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The influence of tumor modulated microenvironment on pancreatic cancer behavior

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Pancreatic stellate cells are activated during the early steps of malignant transformation. In their active state, pancreatic stellate cells produce excessive amounts of extracellular matrix proteins including periostin, collagen type 1 and fibronectin which promote tumor growth under nutrient deprivation, hypoxia and chemotherapeutic pressure. Additionally, periostin creates an auto-feedback loop on pancreatic stellate cells, perpetuating their activity. Because desmoplastic tissue distorts normal pancreatic architecture, the initial tumor-supporting microenvironment favoring growth shifts into a more hostile one selecting aggressive phenotypes. These selected clones apparently retain their ability to stimulate local stromal cells in order to create a similar tumor-supportive microenvironment in the secondary sites. Therefore, cancer clones that can evoke excessive tumor desmoplasia may reflect a more aggressive phenotype. Targeting periostin in order to uncouple pancreatic cancer– pancreatic stellate cells interactions could be an option to mitigate excessive fibrosis, which ostensibly contributes to chemoresistance and metastatic dissemination of pancreatic ductal adenocarcinoma.