The identification of novel MSC regulatory mechanisms in activated pancreatic stroma

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Tumor-associated stroma has emerged as an attractive therapeutic target in several types of cancer including pancreatic. During tumorigenesis, numerous studies have demonstrated fibrogenic/mesenchymal stromal cells (MSCs) acquire "new" properties promoting tumor growth, and these cells express a phenotype reminiscent of wound repair, constituting what is referred to as reactive tumor stroma. These cancer/carcinoma-associated fibroblasts (CAF) or MSCs have been shown to produce growth, angiogenic and chemotatic factors that support and promote tumor growth and progression. Recent studies have shown retinoid signaling impacts pancreatic tumorigenesis in part through its action in the stroma. Using a screen for direct retinoic acid receptor (RAR)-regulated genes, we identified *Emc*, which is epigenetically silenced in a number of tumors including pancreatic. Interestingly, we have found *Emc* expression appears restricted to activated pancreatic stroma in a cerulein-induced model of chronic damage, and *Emc* defines a population of fibrogenic/mesenchymal cells within pancreas. We have utilized several novel transgenic mouse models to track Emc expressing cells in activated pancreatic stroma and FACS sorting to isolate activated stromal cells combined with Illumina sequencing of this population. Preliminary sequencing results of this population showed increased expression of a new repertoire of Emc proteins including S100A4, FAP, in addition to various matrix metalloproteinases (MMPs), which have been shown to lead to extensive remodeling of the local tissue environment. Further characterization of *Emc* and identification of additional downstream targets may lead to novel therapeutic strategies for cancers dependent on the presence of activated stroma.

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