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Regulatory T Cells Reduce Infarct Size, Improve LV Remodeling and Function after Experimental Myocardial Infarction

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Introduction:

Ischemic cardiac damage is associated with upregulation of cardiac pro-inflammatory cytokines, as well as invasion of leukocytes and lymphocytes into the heart and to injured muscle. Regulatory T cells (Tregs) exert suppressive effects on several immune and non-immune cellular elements. We aimed hypothesized that Tregs improve cardiac function after myocardial infarction (MI) with potential alteration of post-ischemic vessel growth.

Methods and Results:

The number and functional suppressive activity of Tregs were assayed in mice subjected to experimental MI (n=40), and to hindlimb ischemia (n=24). The numbers of splenocyte-derived Tregs were significantly higher after the injury, both in MI mice (16±0.6% vs. 12±0.7%, $p<0.01$) and in hindlimb ischemia animals (9.3±0.68% vs. 5±0.83%, $p<0.001$). Treg suppressive properties were significantly reduced in MI mice and in mice that underwent hindlimb ischemia. For adoptive transfer assays, Tregs or PBS were injected to mice and their effect on infarct size and cardiac function after experimental MI and flow recovery after induced hindlimb ischemia were compared. Compared with PBS, Treg transfer to MI mice reduced infarct size as observed by Masson's trichome staining (1.55±0.4 mm^2 vs. 4.1±1.1 mm^2, $p=0.03$) and improved LV remodeling (LVSA, percent of change, 7.8±16% vs. 101±14%) and functional performance by echocardiography (fractional shortening, percent of change, 19.6±18% vs. -32±6%, $p=0.02$). Treg transfer to hindlimb ischemia mice induced improvement in flow recovery compared to PBS transfer (70.74±9.537 vs. 38.21±6.939 % flow, $p=0.02$) at day 14 post procedure.

Conclusion:

Both cardiac and skeletal muscle ischemia increase the number of Treg cells. Tregs play a protective role in two non-overlapping models of ischemia (MI and hindlimb) and may thus be considered as attractive potential therapeutic tools.