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EXPERIMENTAL ARTHRITIS

Endothelin blockade: a new therapy for inflammatory arthritis?

Endothelins might have a role in the pathogenesis of inflammatory arthritis and could represent a novel therapeutic target in this disease, according to data obtained using an antigen-induced arthritis (AIA) mouse model.

"We started this research by wondering what the connection between the immune system and nervous system during inflammatory pain might be," explains Stefan Schulz, who led the investigation. "We decided to use the AIA model and compare gene expression in lumbar dorsal root ganglia from the inflamed versus control sides of mice." First, the researchers found that endothelin (ET)-1 and ET-2 were upregulated in the inflamed side of mice with AIA compared with the control side, so next they investigated the effects of endothelin receptor antagonists in this disease model. Interestingly, in the acute phase of AIA, bosentan—a dual ET_A and ET_B endothelin receptor antagonist—reduced joint swelling and inflammation to a similar degree as dexamethasone, whereas the ET_A-selective antagonist ambrisentan had no such anti-inflammatory effects. Daily administration of bosentan also prevented joint swelling during AIA disease flares (induced by repeated injections of antigen into the joints), whereas control mice developed swollen joints during each flare.

"We were pleased to see that the nonselective ET_A and ET_B receptor antagonist had potent activity in our AIA model, even in flare-ups; this is perhaps the most remarkable finding," says Schulz. "It would be great to see this translated to the clinic".

Jenny Buckland

Original article Imhof, A.-K. *et al.* Potent anti-inflammatory and antinociceptive activity of the endothelin receptor antagonist bosentan in monoarthritic mice. *Arthritis Res. Ther.* **13**, R97 (2011)