

What happens at study section? Behind the scenes of grant review

Robert E. Smith



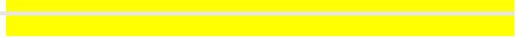
**COLLEGE OF MEDICINE
AND LIFE SCIENCES**

THE UNIVERSITY OF TOLEDO

Disclosure

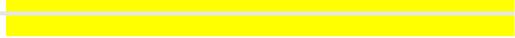
- Grant reviewer for Alkermes
- CSO CRI Genetics
- Founder and board member International Kinome Society





What happens at study section?





Tales from study section:

(1) The reviewer said what!!!

(2) How not to respond to a grant review, and

(3) Tips and tricks for your response to reviewers

Part 1: The reviewer said what??

2. Career Development Plan/Career Goals & Objectives/Plan to Provide Mentoring:

Strengths

- Aspects of training proposed in this application complement each other to allow the candidate to study genetic predisposition, environmental contributions, advanced proteomics, bioinformatics, and behavioral analyses related to psychiatric disease.

Weaknesses

3. Research Plan:

Strengths

- The proposal tests the hypothesis that environmental stress will exacerbate behavioral and cognitive phenotypes in animal models of schizophrenia, using the following approach: 1) examination of the behavioral and cognitive effects of gene x environmental stress, 2) examination of lamina and synapse-specific proteomic changes associated with altered behavioral tasks, and 3) examination of the effects of chronic stress on these factors following rescue of the genetic lesions.
- They will employ a well-characterized chronic stress paradigm with GluN1 knockdown and hDISC1 mutant mice, and genetically rescue the GluN1 knockdown and hDISC1 mutant genotypes prior to chronic stress, to determine the capacity of these animals to recover cognitive plasticity and to characterize the proteomic changes associated with resiliency to chronic stress.

Weaknesses

4. Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):

Strengths

Part 1: The reviewer said what??

Candidate: 5
Career Development Plan/Career Goals & Objectives: 4
Research Plan: 3
Mentor/Co-Mentor(s), Consultant(s), and Collaborator(s): 2
Environment and Institutional Commitment to the Candidate: 2

2. Career Development Plan/Career Goals & Objectives/Plan to Provide Mentoring:

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Weaknesses

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Strengths

Part 1: The reviewer said what??

Overall Impact	High	Medium	Low
Score	1 2 3	4 5 6	7 8 9

e.g. Applications are addressing a problem of high importance in the field. May have some or no technical weaknesses.

e.g. Applications may be addressing a problem of high importance in the field, but weaknesses in the criteria bring down the overall impact to medium.
e.g. Applications may be addressing a problem of moderate importance in the field, with some or no technical weaknesses

e.g. Applications may be addressing a problem of moderate/high importance in the field, but weaknesses in the criteria bring down the overall impact to low.
e.g. Applications may be addressing a problem of low or no importance in the field, with some or no technical weaknesses.

2. Career Development Plan/Career Goals & Objectives/Plan to Provide Mentoring:

Strengths

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Part 1: The reviewer said what?? Example #2

CRITIQUE 2

Significance: 5
Investigator(s): 4
Innovation: 7
Approach: 5
Environment: 1

3. Innovation: Strengths

Weaknesses

- Novelty is low.

4. Approach: Strengths

- Network analysis is a strength

Weaknesses

- Aims are linked

Part 1: The reviewer said what?? Example #2

CRITIQUE 2

Significance: 5
Investigator(s): 4
Innovation: 7
Approach: 5
Environment: 1

3. Innovation: Strengths

Weaknesses

- Novelty is low.

4. Approach:

Strengths

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Weaknesses

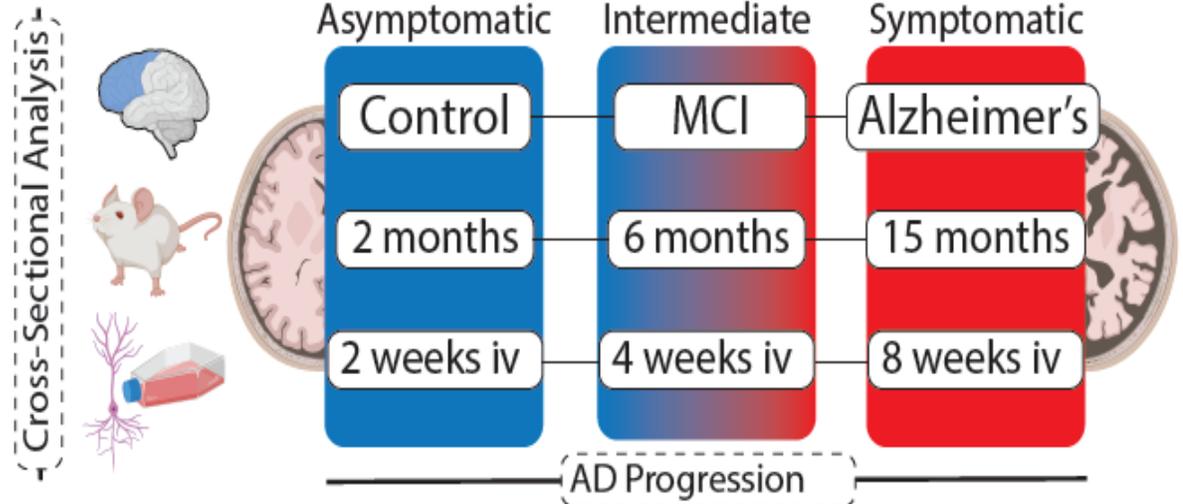
- Aims are linked

CRITIQUE 1

Significance: 2
Investigator(s): 2
Innovation: 3
Approach: 5
Environment: 2

CRITIQUE 3

Significance: 3
Investigator(s): 3
Innovation: 2
Approach: 5
Environment: 2



Part 1: The reviewer said what?? Pop Quiz-

The PI should address the critique that the aims are linked by saying:

- Telling the reviewer they are wrong
- Moving the grant to another study section and avoiding the bad reviewer all together.
- Try to hide that the aims are linked, and rely on one another, avoiding language that suggests this.
- Make each aim an independent experiment with no relationship to other aims.
- Embrace that the aims are linked but bury the reviewers in prelim data supporting each aim being successful.

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Innovation: 7
Approach: 5
Environment: 1

3. Innovation: Strengths

Weaknesses

- Novelty is low.

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Weaknesses

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Part 1: The reviewer said what?? Pop Quiz-

Since SA1 is hypothesis generating, we have designed SA2 for validation and replication, and SA3 for assessment of causality. It follows that our aims are necessarily linked, with clear progression criteria; our approach is rigorous, with complementary omics methods (kinome array and LCMS), and well powered, with appropriate numbers of subjects, mice, and cell lines. While linkage of aims is a standard concern raised in grant review, we address this with *extensive preliminary data in AD subjects* that 1) already identifies targets, based on preliminary data (published or unpublished), to be validated in SA2 and SA3, 2) highlights the potential of our workflow to generate functional proteomic disease signatures that reveal novel pathophysiological insights for AD progression, and 3) shows the feasibility of our methodologies, including kinome array assays and bioinformatics techniques.

CRITIQUE 2

Significance: 5
Investigator(s): 4
Innovation: 7
Approach: 5
Environment: 1

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Weaknesses

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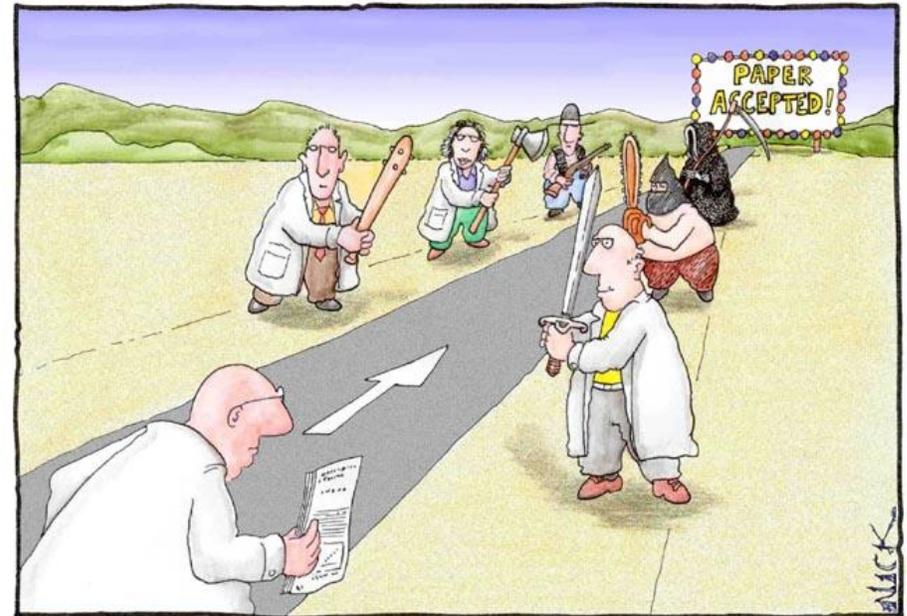
- Network analysis is a strength

Weaknesses

- Aims are linked

Part 2: How not to respond to a grant review

- Introduction to the revised application. 1 pager, 0.5 inch margins 11 point arial (56 lines).
- Talk to your program officer. Often they were listening in-vignette
- Don't tell the reviewer they are wrong!
- Use positive and assertional language: "We agree that . . ."
- Group related criticisms for different reviewers to save space

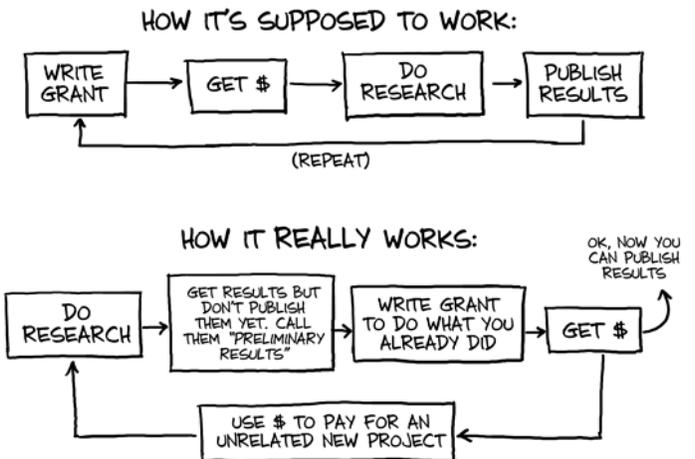


Most scientists regarded the new streamlined peer-review process as "quite an improvement."

Part 2: How not to respond to a grant review

- Briefly summarize positive comments at the top- reviewers have the prior critique so no need to be verbose here.
- No need to use full sentences
- Ok to explain or clarify, but avoid arguing
- Be tactful if the reviewers missed something that was in the grant and said it wasn't there. Grants are complicated and reviewers are human.

THE GRANT CYCLE



Part 2: How not to respond to a grant review

Introduction. Regarding the prior review, the potential impact was described by R1 and R3 as “very high,” while R2 states that “the kinome is clearly important in AD.” However, several valid concerns were raised, particularly with the approach. In response we made substantial revisions indicated by a vertical line in the margins.

Part 2: How not to respond to a grant review

Overarching changes to the approach. We have removed the RNAseq studies and replaced them with phospho-LCMS. This addresses several overlapping concerns raised by the reviewers, including **(R1)** concerns about including mRNA studies, **(R1)** coverage bias for the kinome array, **(R2)** rigor and repro-ducibility, **(R1)** validation, **(R2)** lack of state-of-the-art approaches. The PD/PI has relevant expertise with LCMS, and a long-standing relationship with the proteomics core (led by consultant Dr. Ken Greis) at the University of Cincinnati. We will enrich samples for phospho-peptides, perform shotgun LCMS, and integrate these data with our protein kinase activity-based array datasets. This gives us a second technique to assess/validate the kinome that does not rely on bioinformatic algorithms to make protein kinase assignments.

Part 3: Grantsmanship pearls

- Mechanisms: Internal to Foundation to NIH/NSF
- Be fearless getting feedback at all levels
- Its really a marketing problem (we all have good ideas!)
- Inside and outside readers, especially for SA page

Part 3: Grants review pearls

- Who is reviewing your grant? And where are they reading it?
- Reviewers are tired overworked people!
- Summary/abstract matters. A lot.
- Reviewers hate internal inconsistencies- don't make it easy for them to criticize your grant

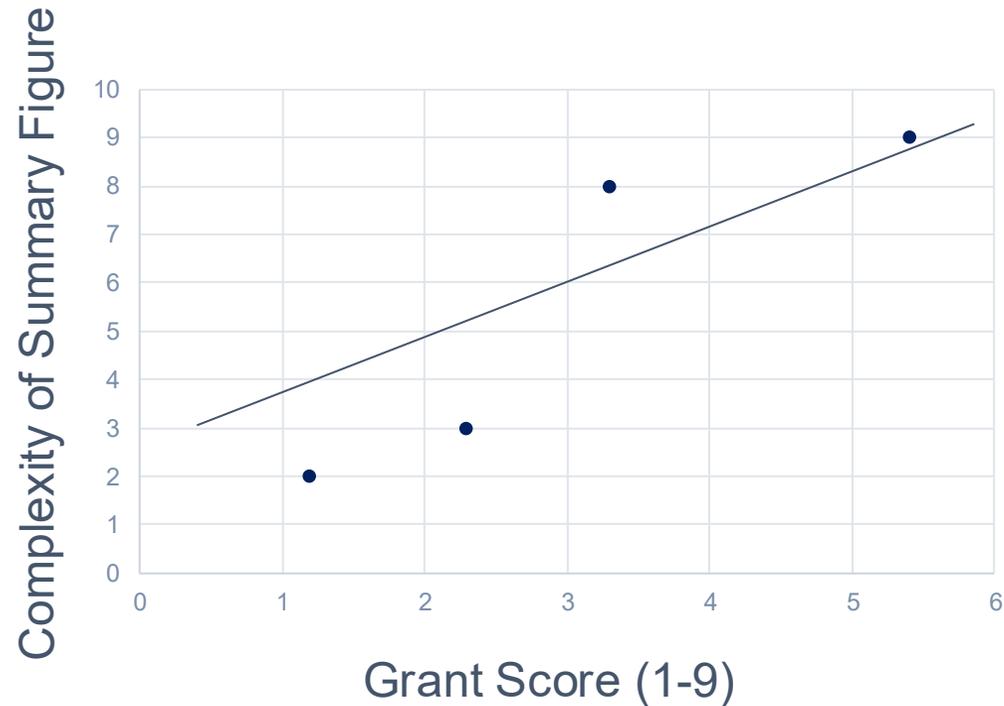
Part 3: Grantsmanship pearls

- At the end of the day the burden of clarity is on the applicant !



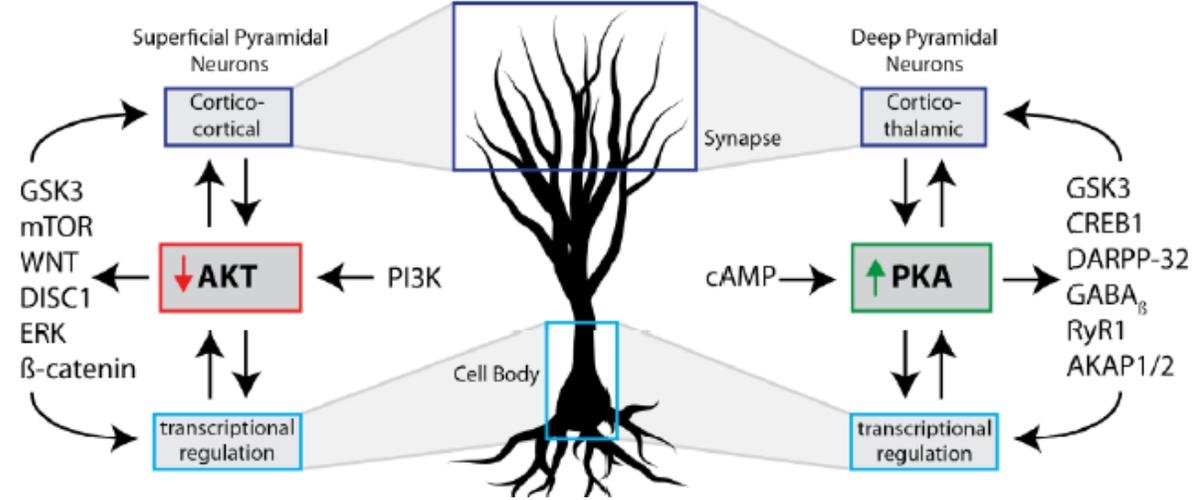
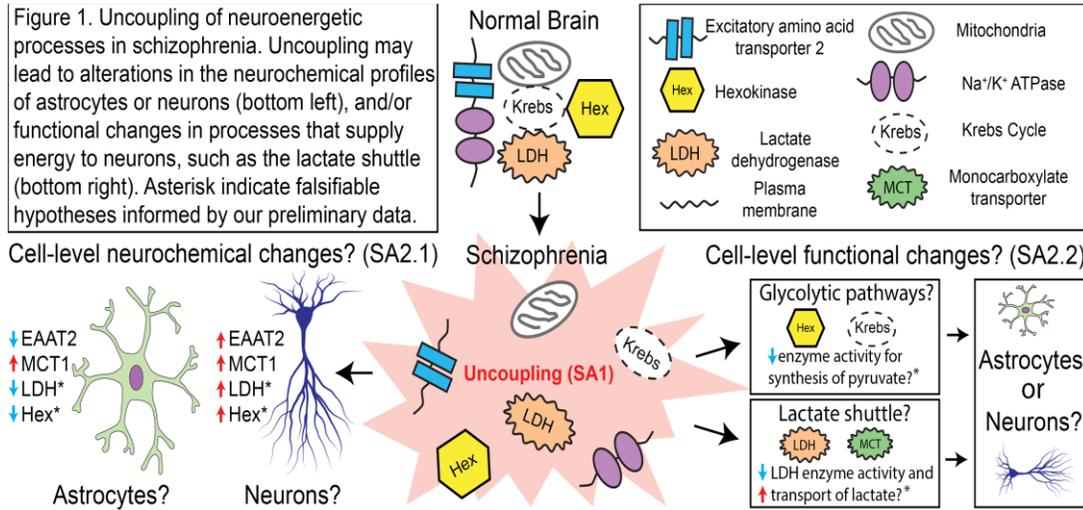
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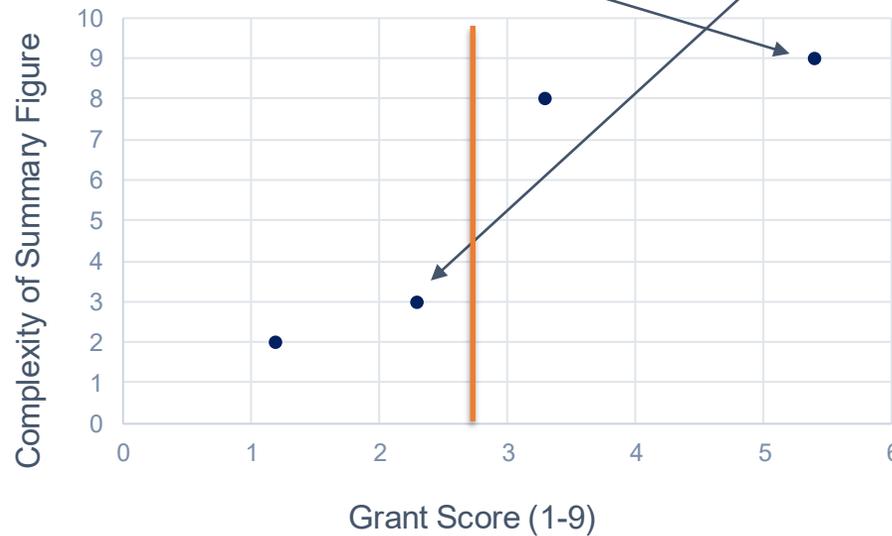
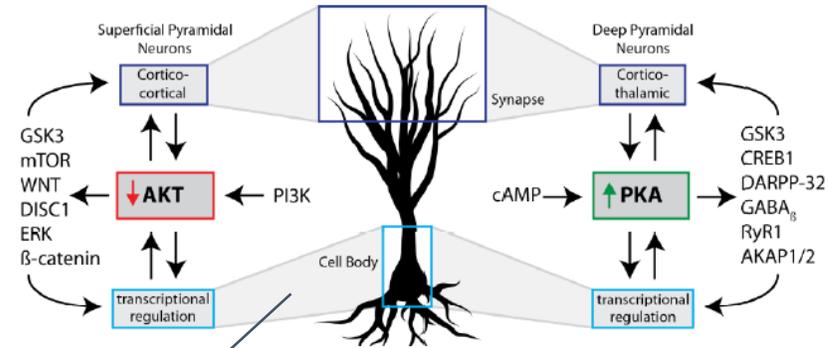
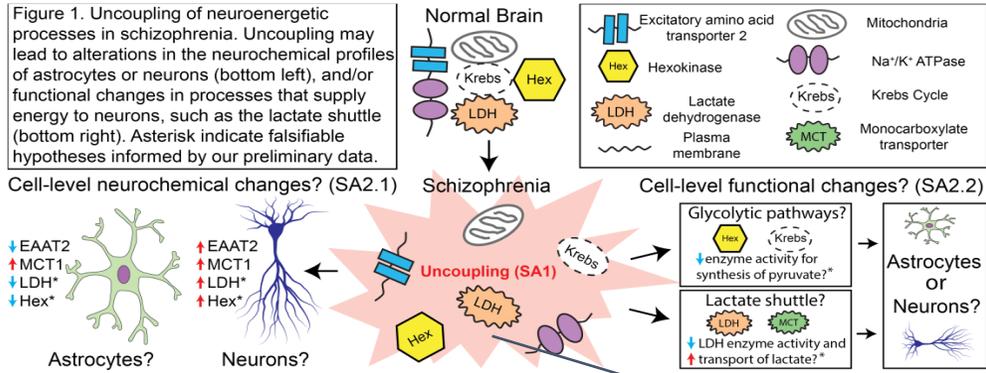
Part 3: Pop Quiz-Which grant got funded?

Figure 1. Uncoupling of neuroenergetic processes in schizophrenia. Uncoupling may lead to alterations in the neurochemical profiles of astrocytes or neurons (bottom left), and/or functional changes in processes that supply energy to neurons, such as the lactate shuttle (bottom right). Asterisk indicate falsifiable hypotheses informed by our preliminary data.



Part 3: Pop Quiz-Which grant got funded?

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Conclusions



The winding road to Hana, Maui.

