#315 iPSC-derived CAR-iNKT cells targeting HER2 show prolonged tumor control and promote durable survival in a tumor xenograft model.

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Introduction

Invariant natural killer T (iNKT) cells are a rare subset of T lymphocytes that express an invariant TCR which recognizes glycolipids presented by the monomorphic MHC like molecule CD1d. iNKT cells can directly kill monomorphic MHC like molecule presenting cells and can also indirectly exert antitumor activity by promoting dendritic cell maturation, priming tumor-specific CD8+ T cells, and reprogramming pro-tumor myeloid cells. iNKT cells do not induce graft-versus-host disease and are a promising strategy for "off-the-shelf" cell therapy platform because of enhanced innate and adapted immunity.

Generation of CAR-iPS-iNKT cells

A schematic strategy to generate CAR-iPS-iNKT. B. Phenotypic analysis of iPSC-iNKT cells with or without gene editing (Unmodified) or HER2-CAR introduced iPSC-iNKT cells (HER2-CAR) by flow cytometry.

Conclusions

This study demonstrated that differentiated CAR-iPS-iNKT cells derived from CAR-iPSC showed potent anti-tumor effects and promoted survival in a tumor xenograft model. Results from in vitro analysis suggest that target-specific killing activity of HER2-CAR-iPS-iNKT cells was derived from increased secretion of Th1 and inflammatory cytokines and NK phenotype such as NKG2D for direct killing. These findings suggest that iPSC-derived CAR-iNKT cells would be a novel allogeneic cell therapy platform because of enhanced innate and adapted immunity.

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References

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