

**Results** Expression of the HERV-K transgene from adenoviral vectors directed high levels of transcripts to the cellular surface and led to the formation of virus like particles. Mutations in the ISD resulted in increased expression of HERV-K in human but not in murine DCs. In addition, ISD mutations increased humoral immune responses to WT Env during recombinant protein immunizations. Adenoviral vectors expressing HERV-K Gag and Env with mutations in the ISD (HERV-K-ISDmut) were highly immunogenic with rapidly induced antibody and T cell responses in mice and break of tolerance in non-human primates. Following prime-boost immunization with selected combinations of checkpoint inhibitors, T cell responses were obtained in the range of 40–50% of circulating CD8+ T cells. As Gag and Env expressing cell lines were rejected in WT mice, we engrafted CT26 cells expressing HERV-K Gag and Env in nude mice and performed adoptive transfer immunotherapy. While initially effective, CD8+ T cells rapidly lost tumor control, whereas combinations of CD8+ T cells with CD4+ T cells and B cells exhibited rapid and sustained tumor control in most animals. **Conclusions** The HERV-K ISDmut antigen holds promise for directing a broad and effective immune response to a large proportion of human cancers.

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**P03.04** **COMBINED SCIB1 DNA VACCINE AND PD-1 CHECKPOINT BLOCKADE FOR THE TREATMENT OF INTRACRANIAL TUMOURS**

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**Background** Intracranial tumours present a significant therapeutic challenge due to their physiological location. Immunotherapy approaches represent attractive treatments for targeting these intracranial tumours due to their tumour specificity relatively low toxicity. The SCIB1 ImmunoBody<sup>®</sup> is a DNA vaccine developed by Scancell Ltd. that encodes a human IgG1 antibody with one TRP-2 two gp100 epitopes engrafted into its complementarity determining regions. SCIB1 has been shown to induce a stronger immune response than

peptide, whole antigen DNA vaccines and peptide pulsed dendritic cells due to Fc-receptor mediated cross presentation. Taking all of this into account, we decided to examine the efficacy of SCIB1 therapy in combination with anti-PD-1 immune checkpoint blockade for the treatment of intracranial tumours.

**Materials and Methods** C57BL/6 HHDII/DR1 mice were immunised with SCIB1 ImmunoBody<sup>®</sup> DNA vaccine and *ex vivo* ELISpot assays were used to assess the immune response while the frequency of TRP-2 specific T-cells was examined via pentamer staining and subsequent flow cytometry analysis. The efficacy of this vaccine was then tested in mice with B16 HHDII/DR1 tumours implanted intracranially. These cells were knockout for murine beta2m and transfected with the chimeric HLA-A2 (HHDII) construct, and naturally express both the TRP-2 and gp100 antigens making it the ideal target for SCIB1 therapy. These mice also received anti-PD-1 therapy, the survival of these mice was then monitored. Immunohistochemical staining for TRP-2 and gp100 was also performed on human GBM tissue micro arrays to study whether SCIB1 could be applicable to this type of cancer. Furthermore, the expression of PD-L1 on GBM tumour cell lines was measured before and after IFN $\gamma$  treatment via flow cytometry. This was done to give an indication of the efficacy of combined anti-PD-1 with SCIB1 vaccination in the GBM setting.

**Results** Here we demonstrate that SCIB1 generates a strong TRP-2 specific immune response in humanised C57BL/6 HHDII/DR1 mice, and this method of vaccination increased the frequency of TRP-2 specific CD8 T-cells. The survival of mice harbouring intracranial B16 HHDII/DR1 tumours was significantly prolonged when SCIB1 ImmunoBody<sup>®</sup> vaccination was combined with anti-PD-1 immune checkpoint blockade compared to mice that received sham vaccination combined with anti-PD-1 and mice that received sham vaccination combined with an isotype control antibody. Our analyses revealed that GBM patients could benefit from SCIB1 ImmunoBody<sup>®</sup> therapy due to the expression of TRP-2 witnessed in GBM tumour tissues. GBM cell lines were also shown to express PD-L1 on their surface and the cell lines studied were shown to upregulate PD-L1 on their surface when exposed to IFN $\gamma$ , providing further evidence for the combination of anti-PD-1 with active immunotherapy such as SCIB1.

**Conclusions** Combinatorial SCIB1 and anti-PD-1 therapy represents an exciting therapeutic intervention for the treatment of intracranial tumours. Our analysis of GBM tumours reveals that this therapy may be applicable to these types of tumours due to their antigen expression profile, because of these findings the efficacy of this combined treatment is now being tested in the GL261 and CT-2A murine GBM models with the aim of moving this combinatorial therapy forward for the treatment of GBM.

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