Driving ADP-A2M4 SPEAR Expression from an Endogenous Hematopoietic Lineage Promotor for “Off-the-Shelf” T-Cell Therapy for MAGE-A4+ Solid Tumors

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Introduction

‘Off-the-shelf’ T-cell therapy is now being adopted as an enabling therapeutic approach in the treatment of a range of cancer types. Therefore TLA (T-cell alloreactive) 4-1BB agonist (4-1BB+CD3) T-cells and SPEAR T-cells (Somatic Peptide Engaged Anti-Receptor) stand out as attractive candidates for application toward a broad range of solid tumors (including melanoma).

Objective

We present data based on a minimal editing strategy that drives the TCR allelic exclusion, which prevents erroneous mitigate the risk of graft versus host disease (GvHD). iT-cells up-regulate activation markers, including CD25 and specifically express the ADP-A2M4 SPEAR as measured by (melanoma-associated antigen A4) peptide (GVYDGREHTV).

Methods

Adaptimmune is currently developing an SPEP (Somatic Peptide-Engaged Promotor) in collaboration with the Endogenous Hematopoietic Lineage Promotor for production of SPEAR iT-cells with anticipated therapeutic

Figure 1. Generation of ADP-A2M4 SPEAR iT-cells from hiPSC clones

We present data based on a minimal editing strategy that driven by TCR allelic exclusion, which prevents erroneous mitigate the risk of graft versus host disease (GvHD). iT-cells up-regulate activation markers, including CD25 and specifically express the ADP-A2M4 SPEAR as measured by (melanoma-associated antigen A4) peptide (GVYDGREHTV).

Figure 2. Summary of the iT-cell differentiation protocol

Figure 3. Expression of ADP-A2M4 SPEAR in differentiation iT-cells

Figure 4. Generation of ADP-A2M4 SPEAR iT-cells from hiPSC clones

Reagents

- Adaptimmune, Abington, Oxfordshire, UK

Figure 5. Edited ADP-A2M4 iT-cells from parental PBMCs

Conclusions

The data presented here demonstrate that: SPEAR iT-cells can be rapidly expanded from WT ADAPi001 hiPSC clones, cells over-expressing the ADP-A2M4 SPEAR and have a strong pro-inflammatory phenotype.

Acknowledgements & Disclosures

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References