Adipose-Derived Secretome as a Therapeutic for Viral Myocarditis

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Background: Viral infection is the most common cause of *Myocarditis*, an inflammatory cardiovascular disease that accounts for over 1 million cases and more than 30,000 deaths globally each year. Yet, there are no FDA-approved treatments specifically for myocarditis. In this study we will investigate if secretome generated from adipose stem cells in vitro reduces inflammatory responses in our viral myocarditis mouse model.

Methods: Secretome, which contains extracellular vesicles and proteins secreted from stem cells, was tested in vitro before being administered to our mouse model. Endothelial proliferation assay and PBMC cytokine assays were utilized to predict the anti-inflammatory effect of the secretome. After quality testing, secretome was administered to 8-week-old male C57BL/6 mice during a clinically relevant time point after infection with coxsackievirus B3 (CVB3) virus at day 0 and harvested at day 10. Endpoints included histology, RT-PCR, and echocardiography.

Results: *In vitro* testing showed secretome decreased TNFalpha secretion from activated PBMCs (p=0.005) and increased endothelial cell proliferation (p=0.003). Mice treated with secretome saw significantly less inflammation, decreased myocarditis, according to histology (p=0.001). RT-PCR analysis showed a significant decrease in immune activity in mice given secretome compared to mice that were untreated (Tlr4, p=0.04; CD45, p=0.02; CD3, p=0.02; Casp1, p=0.02; CD11b, p=0.04). There was no observed significant difference in heart function between secretome-treated and untreated mice.

Conclusion: Adipose-derived stem cell secretome reduced cardiac inflammation severity and immune gene expression while promoting endothelial proliferation in vitro. This combination of anti-inflammatory and pro-reparative activity supports further study of secretome as a therapeutic for viral myocarditis.

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