Background CD112R is an inhibitory immune checkpoint receptor and a putative target for novel immune therapies, but little is known about its molecular epidemiology in healthy and diseased tissues.

Materials and Methods To study the prevalence and expression level of CD112R+ immune cells, we analyzed more than 200 samples of normal lymphatic, inflamed and cancerous tissues in a microenvironment tissue microarray format (4 mm tissue spot diameter) and large sections using fluorescent multiplex immunohistochemistry.

Results CD112R expression was detected at variable intensity levels in 47% of CD8+ cytotoxic lymphocytes, 49% of CD4+ T helper cells, 30% of FOXP3+ regulatory T helper cells and 25% of CD56+ natural killer cells, but no expression was found in the subset of CD8+ cytotoxic T cells with supramaximal CD112R expression. The widespread occurrence of CD112R+ immune cells, we analyzed more than 200 samples of normal lymphatic, inflamed and cancerous tissues in a microenvironment tissue microarray format (4 mm tissue spot diameter) and large sections using fluorescent multiplex immunohistochemistry.

Conclusions These studies indicate that the semi-syngeneic a-PD-1 IgG1e3 ab might be a more efficient and translatable a-PD-1 ab for preclinical in vivo studies, which is important for the future investigation of immune checkpoint inhibitor therapy.

Disclosure Information I. Skandorff Pedersen: A. Employment (full or part-time); Significant; InProTher Aps. K. Orfin: A. Employment (full or part-time); Significant; InProTher Aps. K. Nielsen: A. Employment (full or part-time); Significant; InProTher Aps. P.J. Holst: A. Employment (full or part-time); Significant; InProTher Aps. E. Ownership Interest (stock, stock options, patent or other intellectual property); Significant; InProTher Aps.

P03 Tumor Microenvironment

P03.01 PREVALENCE OF CD112R+ IMMUNE CELLS IN NORMAL LYMPHATIC TISSUES, INFLAMMATION AND THE CANCER MICROENVIRONMENT

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Background CD112R is an inhibitory immune checkpoint receptor and a putative target for novel immune therapies, but little is known about its molecular epidemiology in healthy and diseased tissues.

Materials and Methods To study the prevalence and expression level of CD112R+ immune cells, we analyzed more than 200 samples of normal lymphatic, inflamed and cancerous tissues in a microenvironment tissue microarray format (4 mm tissue spot diameter) and large sections using fluorescent multiplex immunohistochemistry.

Results CD112R expression was detected at variable intensity levels in 47% of CD8+ cytotoxic lymphocytes, 49% of CD4+ T helper cells, 30% of FOXP3+ regulatory T helper cells and 25% of CD56+ natural killer cells, but no expression was seen in CD11c+ dendritic cells and CD68+ macrophages. All analyzed compartments across normal and diseased tissues showed a small subset (CD8: 9±18%, CD4: 5±15%, FOXP3: 2±5%) of immune cells with supramaximal CD112R expression. The highest fraction of cells with supramaximal CD112R expression was found in the subset of CD8+ cytotoxic T cells in the Peyer’s patches of ileum (62%), the intergranuloma area of lymph node sarcoïdosis (27%) and in ovarian cancer (37%). In cancerous tissues, the density and the fraction cytotoxic T cells with supramaximal CD112R expression was highly variable and ranged from 5% in bladder cancer to 3% in lung cancer and 36% in ovarian cancer. A high variability of the number of cells with supramaximal CD112R expression was also seen within every tumor entity.

Conclusions In summary, our analysis shows that CD112R expression is abundant in various subsets of immune cells but identifies a small fraction of cells with exceedingly high CD112R levels. The widespread occurrence of CD112R+ cytotoxic T cells in the cancer microenvironment may suggest considerable opportunities for checkpoint inhibitors targeting CD112R.

signaling. Therefore, inhibition of CD39 and/or CD73 holds exceptional advantages over A2aR blockade as both, A2aR dependent and A2aR independent effects of ATP degradation products are targeted simultaneously.

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Background Secondary lymphoid organs (SLO) are involved in induction and enhancement of anti-tumor immune responses on different tumor entities. Recent evidence suggests that anti-tumor immune responses may also be induced or enhanced in the tumor microenvironment in so called tertiary lymphoid structures (TLS). It is assumed that TLS represent a hotspot for T cell priming, B cell activation, and differentiation, leading to cellular and humoral anti-tumor immune response.

Methods FFPE-slides of 120 primary pancreatic ductal adenocarcinoma (PDAC) patients were immunohistochemically (IHC) stained for CD20, CD3, CD8 and HLA-ABC to analyze spatial distribution of tumor-infiltrating lymphocytes. 5-color immunofluorescence staining was performed to further investigate structural components of TLS in comparison to lymphoid follicles in SLOs. Microscope-based laser microdissection and Nanostring-based RNA expression analysis were used to compare gene expression in PDAC, TLS, SLOs and normal pancreatic tissue.

Results TLS were frequently detected in PDAC and were mainly localized along the invasive tumor margin. In less than 10% of the cases TLS were infiltrating the tumors. Interestingly, 20% of the patients had no TLS. Results of TLS will be correlated with clinical parameters, Immunoscore and PD-L1, it was assessed via expression level (signal intensity), has priority over PanCK. To explore the dynamic range of thresholds generate excluded combinations, priority is given to calls for CD8/FoxP3/PD-1 over CD68, which in turn has priority over PanCK. To explore the dynamic range of PD-L1, it was assessed via expression level (signal intensity), not phenotyping. Spatial analyses and visualizations were performed in R using the phenotyper and phenotyperReports packages, and custom scripts.

Conclusions The results clearly demonstrate close similarities between SLO and TLS in terms of composition, distribution and gene expression patterns.