM
__END__: 6:00 PM or when last app is discussed

1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
064555N	063222N	063222Z	065511Z	064555N	062222Z			066655Z
		062222Z	061111Z					
			063222Z					

__STREAMLINED APPS = 33%__
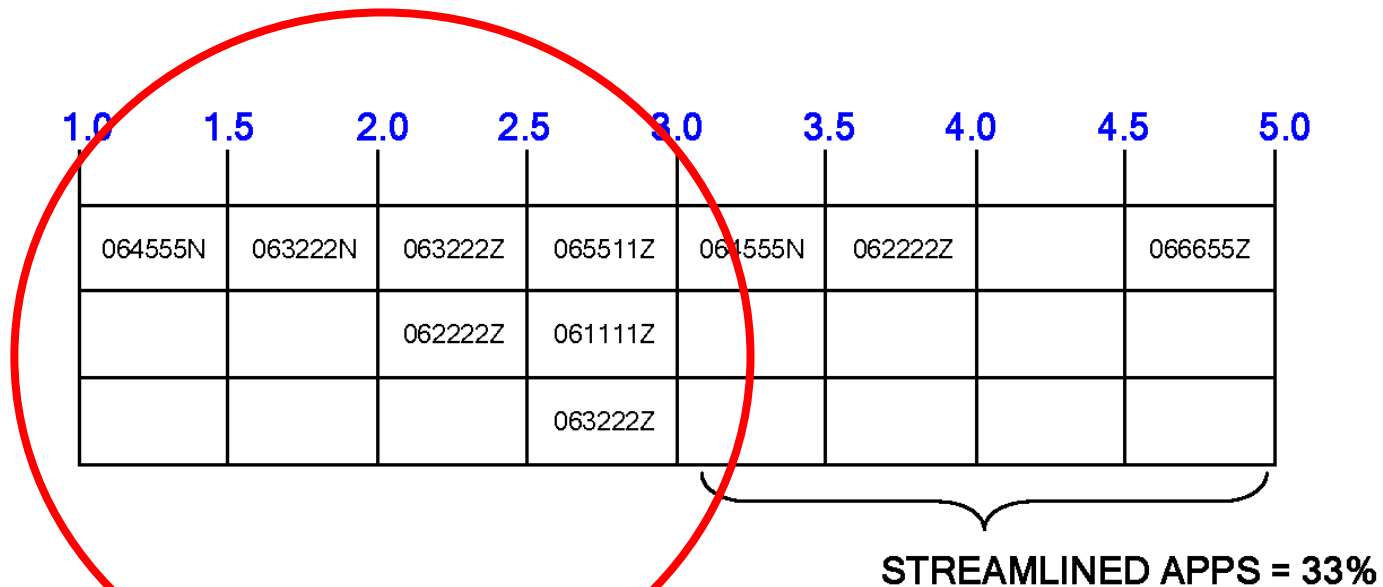
Only if a proposal received 2 or more "streamlines" will it not be discussed.
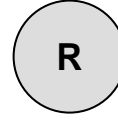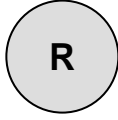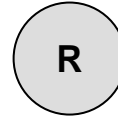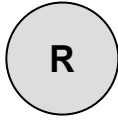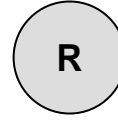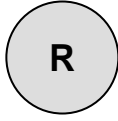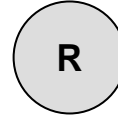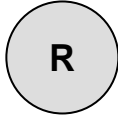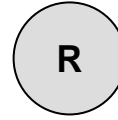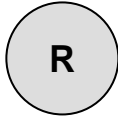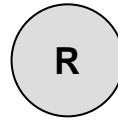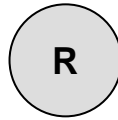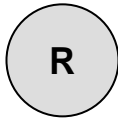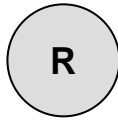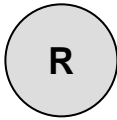
1. Anyone with COI leaves.

2. R1, R2 and R3 state preliminary scores ranges, e.g. R1 "1.9-2.1", R2 "1.6-1.9", R3 "1.7-2.0"

3. R1 gives <5 min summary of grant and 2-3 min discussion of concerns (no more than 10 minutes!)

4. R2 only adds comments that differ from R1 or "in agreement"
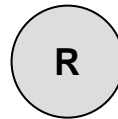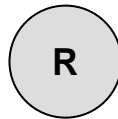
5. R3 adds comments that differ from R1, R2 or "in agreement"

6. R1, R2, R3 restate range of scores.

7. Each reviewer writes down their score.

8. Next application.
    TOTAL TIME FOR YOUR APP = 7-12 min!

You receive your score and critiques via email, What do you do now?

1. <u>Funded</u>: Jump for joy, <u>push on</u>.

2. <u>Not funded</u>: Throw a temper tantrum, blame the world, push on, <u>resubmit</u>!

A large percentage of first-time submissions to the AHA get rejected.

This will happen to you. Breath.

Read your critiques, address every comment and resubmit.

Briefly point out what the reviewers like about the grant and then address every comment.

Walk the reviewer through all of your changes by clearly denoting in the text where the changes were made. *It is likely you will only get 1 of the 3 previous reviewers*.

This is not the time nor place to pick a fight. However, if the reviewer is completely off-base, be respectful. "I respectfully disagree with this comment. It has been shown that…"

Do what the reviewers ask.

NOTE: Revised sections are denoted by *left margin brackets* " ["; Figures are preceded by " ** ".

INTRODUCTION: This is the first resubmission of **RO1 HL081682** by a First-time Investigator. The "Summary of Critique" for the original submission (Oct 1, 2004) was received on **May 20, 2005**. I received a score of ## and the funding payline was ##. The applicant has made significant progress to address the Reviewers' comments and suggestions, providing substantial new preliminary data and greatly improving the focus and quality of this proposal. In general, the major revisions encompassed: 1) general experimental clarification and validation of preliminary studies, 2) "*descriptive nature of Aim 3*", and 3) "*independence of the investigator*".

We thank the Reviewers for their overall enthusiasm for this proposal: 1) *"a highly original and innovative proposal"*, 2) *"employs state of the art methods… and superb models… to address important and novel questions… for understanding phenotypically modulated SMCs"*, 3) *"well crafted research design"* and *"well written"*, 4) *"theory that has clearly been under-investigated"*, 5) *"excellent group of collaborators"* with an *"appropriate"* environment, and 6) *"preliminary data that are supportive of each aim"*.

However, Reviewer 1 and 2 had a major concern regarding the "*descriptive nature of the third specific Aim*". We now provide new preliminary data in this resubmission that will allow us to apply *"transgenic mouse methodology (for) in vivo studies"* to *"advance the work more appropriately and link the studies to the first two Aims"* (below, **pt. 3**). Our overall enthusiasm was also tempered by several excellent concerns and needed clarifications regarding preliminary studies/models raised in **Critique 2** and addressed below:

1. ***"It is not clear whether the applicant can target experiments towards relevant directions and can recognize findings that influence clinical therapy."*** Although it is out of the scope of this proposal to immediately translate findings into a clinical therapy, the new advances we have made in such a short period of time show that we can recognize findings that test mechanisms towards relevant directions. On **page 25**…

2. **"*the conclusion that (S1P effects) are mediated through calcineurin are premature"*.** We have expanded our preliminary results implicating calcineurin as a downstream regulator of S1P mediated SMGX, not depolarization.

Mid-Atlantic and National Affiliate can be on opposite sides of the spectrum

TITLE: Calcium-dependent regulation of smooth muscle phenotype
PI: Brian R Wamhoff

Mid-Atl BGIA
Score: 2.575
Percentile Rank: 58.33
Major Comments:
R1: The experimental plan is not well focussed… and as a result extremely ambitious and lack direction.
R2: …will not do much to bolster independence from current PI…
R3: Clearly at stage for an independent award

National SDG
Score: 1.5182
Percentile Rank: 9.88
Major Comments:
R1: Reasonable approach to test the hypothesis and logically organized.
R2: Supervisor supports the full independence of the researcher.
R3: …rising star…exceptional environment at UVa…

Concluding Remarks

In the end, the best grants/science get funded, for the most part ☺

Have your peers, former and current AHA fellows read your Specific Aims page.   Do they understand what your proposing to do?

Accept criticism openly but know what to filter and what not to filter.

Keep it simple, organized, and structured in such a way that if a Reviewer does not understand what you are proposing to do, it is because <u>you</u> failed, not them ☺

Even if your grant is not funded, you now have a detailed plan for the next 2+ years of your career. Not many people can say that ☺

Acknowledgements

Mike Sturek, PhD, University of Missouri
Gary Owens, PhD, University of Virginia