Grantsmanship and Funding Fest Series
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Presented by
• UCSD Office of Postdoctoral and Visiting Scholar Affairs
• TSRI Office of Career and Postdoctoral Services

THE BASICS OF SCIENCE GRANT WRITING

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THREE GOLDEN RULES:

1. AFTER WRITING EACH SECTION, READ IT AS IF YOU WERE A REVIEWER

2. DISCIPLINE YOURSELF TO FINISH WRITING TWO WEEKS BEFORE DUE DATE

3. PUT IT AWAY FOR A WEEK & GO BACK TO 1
R01- TYPE grants versus Mentored grants

R01:
science > preliminary data > productivity

Mentored grants:
science = PI = mentor/environment

Mentored grants

science = PI = mentor/environment

Science:
Original, feasible, focused, not too much, hypothesis-driven, good training potential

PI:
Strong academics, productive, enthusiastic

Mentor:
Well funded, productive, strong training record, personalized training plan for applicant

F30/F31/F32/F33 Review
If you cannot access the hyperlinks below, visit http://grants.nih.gov/grants/peer/critiques/f.htm

Application #:
Applicant:

Overall Impact
Reviewers will provide an overall impact score (from 1(best) to 9(worst)) to reflect their assessment of the likelihood that the fellowship will enhance the candidate's potential for, and commitment to, a productive independent scientific research career in a health-related field, in consideration of the following scored and additional review criteria. An application does not need to be strong in all categories to be judged likely to have a major impact.

Overall Impact/Merit
• Strengths
• Weaknesses
Scored Review Criteria

Reviewers will consider each of the five review criteria below in the determination of scientific and technical merit, and give a separate score for each.

1. Fellowship Applicant
   - Strengths
   - Weaknesses
2. Sponsors, Collaborators, and Consultants
   - Strengths
   - Weaknesses
3. Research Training Plan
   - Strengths
   - Weaknesses
4. Training Potential
   - Strengths
   - Weaknesses
5. Institutional Environment & Commitment to Training
   - Strengths
   - Weaknesses

Additional Review Criteria

As applicable for the project proposed, reviewers will consider the following additional items in the determination of scientific and technical merit, but will not give separate scores for these items.

- A response for Protections for Human Subjects, Vertebrate Animals, and Biohazards is required for all applications.


Resubmission Comments (if applicable):

- Protections for Human Subjects Comments (Required Unless Not Applicable):
- Vertebrate Animals Comments (Required Unless Not Applicable):
- Biohazards Comments (Required Unless Not Applicable):

Inclusion of Women, Minorities and Children Applicable Only for Human Subjects Research Comments (Required Unless Not Applicable):

Resubmission Comments (if applicable):

- Protections for Human Subjects Comments (Required Unless Not Applicable):
- Vertebrate Animals Comments (Required Unless Not Applicable):
- Biohazards Comments (Required Unless Not Applicable):

Additional Review Considerations

As applicable for the project proposed, reviewers will address each of the following items, but will not give scores for these items and should not consider them in providing an overall impact score.

- Select Agents Comments (Required Unless Not Applicable):
- Responsible Conduct of Research Comments (Required):
- Budget and Period of Support Recommended budget modifications or possible overlap identified:
- Resource Sharing Plans Comments (Required if Unacceptable):
Vascular endothelial growth factor (VEGF) is an hypoxia-inducible endothelial mitogen whose knockout is embryonically lethal. It is thought to be important in maintenance of existing vascular beds and induction of angiogenesis when stimuli are provided.

In many chronic diseases such as COPD, exercise capacity remains impaired even after organ transplant has restored normal primary organ function.
ABSTRACT

BACKGROUND (ctd)
There is evidence that this may be due to skeletal muscle abnormalities, reduced capillarity in particular. We have therefore hypothesized that angiogenesis is impaired in these diseases, and that this is due to altered regulation of VEGF.

SPECIFIC AIMS, PRELIMINARY DATA and DESIGN:

We will test this hypothesis by a combination of basic and clinical approaches. We will first develop a viral construct capable of efficient muscle gene transfer. This will be refined using GFP driven by the CMV promoter, and then will be used to make a Cre recombinase/viral construct. Preliminary data show that adeno-associated rather than adenoviral vectors will be most efficient. We will then create VEGF-loxP transgenic mice. Preliminary work shows that excision of exon 3 will inactivate VEGF, and the loxP flags will therefore be targeted around this exon.

SPECIFIC AIMS, PRELIMINARY DATA and DESIGN:

After this method development, the Cre vector will be directly introduced into regions of skeletal muscle and local VEGF deletion assessed by in situ hybridization for message and immunostaining for protein. Capillarity will then be measured and compared in areas with and without VEGF activity. If our hypothesis is correct, capillarity will be reduced in VEGF-deficient areas. This basic science investigation will be complemented with muscle biopsy studies of VEGF gene and protein response to exercise in patients with COPD, compared to controls. These responses will be related to capillarity and functional estimates of oxygen transport.
SUMMARY: EXPECTATIONS & SIGNIFICANCE

If abnormal VEGF regulation is substantiated and the regulatory pathways can in the future be defined, this should provide the basis for specific therapeutic interventions to restore VEGF activity, enable normalization of muscle function and ultimately improve quality of life for patients with COPD, before and after organ transplantation.

Vascular endothelial growth factor (VEGF) is an hypoxia-inducible endothelial mitogen whose knockout is embryonically lethal. It is thought to be important in maintenance of existing vascular beds and induction of angiogenesis when stimuli are provided. In many chronic diseases such as COPD, exercise capacity remains impaired even after organ transplant has restored normal primary organ function. There is evidence that this may be due to skeletal muscle abnormalities, reduced capillarity in particular. We have therefore hypothesized that angiogenesis is impaired in these diseases, and this block is due to altered regulation of VEGF. We will test this hypothesis by a combination of basic and clinical approaches. We will first develop a viral construct capable of efficient muscle gene transfer. This will be refined using GFP driven by the CMV promoter, and then will be used to make a Cre recombinase/viral construct. Preliminary data show that aden-associated rather than adenoviral vectors will be most efficient. We will then create VEGF-LoxP transgenic mice. Preliminary work shows that excision of exon 3 will inactivate VEGF, and the loxP flags will therefore be targeted around this exon. After this method development, the Cre vector will be directly introduced into regions of skeletal muscle and local VEGF deletion assessed by in situ hybridization for message and immunostaining for protein. Capillarity will then be measured and compared in areas with and without VEGF activity. If our hypothesis is correct, capillarity will be reduced in VEGF-deficient areas. This basic science investigation will be complemented with muscle biopsy studies of VEGF gene and protein response to exercise in patients with COPD, compared to controls. These responses will be related to capillarity and functional estimates of oxygen transport. If abnormal VEGF regulation is substantiated and the regulatory pathways can in the future be defined, this should provide the basis for specific therapeutic interventions to restore VEGF activity, enable normalization of muscle function and ultimately improve quality of life for patients with COPD, before and after organ transplantation.

INTRODUCE BROAD OBJECTIVES, then PRESENT REAL (NOT FAKE) HYPOTHESES FOR EACH HYPOTHESIS, PROVIDE SPECIFIC STUDIES THE MOST IMPORTANT SINGLE PART OF THE APPLICATION. BELIEVE ME. PLEASE.
SPECIFIC AIMS
INTRODUCE BROAD OBJECTIVES:
A short paragraph looking at the forest, not the trees.
What the general problem to be solved is, what the overall approach is to be, what the hoped for outcome will be.

SPECIFIC AIMS
INTRODUCE BROAD OBJECTIVES:
This application seeks to define the importance of VEGF to muscle capillary maintenance. Initial studies in mice will develop and then apply the Cre/LoxP strategy to eliminate VEGF in selected regions of skeletal muscle and examine the consequences for capillarity. Patients with COPD will undergo muscle biopsy before and after an exercise bout. VEGF message and protein responses to exercise will be measured and compared to controls. In addition, VEGF levels will be related to muscle capillarity. These studies should define the importance of VEGF in muscle vascular supply and any abnormalities in VEGF response to exercise in patients with disease.

SPECIFIC AIMS
PRESENT REAL (NOT FAKE) HYPOTHESES
Example: Vascular endothelial growth factor is required for 1) muscle capillary maintenance and 2) the angiogenic response to exercise.
A real hypothesis because there are alternate growth factors such as bFGF etc that could be more important or that could take over if VEGF were eliminated.
SPECIFIC AIMS

PRESENT REAL (NOT FAKE) HYPOTHESES

Fake example: In COPD, angiogenic responses to exercise will or will not be normal. Fake since you have encompassed all possibilities, and the hypothesis lacks any mechanistic basis.

Fake example: Comparative genomics will provide further insight into the molecular basis of pulmonary structure and function changes caused by maternal smoking during pregnancy. Fake because nobody would argue against such a broad non-specific mom & apple pie statement.

SPECIFIC AIMS

LIST SPECIFIC STUDIES FOR EACH HYPOTHESIS

Hypothesis: Vascular endothelial growth factor is required for muscle capillary maintenance.

Aim 1: Develop an Adeno-associated viral vector for skeletal muscle gene transfer. Insert the Cre recombinase gene, and test transfection efficiency.

Aim 2: Create a transgenic mouse with loxP sequences flanking VEGF exon 3.

Aim 3: Delete VEGF by Cre/loxP in selected regions of skeletal muscle, assess adequacy of deletion by ….

Aim 4: Relate presence/absence of VEGF to capillarity

BACKGROUND, SIGNIFICANCE

Give a concise literature review of the area.
Do NOT go on forever.
Feature your own work, but -
Do NOT fail to cite other important references (the reviewer may well be an author in the area!)
Address each piece of the story using subheadings:

VEGF & competitors, in muscle in particular
Exercise limitation in disease
Skeletal muscle function in disease
Gene therapy in muscle (special considerations)
Cre/loxP strategy
PRELIMINARY STUDIES
An increasingly critical part of applications.

Ask yourself:
If you were the reviewer, what are the most ambitious parts of the proposal from a methods point of view, and what are the most critical proof of concept issues to address? What preliminary data would you need to feel comfortable supporting the grant as a reviewer?

Provide those assurances as preliminary data!!!

DESIGN AND METHODS
Make it easy for the reviewer!! ORGANIZE!!

I suggest TWO distinct sections:

1. Experimental design, containing broad protocols, statistical justification of numbers of animals/cells etc. Critical here is to assure a 1:1 correspondence with every single specific aim. Include analysis of outcome and discuss possible problems up front (alternative strategies should your fail should be presented).

2. Specific method “recipes” for technical things like Northern, vector construct, capillary assessment, VEGF-loxP creation, each with its own subheading.

BUDGET
DON’T TRY AND FOOL THE REVIEWER

ASK FOR WHAT YOU REALLY NEED, NO MORE, NO LESS.

DO NOT PLAY THE PADDDING GAME, ie, THINKING THE REVIEWER WILL CUT NO MATTER WHAT YOU REQUEST, SO AS TO TRY AND GET WHAT YOU REALLY WANT.

THIS WILL ONLY ANGER THE REVIEWER
BUDGET: JUSTIFICATION

OFTEN INCREDIBLY POORLY DONE:
A FEW WELL-ARGUED SENTENCES WILL
SECURE BUDGET ELEMENTS THAT WOULD
OTHERWISE BE DISALLOWED

Justify time by figuring out number of studies times hours
per study, including set-up, execution and data analysis

Do NOT BS your way by saying “20% of Joe Boggs is
requested, therefore we ask for 20% of his salary”. Say:
“With 50 studies each lasting one full day (set-up, execution
and data processing), over the year 20% of Joe’s time is
necessary and therefore 20% salary support is requested”.

Justify supplies by figuring out the detailed costs per
animal and multiplying by number of animals.

Do NOT BS your way by saying “$X is requested for
Supplies, in keeping with historical costs”. Say:
“With 50 animals required and a cost of $X per animal,
$50X is requested for supplies. $X is calculated as follows”
and insert the detailed itemized supplies per animal.

FINAL THOUGHTS (1):
WHEN THE GRANT IS TOGETHER, READ IT
AS IF YOU WERE THE REVIEWER AND ASK:

Is it easy to follow, well sequenced? Do the sections link?

Is each section dealing with the right issues?

Is it a good package? This means a convincing rationale,
good background to convince reviewers of novelty, good
preliminary data to prove feasibility and proof of concept,
the best hypotheses & specific aims, and solid methods
with good techniques, protocols, proposed analysis etc.

Can the methods for each aim be easily found?
FINAL THOUGHTS (2):
WHEN THE GRANT IS TOGETHER, READ IT AS IF YOU WERE THE REVIEWER AND ASK:

Are there critical uncertainties in need of resolution?

Is it neither too thin on studies nor too ambitious?

Are the budget requests honest and neither too little nor too much?

RESOURCES

Copy of presentation available at:
• http://research.ucsd.edu/postdoc/training.html

Grant Writing 101 on eLearning at OCGA
• http://ocga.ucsd.edu/eLearning/Overview.html#GPO

All About Grant Writing Tutorial on NIH website
• http://funding.niaid.nih.gov/researchfunding/grant/pages/aag.asp

Grant writing Tutorial by Anthony Coelho
• http://ora.stanford.edu/ora/rad4/nih_04.asp