681 AN EX VIVO 3D TUMOROID MODEL OF FRESH PATIENT TISSUE (3D-EXPLORE) TO ASSESS THE PHAGOCYTIC ACTIVITY OF TUMOR RESIDENT INNATE IMMUNE CELLS

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Background CD47 is an innate immune checkpoint receptor that is overexpressed on tumor cells and contributes to immune evasion through engagement of a myeloid-lineage inhibitory protein SIRPα Blockade of the CD47-SIRPα interaction is proved to enhance the phagocytosis of cancer cells and to induce effective antitumor immune response. Here we developed a novel ex vivo platform using fresh patient tumor samples with intact stromal components and tumor immune microenvironment to assess the therapeutic activity of immunotherapeutic drugs targeting CD47-SIRPα signaling axis in combination with the human IgG1 αPD-L1 antibody avelumab.

Methods All tumor samples were obtained with patient consent and relevant IRB approval. Unpropagated 3D tumoroids with intact TME measuring 150 μm in size were prepared from fresh tumor samples of renal cell carcinoma using proprietary technology developed at Nilogen Oncosystems. Tumoroids prepared from each patient's tumor sample were pooled to represent the tumor heterogeneity and treated ex vivo with phrodo-labeled avelumab alone or in combination with anti-CD47 or anti-SIRPα therapeutics.

Results Multiparameter flow analysis demonstrated tumor binding of avelumab confirming drug penetration into the intact tumor stroma that is further corroborated by high content confocal analysis. Using our confocal-based tumor cell killing assay we were able to quantify drug-induced tumor cell killing ex vivo. We further documented the impact of anti-CD47 and anti-SIRPα therapeutics on phagocytosis of dead tumor cells by tumor resident macrophages and activation of innate and adaptive effector cells by flow cytometry and confocal imaging. Additionally, pHrodo-labeled bioparticles were used to corroborate treatment-mediated changes in the phagocytic activity of tumor resident macrophages.

Conclusions In this comprehensive study we demonstrate that the 3D-EXplore ex vivo platform can be used to assess the efficacy of therapeutic blockade of CD47/SIRPα axis on stimulation of phagocytic process within an intact tumor immune microenvironment.

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