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Secretome from Mononuclear Cells Confers Immunosuppression in a Murine Autoimmune Myocarditis Model

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Background:
Inflammatory dilated cardiomyopathy (iDCM) is a common cause of heart failure in young patients. Experimental autoimmune myocarditis (EAM) is a CD4+ T cell dependent autoimmune model, which mirrors important pathogenic aspects of iDCM.

Objective:
We have recently shown that a high dose application of paracrine factors obtained from mononuclear cells (MNC) modulates the inflammatory response following myocardial ischemia. In this subsequent study, we sought to evaluate possible immunosuppressive features of MNC secretome using the EAM model.

Method and Results:
Cell culture supernatants derived from murine MNC were injected intraperitoneally after induction of autoimmune myocarditis with a cardiac myosin peptide homologue. The inflammatory response was determined by histopathological evaluations and by ELISA. Impact of MNC secretome on proliferation and cell viability of CD4+ T- cells was measured by flow cytometry, ^{3}[H]-thymidine incorporation and histone release assays.
Treatment of EAM mice with a single high dose of MNC secretome resulted in an attenuation of myocardial infiltrate (myocarditis score 2.7±0.4 vs 0.01±0.01; p=0.0089). We further evaluated the effect of MNC secretome on JURKAT cells and purified human CD4+ T cells. Co-incubation of MNC secretome with T-cells led to a caspase-8 dependent induction of apoptosis.

Conclusion:
Our data gives first evidence that secretome obtained from MNC possess immunosuppressive features in an autoimmune myocarditis model. This anti-inflammatory effect of MNC secretome points to a novel and simple potential treatment concept in inflammatory heart diseases.