The Relevance of the Anti-Fibrotic and Other Therapeutic Actions of Relaxin to Atrial Fibrillation

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Originally described for its ability to remodel the birth canal during pregnancy, the hormone relaxin is emerging as both an endogenous inhibitor of collagen turnover and a potential therapy for the progressive fibrosis that occurs during tissue repair and disease processes. Relaxin has been shown to potently and rapidly inhibit fibrogenesis in diverse experimental models of cardiovascular disease. In each case, short-term continuous infusion of relaxin is also able to reverse established fibrosis. Importantly, relaxin only inhibits pro-fibrotic cytokine (angiotensin II, TGF-beta1)-stimulated collagen and fibronectin deposition in primary fibroblast culture models in vitro and animal models of injury/disease in vivo without affecting basal matrix turnover; highlighting its safety as a therapeutic. Consistent with this, relaxin has been evaluated in a number of clinical trials and has demonstrated an excellent safety profile in humans with minimal side-effects. The anti-fibrotic actions of the hormone have been found to primarily involve the down-regulation of Smad2 phosphorylation as a means of interfering with TGF-beta1 signaling and hence, the ability of TGF-beta1 to promote myofibroblast differentiation and collagen production. Additionally, relaxin has been found to promote matrix metalloproteinase expression and activity, while inhibiting the actions of the tissue inhibitors of metalloproteinases to induce collagen breakdown. These combined actions along with its anti-inflammatory and anti-hypertrophic properties highlight its potential as a therapy for atrial fibrillation.

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