Leukocyte Involvement in the Initiation and Maintenance of Pancreatitis

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Pancreatic ductal adenocarcinoma (PDAC) has a low 5-year survival rate, largely due to late detection. Chronic pancreatitis is a risk factor for PDAC; however, the molecular and cellular mechanism(s) underlying this risk remain poorly defined. Since unresolved chronic inflammation, such as chronic pancreatitis, can promote neoplastic progression, we sought to identify critical leukocyte populations or leukocyte-regulated programs involved in potentiating PDAC development. We have previously reported that B lymphocytes foster chronic inflammation that potentiates malignant disease in the skin by activating pro-tumorigenic programs in infiltrating myeloid cells. We have also demonstrated that human PDACs exhibit significant B cell and myeloid infiltration, and B cell-deficient ($JH^{-/-}$) mice have significantly growth-impaired tumors following orthotopic implant. Therefore, we hypothesize that B cells may also play a role in the initiation or maintenance of pancreatitis.

Thus, we are evaluating leukocyte complexity during initiation, maintenance and resolution phases of acute and chronic pancreatitis using immune-competent murine models. Results from these studies are revealing the temporal dynamics of leukocyte presence during discrete phases of pancreatitis, and the role(s) of leukocyte-regulated pathways involved in pancreatic damage and repair. These studies will guide the identification of molecular targets for therapeutic intervention, with the goal of preventing PDAC development.