Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive cancer types with a 5-year survival of only 7% and strongly limited treatment options. A major obstacle for successful treatment is the immunosuppressive nature of the tumor microenvironment in PADC that is characterized by a profound desmoplastic reaction with accumulation of cancer-associated fibroblasts and pancreatic stellate cells. While tumor-associated fibroblasts secrete extracellular matrix proteins and soluble mediators that influence tumor progression, local angiogenesis and antitumor immunity, ablation of the tumor stroma was found to promote tumor growth. These findings are indicative for the presence of both tumor-supportive and tumor-suppressive fibroblastic cell types. Tumor-suppressive fibroblasts are associated with accumulation of highly active T cells and recently CCL19 producing, immune-stimulating fibroblasts that form particular microenvironmental niches and promote protective antitumor immunity have been identified in human lung tumors. The project aims to elucidate the molecular signature of active cellular processes of immune-stimulating fibroblasts and unraveling of the heterogeneity of fibroblast subsets in the context of PDAC. Single cell RNA-seq analysis will be utilized to provide insights into the fundamental molecular process that define the identity of immune-stimulating tumor fibroblasts in PDAC. We anticipate that identification of means to selectively foster the development and activity of immune-stimulating fibroblasts in tumors may significantly enlarge the repertoire of treatment options in PDAC.

**type of project**  fundamental research

**status**  ongoing - recruiting phase

**start of project**  2019

**end of project**  2021

**project manager**  Prof. Burkhard Ludewig