F30/F31/F32/F33 Review

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visit http://grants.nih.gov/grants/peer/critiques/f.htm.

Application #: 1F30HL123456-01

Applicant: Doe, John

OVERALL IMPACT

Reviewers will provide an overall impact score 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 *Write a paragraph summarizing the factors that informed your Overall Impact score.*
This proposal is from an applicant who has shown perseverance and motivation. His academic performance is exemplary in spite of not having a significant prior research experience. The proposed research plan will address the regulation of skeletal muscle metabolism as a result of moderate exercise. The candidate is specifically interested in unraveling the role of dysfunctional fatty acid (FA) metabolism in the development of metabolic pathologies such as obesity, insulin resistance, and cardiovascular diseases; a highly significant study in light of the preponderance of the latter conditions. The mentors are productive with adequate funding to cover the entire requested fellowship period. The amount of data already generated by the applicant is likely to result in high impact publications. That said, several weaknesses have been noted, which detract somewhat from what could have been an outstanding training opportunity to gain cutting-edge research skills, hence dampening my overall enthusiasm. These include **l**ack of expertise in Exercise Physiology and a training plan that does not address the specific needs of this applicant in terms of coursework in molecular biology and developmental cardiology. The research plan with too many biomarkers to determine is deemed overambitious for the proposed two years of training. The proposed animal model for myocardial infarction is questionable and weakens the proposal. Other issues relate to lack of consideration of data analyses, and limited discussion of alternatives in a research plan suffering from interdependent aims.

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

- The scholastic performance of the candidate has improved from many Cs in his undergrad years to straight As in recent years.
- The clinical background of this applicant is adequate for this type of project. This provides assurance that the candidate will be directly involved in generating most of the expected data in this large cohort of patients.
- The letters of recommendations speak highly of his motivation, excellent thinking skills, and strong commitment and enthusiasm to starting the proposed project.

Weaknesses

- The candidate has no prior research experience; however, I do not see this as a significant weakness, since he has just finished his residency.
- The candidate did not state clearly his career goals. These can only be deduced by reading the three letters of reference.

2. Sponsors, Collaborators, and Consultants

Strengths

- The sponsor has an outstanding track record in mentoring young scientists.
- The laboratory is productive with an average of three publications a year.
- The fact that there are 5 post-docs and 2 Assistant Professors, will allow the applicant to have daily interactions with knowledgeable scientists.

Weaknesses

- The sponsor should avoid statements such as the one made: “I will recruit the applicant once he receives this fellowship”. I see this rather as a total lack of commitment from the part of the sponsor.
- Inclusion of an expert in exercise physiologist in the mentoring team is strongly recommended to strengthen the sponsoring team available to the applicant. The sponsor and co-sponsors are cardiovascular surgeons who are not familiar with the intricacies involved with exercise physiology. This can be easily deduced from failure to include the 3-rest timeframes required with this type of exercise. This is even more important given that 50% of the subject population is over 69 years old.

3. Research Training Plan

Strengths

- The result is a significantly improved, much better organized and written application that is likely to generate new and clinically useful results.
- The rationale and background for this work is well described and the preliminary findings support the aims.
- The inclusion of myocardial tissue sampling for assessment of remodeling and heart failure is an important addition.

Weaknesses

- The proposal would have been strengthened by including assessment of stem cell incorporation into the heart as described in reference 2 by the co-sponsor. I assume this will be done.
- Little consideration has been given to statistical methods, and discussion of outcomes and alternatives is rather limited, especially in light of the obvious interdependency of aims. What if aim 1 doesn’t work?
- Page. 18. Myocardial oxygen consumption is the product of coronary blood flow and the AV difference in oxygen content. This product is not divided by the heart rate or multiplied by hemoglobin content as written.

4. Training Potential

Strengths

- There is no doubt that the applicant will learn many new techniques because of his relative limited prior research experience.

Weaknesses

- The application proposes a lot of molecular approaches of which the applicant is unfamiliar with based on the scholastic history he provided. The sponsor could have proposed some coursework in molecular biology, and in cardiovascular development. Inclusion of these courses may help the applicant expand his critical thinking skills while performing the proposed experiments.

5. Institutional Environment & Commitment to Training

Strengths

- The scientific environment is further strengthened by the almost daily scientific seminars that this institution's scientists are accustomed with. The applicant will have ample choice to attend pertinent seminars as suggested in the sponsor's training plan.

Weaknesses

- I do not see how the applicant will drive 35 miles daily from the sponsor's lab located in the main campus to the hospital to acquire the radiographs. It would have been better to perform the exercise tests on patients at the co-sponsor's laboratory which is located in the hospital to save the hassle.

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**.

— A response for Inclusion of Women, Minorities and Children **is required** for Human Subjects Research Applications.

Protections for Human Subjects

Acceptable Risks and Adequate Protections

Comments (Required Unless Not Applicable):

- There are only minimal and acceptable risks associated with the study, mainly as blood draws. The candidate provides adequate protection plans to counter any mishaps with this or with the exercise experiments.

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Not Applicable (No Clinical Trials)

Comments (Required Unless Not Applicable):

-

Inclusion of Women, Minorities and Children Applicable Only for Human Subjects Research
G1A - Both Genders, Acceptable M1A - Minority and Non-minority, Acceptable C3A - No Children Included, Acceptable Comments (Required Unless Not Applicable): • Children have been appropriately excluded from the study. This is justified by the nature of the study addressing myocardial infarct which usually targets older adults.

Vertebrate Animals
Acceptable Comments (Required Unless Not Applicable): • The candidate proposes to use the Meta-Mu rat strain developed in Australian lab. There are no concerns with animal welfare. The five points are adequately addressed. The candidate, however, should have provided justification of numbers under this section and not by simply referring the reviewer to the research plan. I strongly suggest that the five points to be addressed as five and not as seven. Additionally, conventional headings (titles) have not been used, leaving the reviewer to guesses.

Biohazards
Acceptable Comments (Required Unless Not Applicable): • No risks to the staff, and no concerns noted with any of the proposed reagents, vectors, human tissues (blood), or physical procedures (i.e. chest radiographies).

Resubmission
Comments (if applicable): • The applicant has made a serious effort to address issues raised in the previous critique. The result is a much-improved application that will be a strong training vehicle to put the applicant on track to achieving his career goals of becoming an independent academic surgeon.

Renewal
Comments (if 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.

Training in the Responsible Conduct of Research
Unacceptable Comments on Format (Required): • The applicant states that he will train in RCR by daily interactions with the mentor, discussions during lab meetings, and by taking the online IACUC training. The proposed plan does not ensure sufficient formal instruction in RCR. Comments on Subject Matter (Required): • More formal coursework should be taken and which topics should address misconduct in science and other ethical issues, in addition to experimenting with human subjects training, grant writing, authorship, etc. I am personnally aware that the applicant's institution provides such a course. It seems that neither the sponsors or applicant are aware of the existence of the "Survival Skills of a Scientist" course. This course initially developed by Dr Ziegler, is formal, spans over 15 sessions (weeks), and addresses all facets of RCR. Comments on Faculty Participation (Required): • The applicant does not provide any information about faculty participation, except a general statement about discussions during lab meetings. Comments on Duration (Required): • Applicant did not indicate the length of RCR instruction. Comments on Frequency (Required): • As proposed, the applicant meets the frequency requirement for receiving RCR instruction during his current career stage.

Applications from Foreign Organizations
Not Applicable Comments (Required Unless Not Applicable): •

Select Agents
Not Applicable (No Select Agents) Comments (Required Unless Not Applicable): •

Resource Sharing Plans
Not Applicable (No Relevant Resources)

Comments (Required):
•

Budget and Period of Support
Recommend as Requested Recommended budget modifications or possible overlap identified: • It will be challenging for the applicant to recruit 168 patients, performs the exercise test, and determines the 18 proposed biomarkers for each of the patients. The requested two years of fellowship are not enough to complete all of the proposed work. I suggest that the applicant drops the rather weak experiments involving the rat model (to be performed in Australia with no rationale or convincing justification). He should rather focus on the human part of the experimental plan. This should even add some focus to this overambitious plan.

ADDITIONAL COMMENTS TO APPLICANT

Reviewers may provide guidance to the applicant or recommend against resubmission without fundamental revision.

Additional Comments to Applicant (Optional)
• The applicant should drop the rat experiments to bring the project to a more manageable level.

Example posted 8/30/2010