Intracellular trypsinogen activation in phagocytosing macrophages acts as DAMP fueling severe acute pancreatitis

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Introduction
Premature, intraacinar cell trypsinogen activation is dependent on cathepsin B and regarded as an initial event in acute pancreatitis. A second peak of trypsinogen activation is thought to be mediated by infiltrating leukocytes. We have studied the role of protease mediated macrophage (MΦ) activation in experimental pancreatitis.

Macrophages during pancreatitis

Macrophages activate trypsinogen via cathepsin B

Protease activation in MΦ in vivo

Macrophages phagocytose dying acinar cells

Protease activation enhances inflammation

Conclusion
Intracellular protease activation is not restricted to pancreatic acinar cells. In phagocytosing macrophages trypsinogen is activated in a CTSB-dependent manner. Macrophages activating trypsinogen polarise to M1Φ, release pro-inflammatory cytokines and contribute to disease severity. Intracellular active trypsin in MΦ acts as a danger-associated molecular pattern molecule (DAMP).