PANCREATITIS

T cells have a pivotal role in autoimmune pancreatitis in an experimental mouse model

Experimental studies in mice have indicated that T cells have a major role in inducing autoimmune pancreatitis (AIP), and that ciclosporin and sirolimus (also known as rapamycin) could be alternatives to standard steroid treatment.

AIP is a form of chronic pancreatitis that usually responds to steroids, but relapse can occur and little is known about the effectiveness of alternative immunosuppressants. “Analogous to the treatment of IBD, a steroid-sparing therapy is desirable,” says author Julia Mayerle.

Mayerle and colleagues used a mouse model that mimics human type I AIP (MRL/Mp mice). Using this model, they investigated the role of T cells in the development of AIP by blocking CTLA4 (a potent attenuator of T-cell response) and the therapeutic potential of sirolimus, azathioprine and ciclosporin.

Blockade of CTLA4 in MRL/Mp mice led to increased severity of AIP with pronounced organ destruction

and inflammatory cell infiltration.

The composition of T-cell subsets in these AIP mice was also altered; T-regulatory (T_{REG}) cells were suppressed, whereas the effector T-cell response increased.

Treatment with sirolimus and ciclosporin markedly reduced AIP severity, but by different mechanisms; ciclosporin decreased $CD69^+CD4^+$ effector T cells, whereas sirolimus increased T_{REG} cells, which in turn suppressed effector T-cell responses. Azathioprine did not reduce AIP severity, with minimal effect on T-cell populations.

The authors propose that ciclosporin and sirolimus are promising therapeutic candidates in humans with AIP and should be tested in clinical trials.

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Original article Schwaiger, T. *et al.* Autoimmune pancreatitis in MRL/Mp mice is a T cell-mediated disease responsive to cyclosporine A and rapamycin treatment. *Gut* doi:10.1136/gutjnl-2012-303635