Technology Overview

Cancer/testis antigens (CTAs) have been identified as promising immunotherapeutic targets due to their narrow expression profile in malignant tissues and testis. The MAGE family are CTAs expressed in many tumor types, and MAGE-A1 has been shown to drive tumorigenesis directly. Investigators at Fred Hutch led by Dr. Chapuis have identified and generated an engineered version of rare high affinity human donor-derived anti-MAGE-A1 TCRs. Preclinical validation of these MAGE-A1 TCRs displayed strong cytotoxicity towards MAGE-A1+ cell lines and activity in both CD4 and CD8 T cells. These TCRs are being validated and developed for rapid clinical translation.

Applications

∫ Immunotherapy target for tumors expressing MAGE-A1, including triple negative breast cancer (40-60%), non-small cell lung cancer (27-46%), multiple myeloma (10-26%), melanoma (16-51%), ovarian (15-54%), and colon (12-30%)

Advantages

∫ MAGE-A1 expression is strictly limited to testis and tumor tissue which minimizes likelihood of on target off tumor toxicities
∫ HLA-A2 restricted MAGE-A1 peptide is unique to MAGE-A1
∫ Avoids recognition of other MAGE family members

Market Overview

Several companies are developing clinical TCR programs targeting MAGE family members for multiple indications. To our knowledge, Dr. Chapuis has the only program pursuing MAGE-A1 as a clinical target. While CAR-T approaches have had success in liquid tumors, they have demonstrated limited efficacy in solid tumor settings and are limited to recognition of external antigens, which reduces the number of viable targets. In contrast, TCR-based T cell therapies have the potential to overcome many of these barriers and comprise 23% of the T cell immunotherapy pipeline.