Is the rationale sound?	1	4	8
Is the proposal well planned and designed?	0	6	7
Is the proposal feasible?	2	2	9

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

- The proposal focuses on the treatment of melanoma.
- A strength of the proposal is the PIs recent work showing that CD47 is expressed at higher levels in metastatic melanoma cell lines and samples, and the preliminary data showing that blocking CD47 increases phagocytosis of these cell by macrophages.
- The resources at the institution are excellent.
- The use of the GMCSF and SCF modified NSG mouse for CD34+ transplantation is a good idea, and should help with the otherwise defect in myeloid function in standard NSG mice. The BLT mouse model is considered as an alternative.
- The PI provides careful consideration to the potential problems of using anti-CD47 treatments and gives alternative dosing treatments.

Concerns

- This proposal will examine the effects of blocking CD47 on human melanoma cells to treat metastatic outcomes using a humanized mouse model.
- The applicability to stem cells is limited to the use of human HSCs to develop a model to test CD47 cells. This may allow the interaction between macrophages and tumor cells, but it is unlikely that anti-tumor T cells will be present.
- Immuno-oncology is a crowded area.
- CD47 blocking antibodies are being studied by several companies.
- The investigator is relatively inexperienced in this field of research.
- The proposed work is focused on immune-therapeutic approaches, and not really aimed at understanding the cancer stem cell properties that lead to CD47 increased expression.
- The preliminary data showing a change in MDSC to macrophage ratio in anti-CD45 treated tumors are quite striking, and it is curious that the PI does not follow up on this finding.