**INDUCTION OF IL-17 SIGNALLING IN THE RAT HEART EXPOSED TO IN VIVO ISCHEMIA/REPERFUSION INJURY PROMOTES NECROTIC AND APOPTOTIC CELL DEATH**

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Background: L-17A and IL-17F are pro-inflammatory cytokines exerting a pathogenic role in arthritis, multiple sclerosis and inflammatory bowel disease.

Aims: To investigate the role of IL-17 cytokines in myocardial ischemia/reperfusion injury (IRI).

Methods and Results: Expression of IL-17A, IL-17F and the IL-17 receptor (IL-17RA) was dramatically increased (>7 fold) in rat hearts exposed to in vivo IRI (30 minutes ischemia and 2 hours reperfusion), as documented by affymetrix microarray analysis and confirmed by quantitative RT PCR. Several IL-17 target genes were also upregulated following IRI, including KC (Cxcl1), Cxcl2, Cxcl3, Ccl2 (MCP-1), IL-1â, iNOS, IL-6, S100a8, S100a9, Ccr1, P-selectin, ICAM-1, MMP-8, MMP-9, Ptgs2, Timp1, lcn2, Cotl1 and Spsb1. IL-17A promoted the expression of KC and IL-6 in isolated cardiac mycoytes in a MAPK and PI(3)K dependent manner. IL-17A and IRI were found to have an additive effect on KC expression, suggesting that IL-17 may enhance myocardial neutrophil recruitment following IRI. Although cardiac myocytes were found to express relatively low levels of IL-17A mRNA, IL-17F and IL-17RA were induced by IRI injury in these cells. Likewise, protein levels of both IL-17R and IL-17A were enhanced following in vivo IRI. Finally, intraperitoneal injection of IL-17 blocking antibody prior to in vivo IRI promoted postischemic hemodynamic recovery, minimized infarct size and reduced the extent of myocyte apoptosis.

Conclusions: IL-17 cytokines and their receptor are induced following myocardial IRI and promote myocyte necrosis and apoptosis. Strategies aimed at modulating the expression of IL-17 cytokines may be clinically useful to promote cell survival following IRI.