Both allogeneic and syngeneic induced pluripotent stem cell (iPSC) vaccines decrease tumor growth and improve survival in a prophylactic mouse model of breast cancer

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Background: Extensive data on gene expression, metabolic state and glycosylation of cancer cells suggest that cancer represents a reversion of adult cells to an embryonic state and that induced pluripotent stem cells (iPSC) model this state. In contrast to cancer cells, iPSC have never undergone immunoediting and therefore present hundreds of oncofetal antigens in their native conformations. Previous studies have demonstrated the efficacy of syngeneic iPSC vaccination in a variety of cancer models. In this study, we administered vaccines comprising syngeneic or allogeneic iPSC together with the Toll-like receptor (TLR) 9 agonist CpG1826 (CpG) as an adjuvant and compared their immunogenicity and preclinical efficacy in a prophylactic mouse model of breast cancer.

Methods: FVB mice (n=10) received a course of 6 weekly injections with previously cryopreserved 10^7 irradiated (60Gy) allogeneic (C57BL/6) or syngeneic (FVB) iPSC admixed with 1nmol CpG, or CpG alone as control. After the 5th treatment, mice were injected with 5x10^5 DB7 syngeneic breast cancer cells s.c. Tumor growth and survival were monitored for 60 days post tumor injection. Mice were euthanized when tumor volume reached 2000 mm^3. IgG antibody binding to iPSC, syngeneic DB7 cells and other cancer cells from sera collected before the 5th treatment was studied by flow cytometry. T cell responses were evaluated by γ-interferon-ELISPOT and cytotoxicity assays.

Results: Both allogeneic and syngeneic iPSC+CpG vaccination significantly delayed tumor growth and increased survival in DB7 breast cancer mouse model as compared to CpG control. 70% of the mice injected with syngeneic and 60% of mice with allogeneic iPSC vaccine survived up to day 60 as compared to only 20% of CpG controls (p=0.0244, Mantel-Cox test) (figure 1). No statistically significant difference between allogeneic and syngeneic iPSC vaccination was detectable (p=0.6128). Similar results were obtained for the tumor growth. Serum IgG binding to DB7 cancer cells increased ~30-fold after allogeneic and syngeneic iPSC+CpG vaccination compared to CpG control. No significant difference in the IgG antibody response between syngeneic and allogeneic iPSC vaccines were observed (p=0.4743, One-way ANOVA).

Conclusions: Irradiated allogeneic and syngeneic iPSC admixed with TLR9 agonist CpG1826 induced similar antibody and T cell responses to iPSC, DB7 and other cancer cell lines. Allogeneic iPSC vaccine was as effective as syngeneic iPSC vaccine in delaying and decreasing tumor growth and in increasing survival in a prophylactic model of breast cancer. These results warrant further investigation of allogeneic iPSC vaccines in clinical trials for a variety of cancers.

Ethics Approval: The study was approved by Valley Bio Services’ Institutional Animal Care and Use Committee; approval number VBS1002.