IL-7 and CCL19 Expression in Specific Peptide Enhanced Affinity Receptor T-cells Targeting MAGE-A4 Display Improved Survival and Ability to Induce Migration of Immune Cells

Introduction

- Specific peptide enhanced affinity receptor (SPEAR) T-cells are engineered with T-cell receptors (TCRs) designed to target tumor cells with specific antigens presented on their surface by human leukocyte antigen (HLA) molecules.
- In this study, we evaluated the biological efficacy of ADP-A2M4N7X19 by determining the functional effects of IL-7 and CCL19 on T-cell survival and proliferation.

Methods

T-cell Expansion as a Function of IL-7 Production

- ADP-A2M4, ADP-A2M4N7X19, and ADP-A2M4IL7 T-cells were stimulated with irradiated A375 (MAGE-A4 positive) cells.
- rhIL-7 and rhCCL19 were added to independent wells as a positive control.

IL-7 plays a role in stimulating proliferation and supporting the survival of T-cells, and CCL19 induces the migration of immune cells.

Tumor Exposure

- Supernatants were collected on Days 1, 7, 8, 14, 15, 21, 22, and 28, and cytokine levels (pg/mL) determined on supernatants (data not shown).
- Differences in cytokine production were assessed by a trans-well migration assay.

Figure 4

Conclusions

- Transduction of SPEAR T-cells with PRIME technology increases T-cell engraftment, functionality, and improves observed in vivo T-cell infiltration into the tumor, which is hypothesized to lead to improved anti-tumor activity in the clinic.

ADP-A2M7N19 T-cells need both antigen exposure and IL-7 signaling to survive, suggesting that increased T-cell activity will only occur in the presence of MAGE-A4 antigen.

Based on results presented here, a Phase 1 clinical trial will be initiated with ADP-A2M7N19 in multiple indications.

Acknowledgements and Disclosures

We thank Hodi-Immune Biotech for utilization of their PRIME technology. Writing assistance was provided by Gabrielle Kröller, MSc, PhD, of Exell Scientific Solutions, which was contracted and compensated by Adaptimmune for these services.

George R. Pope,1 Sebastian Laycock-van Spyk,1 Annette Pachnio,1 Katherine Adams,2 Vicki Jefferson,2 Neil Cartwright,1 Phillip Debnam,1 Jonathan D. Silk,2 Ciara Morris,1 Bryan Jackson,1 Karen Miller,1 Joseph Sanderson1

1Adaptimmune, Abington, Oxfordshire, UK; 2Adaptimmune, Abington, Oxfordshire, UK, at the time the study was conducted

References