Background Cancer Testis Antigens (CTAs) are highly expressed in multiple different tumor types, but silent in normal tissue, except the testis. This tumor-restricted expression pattern makes them an ideal target for adoptive T-cell therapy. Preliminary data supports the hypothesis that low tumor dynamics are associated with favorable outcomes of CD19 CAR T cell therapy.


P07.02 HIGH-AFFINITY TCRs SPECIFIC FOR CANCER TESTIS ANTIGENS AS A THERAPY FOR MULTIPLE MYELOMA AND SOLID TUMORS

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Background Cancer Testis Antigens (CTAs) are highly expressed in multiple different tumor types, but silent in normal tissue, except the testis. This tumor-restricted expression pattern makes them an ideal target for adoptive T-cell therapy. However, the responsiveness in clinical setting may be hampered because high-affinity T cells against self-antigens presented in the context of self-HLA are deleted in the thymus by negative selection. In this study, we aim to identify high-affinity T cell receptors (TCRs) specific for CTAs from the allogeneic-HLA repertoire.

Materials and Methods In this study, HLA class I binding peptides derived from different CTA genes were identified by HLA-peptide elution experiments and subsequent mass spectrometric analysis. From the identified peptides HLA tetramers were generated to isolate peptide specific CD8+ T cells from healthy allogeneic donors. Efficacy and safety of the TCRs was determined by various different stimulation assays. The most potent TCRs were sequenced, analyzed and transduced into peripheral CD8+ and CD4+ T cells to confirm CTA specific cytokine production and cytotoxicity.

Results MAGE and CTAG peptides were eluted from multiple myelomas, EBV-transformed lymphoblastic cells, acute myeloid leukemia and ovarian carcinomas. We selected TCRs recognizing 3 different MAGE-A1 peptides in the context of HLA-A*02:01, HLA-A*03:01 and HLA-B*07:02. Furthermore, we selected TCRs specific for MAGE-A3 in the context of HLA-B*35:01 and HLA-A*01:01; TCRs specific for MAGE-A9 in the context of HLA-A*01:01 and TCRs specific for CTAG1 in the context of HLA-A*02:01. The selected T-cell clones demonstrated efficient recognition of MAGE-A1, MAGE-A3 or CTAG1 positive multiple myeloma and solid tumor cell lines without detectable cross-reactivity.

Conclusions We identified multiple different TCRs from the allogeneic-HLA repertoire specific for CTA genes. These TCRs demonstrate efficient recognition and killing of CTA positive multiple myeloma and solid tumor cell lines and did not show any cross-reactivity. The peptides recognized by the TCRs are presented in different HLA alleles. Since, 71% of the world population contains one of these HLA-alleles, a large percentage suffering from a MAGE or CTAG positive tumor could potentially be treated with the identified TCRs by TCR-gene therapy.


P08 Combination Therapy

P08.01 LOW-DOSE CHECKPOINT INHIBITORS WITH HYPERTHERMIA AND IL-2 ARE SAFE AND EFFECTIVE IN STAGE IV CANCER WITH UNFAVORABLE IMMUNOLOGICAL PROFILE (MSILOW, PD-L1 UNDER 1%, TMBLOW) – A SINGLE-INSTITUTION EXPERIENCE FROM 2015 TO 2020

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Background Close to 10 million cancer deaths occurred worldwide in 2017 primarily due to stage IV disease, the management of which is still palliative by intent. Differently from melanoma and non-small cell lung cancer, where the use of ground-breaking immune checkpoint inhibitors (ICI) results in a relatively high efficacy, the response rate in many other stage IV tumors, such as gastrointestinal cancers, breast cancers, sarcomas, and part of genitourinary cancers remains low. In addition, administration of this type of cancer immunotherapy is known for its potentially severe and even fatal side effects due to their severe immune-related adverse events (irAEs).

Materials and Methods Here, we report a retrospective analysis of 129 patients with stage IV cancer who exhausted conventional treatments, who were treated by a low-dose ipilimumab (0.3 mg/kg) plus nivolumab (0.5 mg/kg) blockade in...