COMMONLY HEARD COMMENTS AT STUDY SECTION MEETINGS

**SIGNIFICANCE:** Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effects of these studies on the concepts or methods that drive this field?

This will have a huge impact and fill a big gap in the field. The potential benefit of new targets for understanding and treating these diseases is enormous. This is extremely important work that few people are doing but that needs to be done. Why didn’t I think of this? Even if all the experiments work, no one will care or use these data. The results will be only incremental extensions of what is already known. The results will generate very limited interest and not be applicable to other systems/organisms. The prior success in other laboratories diminishes the significance of this effort.

**APPROACH:** Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

This grant application was a pleasure to read because the PI considered the possible results, their interpretation, the potential weaknesses of the approach, and other independent methods to test the hypothesis. Well thought-out and well written. The PI takes a highly mechanistic approach toward analyzing these reactions, thereby providing a framework upon which future discoveries and applications will emerge. Proof of principle has already been demonstrated. The experiments proposed are clearly presented, logical, and demonstrate considerable creativity. These experiments do not directly or appropriately test the hypothesis. The experiments are hard to follow. More preliminary data showing the feasibility of the approach would improve this aim. It is not clear what new insight will be gained about possible mechanisms. The “Approach” Section reads like a list of methods with too many irrelevant details. The results will be indirect or descriptive. There is an over-reliance on a single method. This aim does not fit in with the other aims. There are major concerns that the aims will not be accomplished using this approach. This proposal deals with very complex, interdependent systems. Thus, while the application was insightful, the approaches are frequently tedious and difficult to follow. The proposal is strong on theory and speculation, but somewhat less impressive on supporting evidence. This application is overly ambitious, with too many experiments for the proposed project period. The PI should have included a stronger rationale for these experiments. The PI does not indicate how data gained from these experiments would be interpreted. These studies are not worth the time relative to the amount of information they will produce.
**INNOVATION:** Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

The PI will develop new approaches to answer previously unanswerable questions. This is a novel mechanism that has the potential to explain previously perplexing results. This is a crazy idea that just might work. These new or modified methods will have wide application and impact. Exceptional opportunities for innovation characterize a well-organized and polished presentation. The methods are standard, but the questions asked are novel and the results will have wide impact. The results are derivative and would corroborate what is already known. These questions and approaches have been asked and used by other laboratories.

**INVESTIGATOR:** Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

The PI has a strong record of research productivity in the field. Careful, rigorous, exciting research is a hallmark of this investigator. The recipient of a CAREER Award from the NSF, this investigator has supervised 10 undergraduates in the last three years and should be an excellent mentor. The collaborators have had a longstanding research relationship with the PI. The expertise of the collaborators is complementary to that of the PI. Productivity has been very low in the past several years and there is no indication that this will change. The investigator/collaborator does not have the expertise required for the proposed research. The PI seems to lack the background, experience and perspective required to succeed on this project. The PI’s postdoctoral experience would presumably prepare him to conduct the proposed studies; however, he lists only one publication as an independent PI in four years, and so it is difficult to assess his potential. There are no letters from the listed collaborators. There are letters but little information about the collaborators’ roles. The collaborator is very busy so it is not clear what the commitment is to the proposed research.

**ENVIRONMENT:** Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

The institution has provided all the resources necessary for the PI to succeed. The PI’s limited expertise is balanced by the availability of the institution’s resource center and its director. Institutional support is provided through a reduced teaching load for the PI and through equipment purchase. Resources at the home institution are limited, but the PI has arranged to use facilities at other institutions and at a nearby company. The past record of good student interest in research and the availability of qualified collaborators bodes well for the success of this AREA grant application. The institution has an exceptional record of educating students going on to Ph.D. or M.D. degrees. The PI has limited access to the required equipment so there are concerns about potential productivity. The existing computer is not suitable to run up-to-date programs and is too slow to compute the proposed structures. The contribution of institutional support is extremely vague and should be clarified. The PI has not taken advantage of potential collaborators available in the same institution. The research environment does not seem to be very supportive.