PANCREAS

# New antibody may aid diagnosis of autoimmune pancreatitis

An antibody present in almost all patients with autoimmune pancreatitis may be the most specific serologic marker yet identified for this disease, report Antonio Puccetti and colleagues in *The New England Journal of Medicine*.

The pathogenesis of autoimmune pancreatitis is not well understood, and although an autoimmune etiology has been suggested, it has never been proved.Focal autoimmune pancreatitis, which occurs in about 60% of cases, is difficult to distinguish from pancreatic cancer. "The identification of a serologic marker for autoimmune pancreatitis remains a major goal in clinical research," stress Puccetti and co-workers. In particular, these researchers were looking for a serologic test that would be able to discriminate this disease from pancreatic cancer.

These investigators, from the Universities of Verona and Genoa, have been working on the identification of novel disease-specific autoantigen targets associated with autoimmune diseases. The peptide library approach they use "allows the detection of peptides recognized by the sera immunoglobulins of patients suffering from the disease of interest," explains Puccetti. In earlier studies, these researchers have successfully used this approach in diseases such as systemic sclerosis, Sjögren syndrome, celiac disease and Cogan syndrome.

In the current study, the researchers screened a random library of dodecamer peptides with pooled immunoglobulins purified from serum samples from 20 patients with focal autoimmune pancreatitis. The most promising peptide they identified was recognized by the serum from 18 of 20 patients with autoimmune pancreatitis (90%), whereas only 4 of 40 serum samples from patients with pancreatic cancer (10%) contained such antibodies. Serum samples from patients with other pancreatic diseases or from healthy controls showed no reactivity to the peptide.

The researchers found that the sequence of this peptide was very similar to a portion of the PBP protein of *Helicobacter pylori* and also to part of the human UBR2 protein, which is highly expressed in pancreatic acinar cells. Overall, after the inclusion of an independent group of patients for validation, these researchers reported that 33 of 35 patients with autoimmune pancreatitis (94%) had serum antibodies against PBP, whereas 5 of 110 patients with pancreatic cancer (5%) tested positive for such antibodies. Interestingly, 22 of the 35 patients with autoimmune pancreatitis also had antibodies against UBR2, which were not detected in serum from patients with other pancreatic diseases. Together, these findings "suggest that *H. pylori* may be involved in the pathogenesis of the disease through a mechanism of molecular mimicry," says Puccetti.

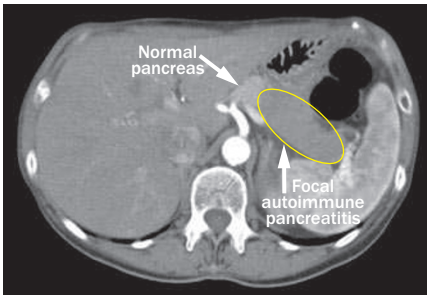


Image courtesy of A. Puccetti

As a few patients with pancreatic cancer did harbor antibodies against PBP, serologic testing for these antibodies alone cannot reliably discriminate between this condition and autoimmune pancreatitis.

Further work is needed to establish the clinical utility of this new serologic test for the diagnosis of autoimmune pancreatitis. Next, Puccetti explains, "the test needs to be validated in a larger cohort of patients from different countries with different genetic backgrounds." Puccetti and his research group also plan to test patients' sera before and after steroid treatment, and will further investigate the putative role of *H. pylori* in the pathogenesis of autoimmune pancreatitis.

*Joana Osório*

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