RSNA R&E Foundation
Grant Application Review Form

Application ID: ---
Name: ---
Title: Peroxisome Proliferator-activated Receptor-gamma (PPAR-gamma) Agonists Combined with Radiotherapy for the Treatment of Cachexia-inducing Non-small Cell Lung Cancers
Institution: ---
Department: ---

Overall Impact

Overall Impact (rate 1-9):
After considering all of the scored review criteria, briefly summarize the significant strengths and weaknesses of the application and state the likelihood of the project to exert a sustained powerful influence on the field.

Overall Impact: 7

Strengths:
• This research area linking cachexia and response to treatment appears to be quite novel.
• Strength of this application lies in the experience and dedication of the applicant

Weaknesses:
• The project is overambitious, with specific aims which are not clearly defined. There is no justification of the choice of experimental models to simulate the clinical situation.
• The research environment is not well-described.
• The mentoring plan, though adequate would be improved by the addition of a radiation biologist familiar with the cellular studies and the study of tumor growth delay following irradiation.

Potential Impact:
• Unless it is shown that TZDs might have a significant role in improving the response of lung cancers to radiotherapy, this project is likely to have a low impact.

Scored Review Criteria
Scored individually and considered in overall impact/priority score

Research Plan (rate 1-9)
Evaluate the proposed research project as suitable for a faculty member to obtain preliminary data with the anticipation of a future submission for additional funding from corporations, foundations or governmental agencies. If the research is part of a larger effort in an established lab, is the project for which the applicant is responsible clearly defined? An evaluation should include, but is not limited to the following criteria:

Significance and Innovation: Greater emphasis should be placed on the significance, innovation and impact of the proposed research effort compared to a resident or fellow grant. Does the research address an important and relevant problem in the radiologic sciences? What is the likely impact on clinical care or advancing radiologic science if successful? Is the research to be considered innovative? What is the likelihood for future funding if successful?

Approach: Is the hypothesis clear and well developed? Are the experiments well designed and appropriate to test the hypothesis? Is the proposed statistical analysis of the data appropriate for the study design? Is there a reasonable chance of completion within the time frame of the grant? Is the budget realistic for the research proposed? Proposals that are well beyond the experience of the faculty, and cannot be completed in the timeline of the proposal and grant period, should be discouraged. Is there a suitable plan for the protection of human subjects as well as does the investigator address issues related to inclusion based on gender, minorities and children?
Research Plan: 8

Strengths:

- The idea behind the project is original.
- The project aims ultimately to address a clinical issue, namely the poorer response to therapy in lung cancer patients suffering from cachexia.

Weaknesses:

- The project appears to be overambitious.
- The Specific Aims are not clearly described.
- Aim 2 appears to be dependent on a positive outcome from Aim 1. It is not clear from the description precisely what the in vitro studies are offering, especially since preliminary data in vivo are already being shown so the models must be available for use.
- In the animal models, the tumors are apparently growing in the flanks and not the lungs, which makes application of data to predicting lung-tumor response suspect.
- It is a big leap from in vitro models and animal models to human lung cancer. Though weight loss has been correlated with a poorer response to therapy, it is not clear if this also applies to clinical radiotherapy, and mouse may not predict human in this area. The principal hypothesis is speculative.
- It is not clear why a drug used to treat diabetes, causing blood sugars to decrease, should be better than other anti-inflammatory agents, if this is being proposed as the rationale for their use in lung cancer therapy.
- Preliminary data indicating a possible effect of TZDs on radiation response would be supportive.
- The following sentence provides an example of the lack of clarity in the proposed radiation studies. *We hypothesize that treating with radiotherapy at this point would help to potentiate further tumor inhibition and potential cell death.*
- A rewrite of the experimental methods associated with both aims would benefit from consultation with a radiation biologist familiar with these studies.
- Additionally, the system for scoring cachexia is poorly described. Radiation sensitization not adequately evaluated.
- Time course: optimistic for the cell biology studies
- The proposed drug and radiation interaction studies are difficult to characterize in any useful way'
- Possible confounding events and effects as well as back-up plans are not discussed.

Applicant and Advisors (rate 1-9)

Evaluate the suitability of the applicant as it relates to the proposed research. Will this experience enhance the applicant's investigative or educational skills? Will the experience increase the likelihood of establishing an independent research focus? What is the likelihood that the research will be suitable for future funding upon completion of this grant cycle? Is the time commitment realistic? Has the applicant sought out suitable experienced advisors that can help them through the process? Does the scientific advisor have background knowledge and experience related to the proposed project, with evidence of ability and commitment to mentoring.

Applicant and Advisors: 4

Strengths:

- The applicant is an MD, PhD with lab experience.
- Applicant will devote 90% of a 1 year research rotation to the project.
- The scientific advisor is an MD, PhD with his own lab.

Weaknesses:

- The Scientific Advisor is an assistant professor and appears to be in early career and therefore with less experience in mentoring residents.
Facilities (rate 1-9)
Evaluate the commitment of the institution, the department and individual research labs, if applicable, to provide adequate support for the applicant. Is appropriate space and equipment available? Are the support faculties such as computer services and statistical assistance adequate?

Facilities: 3

Strengths: Outstanding facilities and support should in principle be accessible at this prestigious institution.

Weaknesses: It is not clear exactly what facilities and support will be available for this project, not well described. Biostatistics support is likely available though not delineated.

Additional Comments
Add any additional comments you may have for the reviewers and/or comments or advice you may have for the applicant. Reviewers may recommend against resubmission without fundamental revision.

Proposal is well thought out. I would question the time commitment of the resident and the ability of the department to support the project (although the latter appears it will). Is this a year of research?