Interleukin 10 administration after MI improves left ventricular function in rodents

Interleukin (IL)-10 exerts potent anti-inflammatory effects *in vivo* via inhibition of the production of various cytokines and chemokines. Serum levels of this molecule have been shown to correlate with prognosis in patients with acute coronary syndromes. IL-10 administration is, therefore, considered a potential treatment for patients after myocardial infarction (MI). Two recent rodent studies have reported beneficial effects of IL-10 therapy on inflammation and remodeling after MI.

In humans, intracoronary transplantation of bone-marrow-derived progenitor cells after acute MI results in improved left ventricular function. Bone-marrow-derived progenitor cells express high levels of IL-10 and Burchfield *et al*. hypothesized that IL-10 mediates much of the beneficial effect of these cells in patients after MI. Bone marrow mononuclear cells (BM-MNCs) were isolated from IL-10-deficient and wild type (control) mice to test this hypothesis.

Ligation of the left anterior descending coronary artery was performed in female mice to result in MI. This procedure and was immediately followed by intramuscular injection of diluent with and without BM-MNCs from wild type or IL-10-deficient mice into the infarcted area. IL-10 was required for the protective effects of BM-MNCs on left ventricular function; this protection possibly resulted from IL-10 suppression of T-cell infiltration, but not from limitation of neutrophil infiltration. IL-10 was not required for BM-MNC-stimulated neovascularization or for BM-MNC secretion of the proangiogenic cytokines IL-6, monocyte chemotactic protein 1, vascular endothelial growth factor and insulin-like growth factor 1.

Stumpf and colleagues' approach to studying the effects of IL-10 therapy on inflammation and remodeling after MI was to treat rats with a subcutaneous injection of recombinant human (rh) IL-10 immediately after induction of MI (via ligation of the left anterior descending coronary artery) and then to inject rhIL-10 subcutaneously every day for the next 4 weeks. Animals were assessed at the 4-week time point.

In agreement with the results from Burchfield and colleagues' study of BM-MNC-secreted IL-10, administration of rhIL-10 protected rats from MI-induced left ventricular dysfunction. In rats that underwent ligation of the left anterior descending coronary artery but received no IL-10, membrane-bound and circulatory concentrations of tumor necrosis factor and IL-6, as well as serum levels of monocyte chemotactic protein 1, were substantially increased after MI. Interestingly, membrane-bound and soluble IL-10 levels were decreased. Subcutaneous administration of rhIL-10 attenuated the increases in tumor necrosis factor, IL-6 and monocyte chemotactic protein 1 that were associated with MI. In line with these findings, IL-10 suppressed macrophage infiltration after MI.

IL-10, therefore, exerts protective effects on left ventricular function when administered after MI, possibly by suppression of T-cell and macrophage infiltration. These studies suggest that IL-10 could be a good therapeutic option for patients who have undergone MI.

Original articles Burchfield JS *et al.* (2008) Interleukin-10 from transplanted bone marrow mononuclear cells contributes to cardiac protection after myocardial infarction. *Circ Res* **103:** 203–211
Stumpf C *et al.* (2008) Interleukin-10 improves left ventricular function in rats with heart failure subsequent to myocardial infarction. *Eur J Heart Fail* **10:** 733–739

Limiting myocardial infarct size: a new role for cyclosporine

Experimental studies have indicated that the immunosuppressive drug cyclosporine could limit myocardial reperfusion injury through inhibition of the mitochondrial permeability transition pore. Piot and coworkers conducted a prospective, multicenter, pilot study to investigate whether cyclosporine reduces infarct size in patients who undergo percutaneous coronary intervention after myocardial infarction.

Patients (mean age 58 years; 79% male) were randomly assigned to receive intravenous 2.5 mg/kg cyclosporine ($n = 30$) or placebo ($n = 28$) during angioplasty. Infarct size was determined by the measurement of levels of the cardiac biomarkers creatine kinase and troponin I. At 3 days after percutaneous coronary intervention, creatine kinase release was significantly lower for the cyclosporine group than for the placebo group (138,053 versus 247,930 arbitrary enzyme units, $P = 0.04$). This difference equates to a 40% reduction in infarct size among patients who received cyclosporine. By contrast no significant difference between the

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