

Pennsylvania Department of Health Final Performance Summary Report Formula Grants

Overview of the Health Research Project Performance Review Process and Criteria

An applicant that receives a health research grant under Tobacco Settlement Act / Act 77 of 2001, Chapter 9, is subject to a performance review by the Department of Health upon completion of the research project. The performance review is based on requirements specified by Act 77 and criteria developed by the Department in consultation with the Health Research Advisory Committee.

As part of the performance review process, each research project contained in a grant is reviewed by at least three experts who are physicians, scientists or researchers. Reviewers are from the same or similar discipline as the research grant/project under review and are not from Pennsylvania. Reviewers use the applicant's proposed research plan (strategic plan), the annual progress report and final progress reports to conduct the review. A grant that receives an unfavorable performance review by the Department may be subject to a reduction in funding or become ineligible for health research funding in the future. The overall grant evaluation rating is based on the ratings for the individual research projects contained in the grant.

This performance review report contains the outcome of the review for the grant as a whole (outstanding, favorable, or unfavorable), strengths and weaknesses of each research project, as well as recommendations for future improvement.

The following criteria were applied to information submitted by research grant recipients:

- **Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?**
 - Did the project meet the stated objectives?
 - Were the research design and methods adequate in light of the project objectives?
 - Consider these questions about data and empirical results: Were the data developed sufficiently to answer the research questions posed? Were the data developed in line with the original research protocol?
 - If changes were made to the research protocol, was an explanation given, and, if so, is it reasonable?
 - Consider (only for clinical research projects) the extent of laboratory and clinical activities initiated and completed and the number of subjects relative to the target goal.
 - Were sufficient data and information provided to indicate or support the fact that the project met its objectives or made acceptable progress?
 - Were the data and information provided applicable to the project objectives listed in the strategic research plan?

- **Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?**
 - What is the significance of this project for improving health?
 - Consider the value of the research completed towards eventual improvement in health outcomes.
 - Consider any changes in risk factors, services provided, incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of impact and effectiveness of the research being conducted.
 - Consider any major discoveries, new drugs and new approaches for prevention, diagnosis and treatment, which are attributable to the completed research project.
 - What are the future plans for this research project?

- **Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?**
 - If leveraging of funds were expected, did these materialize?
 - Are the researchers planning to apply for additional funding in the future to continue or expand the research?

- **Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted/filed?**
 - If any of the above listed were expected, did these materialize?
 - Are the researchers planning to submit articles to peer-reviewed publications, file for any licenses, or patents or begin any commercial development opportunities in the future?
 - Consider the number/quality of each.

- **Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?**
 - Were there improvements made to infrastructure?
 - Were any new investigators added or were any researchers brought into the institution to help carry out this research?
 - Were funds used to pay for research performed by pre- or post-doctoral students?

- **Criterion 6 - Did the project lead to collaboration with research partners outside the institution, or new involvement with the community?**
 - Are the researchers planning to begin any collaborations as a result of the research?
 - For clinical research only: consider the number of hospitals and health care professionals involved and the extent of penetration of the studies throughout the region or the Commonwealth.

Overall Evaluation Rating

An overall evaluation rating is assigned to each research project. The rating reflects the overall progress the project attained in meeting the stated goals and objectives. The rating is based on a scale of 1–3, with 1 being the highest. An average rating is obtained from all the reviews (minimum of 3) of each project and is the basis for the determination of the final overall rating for each project as follows:

1.00 – 1.33 = *Outstanding*

1.34 – 2.66 = *Favorable*

2.67 – 3.00 = *Unfavorable*

The grant level rating is an average rating from all projects as above. The numerical rating appears in parentheses for the grant and each project in the ***Overall Grant Performance Review Rating*** section of the report.

Overall Grant Performance Review Rating

Grant Rating: Favorable (2.00)

Project Rating:

| Project | Title | Average Score |
|----------------|---|----------------------|
| 1168101 | Electrospun Scaffold Substrata for Culture of Osteoprogenitor Cells | Favorable (2.00) |

Project Number: 1168101
Project Title: Electrospun Scaffold Substrata for Culture of Osteoprogenitor Cells
Investigator: Koepsel, Richard

Section A. Project Evaluation Criteria

Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?

STRENGTHS AND WEAKNESSES

Reviewer 1:

The investigators found that the original objective proved more difficult than anticipated. During the course of the study, it was discovered that the electrospun collagen/HA scaffolds dissolved in culture media over a very short time. Upon confirming that solubility of the scaffold was an issue, the investigators changed their strategy and incorporated a crosslinking step into their protocol. While this was in process, another group published a paper which largely duplicated what they were trying to accomplish.

The investigators then deviated from the original aim for the project and focused on developing a polymer which would be constructed so that it would attach to cells on one end, have a spacer in the middle, and on the opposite end there would be a bone binding region that conceptually would be based on bisphosphonate chemistry. This was proposed as a mechanism for attaching cells to the electrospun collagen/HA scaffold. The remainder of the study was devoted to synthesizing this polymer and testing its ability to bind to mesenchymal stem cells (MSC) and its effect on MSC behavior (in particular, differentiation into osteoblasts and adipocytes).

The investigators made a reasonable effort to accommodate the unexpected event(s) and made good progress toward their overall aim of 1) developing a unique collagen/HA scaffold using electrospinning and 2) developing a novel polymer for binding cells to the collagen/HA scaffold. The final report fails to describe the methods and results in adequate detail.

Reviewer 2:

In general, the objective of this project was to electrospin scaffold substrata for culture of osteoprogenitor cells. In the year that the project was funded, the Principal Investigator did attempt to fabricate scaffolds through electrospinning. Additionally, in the first six funded months, the Principal Investigator also attempted to seed osteoprogenitor cells on the electrospun scaffolds. In the evaluation of the scaffolds produced, the Principal Investigator discovered that the structural integrity of the electrospun scaffolds was not sufficient for cell attachment. As such, changes in the research protocol was expressed in the last progress report, with the PI attempting to focus their efforts on the production and analyses of the polymer coated cells before re-focusing on the electrospun scaffolds. Data produced on the revised protocol indicated that the PI had successfully coated cells with the polymer.

Reviewer 3:

Overall, the project met the original goals well. The team has made a significant contribution during the year. Although the initial plan with hydroxyapatite doping into collagen for nanofiber production did not lead to the original expectation, they still successfully obtained nanofibers. If they add materials into the collagen mixture to enhance the physical crosslinking and chemical crosslinking, some new discovery may be possible. In addition, they developed a new cell-painting material which may improve the osteo-differentiation. This novel cell painting concept is very interesting. And hopefully, they will publish work in this area soon. The research design and methods used are sound, although not thoroughly explored due to the time limit (only 1 year). The data obtained are appropriate for answering the questions. Some data were obtained based on original research protocols. Due to some difficulties in maintaining the electrospun structures, data are not desirable so far. But they are on the right track and just need more time and more explorations in that direction. In addition, they made reasonable changes to their protocol with good explanations and advanced the field greatly with a new cell painting concept. They have met the goal of the project well, and the data are exceptional based on the funding level and time used. The progress is outstanding. The data provided is applicable to the project objectives listed in the strategic research plan.

The major weakness is the exploration on maintaining nanofiber structure is not sufficient, and some details in removing the solvents are not well studied.

Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?

STRENGTHS AND WEAKNESSES

Reviewer 1:

The likely beneficial impact of this project is relatively small. There are no anticipated publications or patents resulting from this project. During the funding period (one year; approximately \$8000), one NIH grant application was submitted.

Since the budget was quite modest, this level of impact is not a weakness.

Reviewer 2:

Large bone repair has always been an issue, since defects in large bone do not usually heal on their own. Autografts are usually a problem, especially when a large volume of bone is needed for the defect site. There is also a concern with allografts, especially with the transmission of diseases. The successful completion of this project would mean the elimination of allograft and autograft uses.

Reviewer 3:

They have made two major contributions. One is the doping bioceramics into collagen for composite nanofiber fabrication. Although, the results are not perfect yet, they are on the track to getting the composite nanofiber optimized. The other contribution is developing a new material that can be used to coat cells with tracing and osteo-promoting functions. The benefit from these two contributions well justified the dollars spent. Both contributions may benefit the

life science and healthcare in the long run, since both technologies may be used in tissue regeneration applications. These two technologies may be used to improve healthcare and reduce the complications. Both technologies developed here may be used for the treatment of bone diseases. They have planned to combine these two technologies for bone regeneration, which is plausible.

The only weakness is that the exploration is still quite immature. More in-depth research is needed.

Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?

STRENGTHS AND WEAKNESSES

Reviewer 1:

The investigator applied for one NIH grant, but does not intend to submit any other applications.

Reviewer 2:

Funds from the NIH were used as leverage. It was not indicated that additional funding in the future would be continued. There was also no indication that the research would be expanded in the future.

Reviewer 3:

They have submitted an R21 proposal to NIH. Although they have not obtained any funding support at the time of submitting the final report, their data in cell painting is very encouraging. With new funding in the future, they will be able to expand this research.

The only weakness is that they should focus on getting more data for a good publication to support new proposals.

Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted / filed?

STRENGTHS AND WEAKNESSES

Reviewer 1:

There were no publications, licenses, patents, etc., resulting from the project.

Reviewer 2:

No peer-reviewed publications, licenses, patents, or commercial development opportunities were indicated.

Reviewer 3:

Although there is no new publication or patent submitted yet at the time of final report, the data obtained are quite encouraging and may support a new publication and a new patent in the near future when more data are obtained.

The only weakness is that they need to focus on technology one-by-one and get the technologies matured one-by-one. Then submit patent and manuscripts.

Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?

STRENGTHS AND WEAKNESSES

Reviewer 1:

The project did not produce any tangible increase in quality or capacity for research at the grantee's institution. No pre- or post- doctoral students were supported by this grant. The only potential future enhancement will be if the submitted NIH application is funded.

Reviewer 2:

Other than providing training for a post-doctoral fellow and a technician, the project did not enhance the quality and capacity for research at the grantee's institution.

Reviewer 3:

The funds were used to support the PI's summer salary. And in the meantime, it allowed for the generation of new data in a new direction, which enhances the quality and capacity for research at the grantee's institution. The funds were not used to improve infrastructure, to hire new researchers, or to support post-doc or graduate students due to the limited funds available.

Criterion 6 - Did the project lead to collaboration with research partners outside of the institution or new involvement with the community?

STRENGTHS AND WEAKNESSES

Reviewer 1:

The investigators do not report any additional outside collaborations resulting from this project.

Reviewer 2:

No collaborations were indicated in the progress report as a result of the research.

Reviewer 3:

Due to the limitation on the dollar amount, this project did not lead to any new collaboration with research partners outside of UPMC.

Section B. Recommendations

SPECIFIC WEAKNESSES AND RECOMMENDATIONS

Reviewer 1:

I think the investigators did a good job of transitioning the project from producing the electrospun scaffold to synthesis of the cell attachment polymer. The results are intriguing.

What I identify as a significant weakness is the write-up of the results (see section 17 of the Final Report). The instructions call for a detailed report of the methods and findings. A report on how the electrospun scaffolds were prepared and characterized should be provided, in detail. Similarly, the production of the polymer for linking the cells to bone and its characterization using stem cells should be provided (doesn't MSC-12kD-PBP-F3-NHS, in Figure 3, bind better than the other versions of the polymer?). As one example, the isolation of the MSCs and their characterization is missing. A reference to the literature would be helpful. Lastly, the figure legends are woefully inadequate. In fact, legends for Figures 4-6 are completely missing. As this document will survive in perpetuity, the public who funded this project are deserving of a reasonable and complete report.

Reviewer 2:

1. The PI needs to state the number of formulations fabricated, since it is stated in the grant that mixtures of collagen type 1 and hydroxyapatite will be used for the fabrication. Since structural integrity of the composite scaffold is dependent on the filler-matrix ratio, it is not known if such ratios have been optimized.
2. In addition, the porosity of the scaffolds and the distribution of the hydroxyapatite need to be reported, especially when the criteria for the selection of the scaffolds for cell culture requires a porosity of greater than 5 microns. It is not known if these criteria were met prior to performing the cell culture.
3. Given that this project is leveraged with a NIH grant, the funds from this agency should still result in data that needs to be disseminated to fellow researchers and scientists. It is recommended that the PI should report these data in peer-reviewed conferences or journals that would partially acknowledge support from this agency, in addition to the NIH.

Reviewer 3:

1. It is suggested to explore different crosslinking technologies, including both chemical and physical crosslinking, to obtain stable nanofiber structure from collagen and hydrogapatites.
2. Expand the work on the cell painting concept, which may be a great direction in which to go.

Generic Recommendations for the Pittsburgh Tissue Engineering Initiative

Reviewer 2:

With the understanding that the results of this project did not turn out as expected as well as the budgetary constraints and the grant period, the outcome may have been more favorable if the grant period had been extended beyond a year to allow the PI to work out their experimental issues. As such, I am recommending that the institution focuses on projects that are beyond a 1-year period.

Reviewer 3:

With the limited amount of support, the PI made two major contributions in the area of bone tissue engineering. The outcome is great.

ADDITIONAL COMMENTS

Reviewer 2:

Although some progress was made in the grant with respect to its original objectives, some of the measurements stated were not reported. For example, the PI had indicated that he would be producing electrospun materials from mixtures of collagen type 1 and hydroxyapatite, but the report only indicated data from the collagen type 1 scaffold and one collagen-type 1-HA scaffold. It is not known as to how many formulations of collagen type 1 and hydroxyapatite were fabricated. The grant also indicated that porosity of the scaffolds as well as distribution of the HA would be reported, but this information is absent in the progress report.