

## AB011. S011. Mesenchymal pancreatic cancer cells inhibit pancreatic stellate cell activation

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**Abstract:** Pancreatic ductal adenocarcinoma (PDAC) is a malignancy with a poor prognosis. Resection is the only curative option and even then, reported 5-year survival rates are less than 10%. Most patients present with advanced disease and these rarely respond to chemotherapy. This lack of response is thought to be, at least in part, related to the abundant stromal tissue surrounding the tumor cells but tumor-restraining aspects have been attributed to the stroma as well. Pancreatic stellate cells (PSCs) are the main constituent of the PDAC stroma and are involved in

remodelling the extracellular matrix. The crosstalk between tumor cells and PSCs has been studied extensively, but this has focused on PSC activation. Surprisingly, we now find that conditioned medium from mesenchymal but not from epithelial pancreatic tumor cell lines inactivates PSCs. This effect is stronger than that of known inhibitors such as retinoic acid and vitamin D, as determined by cell number and stromal activation marker expression. By differential filtration of the tumor cell conditioned medium, we find that the unknown protein should be between 30 and 50 kDa and using gene expression data a small selection of candidate proteins has been established. Validation experiments to identify the candidate protein are ongoing. Identification of this molecule can be used to devise novel therapeutics that act specifically on activated stroma and provide a more specific anticancer treatment.

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