Specific Peptide Enhanced Affinity Receptor (SPEAR) T-cells Targeting MAGE-A4

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**Objectives**

- Determine the frequency of MAGE-A4 expression in NSCLC, identify patients likely to benefit from SPEAR T-cell therapy, and establish the safety and efficacy of NSCLC T-cell assays.

**Methods**

- NSCLC selection: A panel of 534 resected NSCLC cases (stage I–IV) with histological diagnoses and clinicopathologic details was analyzed for MAGE-A4 expression.
- In vitro peptide processing and presentation: The peptides identified in tumor cell lines were overexpressed in tumor cell lines. The HLA-A2.1 peptide was used as a positive control.
- Alloreactivity testing: Alloreactivity was observed in antigen-negative cells expressing MAGE-A4.
- Potential peptide sequences that could be searched against TCR motifs were identified.
- Cell death: The Cytotoxicity of antigen-positive tumor lines by MAGE-A4 SPEAR T-cells was measured by time-lapse microscopy.

**Results**

- MAGE-A4 expression screening in the NSCLC cohort.
- TCR-transduced T-cells added as positive controls (T2).
- Percent survival of MAGE-A4+ T-cells in 3-D microtissues derived from MAGE-A4+ melanoma cell line A375, as determined by time-lapse imaging of T-cell donor 4.

**Conclusions**

- MAGE-A4 is a promising target for SPEAR T-cells.
- The peptides identified in this study are expected to improve the current repertoire of SPEAR T-cells.
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**Disclosure**

- All authors have declared no conflicts of interest for this study.
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**Reference**


**Figure 1.** NSCLC cohort clinicopathological details. Of the 534 resected NSCLC cases, the majority were either adenocarcinoma (8%) or squamous cell carcinoma (34%). Of the 534 resected NSCLC cases, the majority were either adenocarcinoma (8%) or squamous cell carcinoma (34%).

**Figure 2.** MAGE-A4 expression screening in the NSCLC cohort. MAGE-A4 expression was observed in 25% of all NSCLC cases, with higher expression observed in SCC (7%) than in adenocarcinoma (5%).

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**Figure 12.** MAGE-A4 expression screening in the NSCLC cohort. MAGE-A4 expression was observed in 25% of all NSCLC cases, with higher expression observed in SCC (7%) than in adenocarcinoma (5%).