Loss of Ifnar1 in Pancreatic Acinar Cells Ameliorates the Disease Course of Acute Pancreatitis.

Abstract:
Type I interferon constitutes an essential component of the combinational therapy against viral disease. Acute pancreatitis is one side effect of type I interferon-based therapy, implying that activation of type I interferon signaling affects the homeostasis and integrity of pancreatic acinar cells. Here, we investigated the role of type I interferon signaling in pancreatic acinar cells using a caerulein-induced murine model of acute pancreatitis. Pancreas-specific ablation of interferon (alpha and beta) receptor 1 (Ifnar1) partially protected animals from caerulein-induced pancreatitis, as demonstrated by reduced tissue damage. Profiling of infiltrating immune cells revealed that this dampened tissue damage response correlated with the number of macrophages in the pancreas. Pharmacologic depletion of macrophages reversed the protective effect of Ifnar1 deficiency. Furthermore, expression of chemokine (C-C motif) ligand 2 (Ccl2), a potent factor for macrophage recruitment, was significantly increased in the Ifnar1-deficient pancreas. Thus, type I interferon signaling in pancreatic acinar cells controls pancreatic homeostasis by affecting the macrophage-mediated inflammatory response in the pancreas.

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