**RESULTS**

**A. Immunoregulatory interaction**

- **Inhibition of the TGFβ dependent pathway**
- **Peptide MHC class I binding receptors**

**B. GPCR Binding**

**C. Immune Response**

**METHODS**

- Patient biopsies were surgically implanted subcutaneously into the right rear flanks or into their respective orthotopic location (e.g., into the stomach for gastric PDX CRT00292 (Baylor™ model) of the female NDG mouse). To monitor tumor growth, SC tumors were resected twice weekly, and Ortho tumors were imaged with the M3™ compact MRI from Aspect Imaging. For the humanized study, i.e., SC-5e6 and Ortho-5e6 PBMCs were injected intravenously via tail vein before or after tumor implantation depending on respective tumor growth. Therapeutics were formulated and administered per manufacturer’s instructions or past publications. To determine %hCD45 cellularity, weekly NBS blood samples were collected, and RBC lysed per manufacturer’s protocol (Thermo Fisher Scientific) and further processed by standard flow cytometry protocol. For RNA-Seq analysis, mouse contamination was removed (Xenos) and aligned to Human GRCh38 genome using STARaligner, and differential gene expression was performed using edgeR against matched normal tissue from the Genotype-Tissue Expression (GTEx) project. Gene set enrichment analysis (GSEA) was performed to find enriched pathways (KEGG). For tumor-infiltrating lymphocyte (TIL) analysis, tumors were surgically removed and dissociated into single cell suspension using the Miltenyi Biotec gentleMACS™ Dissociator. Immune populations were analyzed using the Cytek™ Biosciences Aurora 3 spectral flow cytometry.

**CONCLUSIONS**

- Tumor implantation site determines the outcome of therapeutic response including immune check point inhibitors. Differences in response is driven by differential gene expression. T cell recruitment, infiltration and functional status. Orthotopic PDX models provide a clinically relevant and translational platform for advancing various cancer therapeutics, including immunotherapies.

**REFERENCES**


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