

DEVELOPMENT OF A PANCREATITIS-INDUCED LUNG INJURY MODEL

Qinxiao Wu¹, Marissa Pokharel¹, Baron Osborn¹, Jennifer Lundberg², Jessica C. Cardenas¹

1. Department of Surgery, University of Colorado Anschutz Medical Campus
2. Department of Internal Medicine, University of Nebraska Medical Center

Abstract

Acute pancreatitis (AP) is one of the leading causes of gastrointestinal hospitalization and is frequently complicated by systemic inflammatory responses and multi-organ dysfunction, with acute lung injury (ALI) and progression to acute respiratory distress syndrome (ARDS) accounting for nearly one-third of AP-related deaths. Despite its clinical significance, the mechanisms driving remote organ injury remain poorly understood, and growing evidence implicates endothelial dysfunction in amplifying systemic inflammation and vascular permeability. To address this gap, we developed a reproducible murine model of AP-associated lung injury to investigate endothelial pathways, focusing on the HS3ST1 gene, which regulates the synthesis of 3-O-sulfated heparan sulfate, a key mediator of endothelial barrier stability and anti-thromboinflammatory signaling. Male and female C57BL/6 wild-type (WT) and HS3ST1 knockout (KO) mice were subjected to caerulein-induced AP (1.5 mg/kg, 4×/day for 2 days), with PBS-injected mice as controls, and monitored for weight loss, lethargy, and dehydration. Primary endpoints included plasma pancreatic lipase levels, histologic pancreas and lung injury scores, indices of vascular permeability, and inflammatory profiling, including IL-6 quantification to assess systemic and organ-specific responses, as well as Ptf1a expression as an acinar cell marker of AP severity. Caerulein-treated mice demonstrated significant weight loss, elevated pancreatic lipase levels, and marked pancreatic injury compared to controls, confirming successful AP induction. Preliminary analyses suggest that HS3ST1 deficiency exacerbates inflammatory responses and compromises vascular integrity, supporting its potential role in protecting against AP-associated multi-organ dysfunction. This model provides a valuable platform to show endothelial contributions to systemic inflammation and identify novel therapeutic targets to prevent remote organ injury and improve patient outcomes.