Fakultät für Medizin

Dokumenttyp: journal article

Autor(en) des Beitrags:
Löhr, JM; Faissner, R; Koczan, D; Bewerunge, P; Bassi, C; Brors, B; Eils, R; Frulloni, L; Funk, A; Halangk, W; Jesnowski, R; Kaderali, L; Kleeff, J; Krüger, B; Lerch, MM; Lösel, R; Magnani, M; Neumaier, M; Nittka, S; Sahin-Tóth, M; Sänger, J; Serafini, S; Schnölzer, M; Thierse, HJ; Wandschneider, S; Zamboni, G; Klöppel, G

Titel des Beitrags:
Autoantibodies against the exocrine pancreas in autoimmune pancreatitis: gene and protein expression profiling and immunoassays identify pancreatic enzymes as a major target of the inflammatory process.

Abstract:
OBJECTIVES: Autoimmune pancreatitis (AIP) is thought to be an immune-mediated inflammatory process, directed against the epithelial components of the pancreas. The objective was to identify novel markers of disease and to unravel the pathogenesis of AIP. METHODS: To explore key targets of the inflammatory process, we analyzed the expression of proteins at the RNA and protein level using genomics and proteomics, immunohistochemistry, western blot, and immunoassay. An animal model of AIP with LP-BM5 murine leukemia virus-infected mice was studied in parallel. RNA microarrays of pancreatic tissue from 12 patients with AIP were compared with those of 8 patients with non-AIP chronic pancreatitis. RESULTS: Expression profiling showed 272 upregulated genes, including those encoding for immunoglobulins, chemokines and their receptors, and 86 downregulated genes, including those for pancreatic proteases such as three trypsinogen isoforms. Protein profiling showed that the expression of trypsinogens and other pancreatic
enzymes was greatly reduced. Immunohistochemistry showed a near-loss of trypsin-positive acinar cells, which was also confirmed by western blotting. The serum of AIP patients contained high titers of autoantibodies against the trypsinogens PRSS1 and PRSS2 but not against PRSS3. In addition, there were autoantibodies against the trypsin inhibitor PSTI (the product of the SPINK1 gene). In the pancreas of AIP animals, we found similar protein patterns and a reduction in trypsinogen.

CONCLUSIONS: These data indicate that the immune-mediated process characterizing AIP involves pancreatic acinar cells and their secretory enzymes such as trypsin isoforms. Demonstration of trypsinogen autoantibodies may be helpful for the diagnosis of AIP.