

## Pro-inflammatory Cytokine Interleukin-6 is Upregulated in Early Stage Type 1 Diabetic Rats

YU HUO, MICHELLE L. HARRISON, and AUDREY J. STONE

Autonomic Control of Circulation Laboratory; Department of Kinesiology and Health Education; University of Texas at Austin; TX

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Advisor / Mentor: Stone, Audrey ([audrey.stone@austin.utexas.edu](mailto:audrey.stone@austin.utexas.edu))

### ABSTRACT

Type 1 diabetes (T1DM) is an autoimmune disease characterized by systemic inflammation. T1DM patients are at a higher risk of cardiovascular disease and chronic inflammation, and this is reflected by increased levels of circulating pro-inflammatory cytokines IL-6, IL-1 $\beta$ , and TNF- $\alpha$ . However, the time point at which these pro-inflammatory cytokines become elevated is not known. **PURPOSE:** The purpose of this study was to determine the concentration of circulating pro-inflammatory cytokines IL-6, IL-1 $\beta$ , and TNF- $\alpha$  in the early stage of T1DM. **METHODS:** We injected (i.p) 50mg/kg of Streptozotocin (STZ) or the vehicle (CTL) into male and female Sprague Dawley rats and waited one to three weeks before drawing blood. Blood was drawn from the carotid artery into a serum separator vacutainer, centrifuged, and then the serum was aliquoted into tubes and frozen at -80°C for subsequent batch analyses. A rat cytokine multiplex kit (RADPKMAG, EMD Millipore) was used to determine cytokine concentrations in the aliquoted samples. Samples were analyzed using a Luminex 200 instrument (Luminex Corp) according to manufacturer's instructions. **RESULTS:** STZ rats had significantly higher blood glucose (CTL=200 $\pm$ 15 mg/dl, n=14; STZ=523 $\pm$ 14 mg/dl; n=14; p<0.01) and % HbA1c (CTL=4.3 $\pm$ 0.1%, n=10; STZ=8.7 $\pm$ 0.7%; n=11; p<0.01) than CTL rats. STZ rats had significantly lower insulin (CTL=1259 $\pm$ 500 pg/ml, n=8; STZ=200 $\pm$ 182 pg/ml, n=14; p<0.01) than CTL rats. We found that serum IL-6 was increased in STZ rats (222 $\pm$ 205 pg/ml; n=11; four samples with undetectable concentrations were excluded) compared to CTL rats (116 $\pm$ 69 pg/ml; n=10; one sample with undetectable concentration was excluded), p=0.06. In contrast, we found that IL-1 $\beta$  (STZ: 4.9 $\pm$ 4 pg/ml, n=14; CTL: 4.6 $\pm$ 3 pg/ml, n=7, p>0.05) and TNF- $\alpha$  (STZ: 15.6 $\pm$ 12 pg/ml, n=14; CTL: 14.3 $\pm$ 9 pg/ml, n=13, p>0.05) were not significantly different between STZ and CTL. **CONCLUSION:** We conclude that serum IL-6 concentrations are trending toward being greater in the early stage of T1DM. However, serum levels of IL-1 $\beta$  and TNF- $\alpha$  do not appear to be elevated at this stage of the disease. Further studies are needed to determine if concentrations of pro-inflammatory cytokines fluctuate during the progression of the disease.