Reviewer Comments

The Following is a compilation of comments provided by multiple reviewers following the panel's discussion and scoring of the application. All reviewers were asked to provide brief bullets on key strengths, concerns, or recommendations related to the proposal that CIRM compiled and edited for clarity.

Strengths

- A solid, integrated project to address the entire "ecosystem" or "biological environment" for regenerating cartilage---electro-spinning/ -spraying/ cellular constituents/ growth factors.
- The project is logically organized with a very aggressive timeline which should be implementable.

Concerns

- The potential immunogenic responses to the MSCs, despite the short-term sheep data, are concerning. Furthermore, in preparation for the pre-IND meeting, there will need to be much more specificity about the methodology within the protocol (i.e., dose of growth factors, duration of electrospraying, etc).
- The applicants claim “no evidence of cell migration out of electrospun scaffold in *in vivo* experiments”, but data is not shown (in addition, Fig 3 claims to show a 4-week time point but the image is of 3-week tissue).
- Figures 4-7 (there are two figure 6s), appear to support the use of cells to heal damaged tissue. These data are poorly described and the figures are not referenced in the text.
- It is not clear where the large animal work (sheep) will be performed.
- It is not clear who on the team has expertise in creating meniscal tears and working with the model system.
- The imaging center specifically says that it can do small animal imaging. No mention of large animal imaging. Unclear how sheep samples will be processed.
- The choice of cells is a major issue.
- There is a lack of experimental details.
- The proposal lacks novelty. Electrospinning and electrospraying has been used before.
- The proposal is poorly written. There are several grammatical errors in the proposal.