Advice on Rigor and Reproducibility in NIH Grants

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Significance
• Include bold headings of paragraphs with titles such as:
  o "Rigor of work demonstrating the importance of..."
  o "Rigor of data indicating that..."
  o "Rigor of work highlighting the importance of..."
• Focus on key data that must be solid for the proposed work to go forward.
• Consider adding a figure or two if they are essential to making your case to the reviewers, especially if this point was criticized in a previous submission.
• Consider adding a newly published figure if it’s essential for the foundation of the work.
• Point out gaps in knowledge that you will fill.
• Try to keep this section to ~1.5 pages.

Approach
• Sprinkle comments such as these (with formatting for emphasis) throughout:
  o "To ensure rigor and reproducibility, we will..."
  o "To rigorously test the hypothesis that..., we will..."
• Can also include a general section such as this:
  o Rigor and Reproducibility: As specified for each experiment, we will use appropriate numbers of animals or human samples for all experiments, investigators will be blinded to treatment groups, and a statistician (first last, PhD) has worked with us on designing the experiments and will guide our data analyses.
• Provide sample sizes for all experiments, including animal experiments.
• Provide justification for the sample size (a priori power analysis or indication of the effect size you’ll be able to detect).
• Include a solid "anticipated outcomes, potential challenges, and alternative approaches" section for each aim.
• Provide a strong statistical analysis section. If the analysis is unusual, go into more detail.
• Have a statistician read the grant and help with analysis section, and name that person on the grant.
• Sex as a biological variable: include this as a section heading even if the work is clearly only in one sex!
Review comments you do NOT want:

- There are gaps in clarity regarding the scientific premise underlying the proposed work that negatively impact enthusiasm.
- Despite overall enthusiasm for the line of investigation there are some gaps in presentation and analysis, particularly of the preliminary data in Figure 1 that are fundamental to the premise.
- After many cycles the evidence that XXX play a significant role in YYY remains to be provided.
- Sex as a biological variable was not mentioned.
- The application seems to suffer from extrapolation of literature in other XXX to the bench prior to ascertaining whether the experiments are biologically and physiologically relevant in the human YYY.
- There are limitations in the study design and the rigor of citing references that support the hypothesis.

Review comments you do want:

- Outstanding rigor and attention to power calculations in mice and human samples to detect statistically significant differences.
- Replicate experiments are proposed to increase rigor. Multiple complementary approaches are proposed.
- Power calculations and statistical analysis methods are stated, also increasing rigor.
- Reviewers noted the rigor of the prior research was built upon compelling preliminary data and numerous publications.
- Reviewers lauded the comprehensive and rigorously designed research plan.
- The development of the aims follows a solid rationale and are supported by strong preliminary data and recent publications from this laboratory.
- The scientific rigor of prior work is strong and justifies a new model...
- A strong case is made for the proposed model that....
- The rationale was well elaborated, and experiments were rigorously and logically designed, with necessary replicates, enough details of methodologies, and well-thought-out pitfalls, alternative strategy and data analysis plan.