**PREVENTION OF MYOCARDITIS/DCM USING REGENERATIVE MEDICINE THERAPY**

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**Objective:** Myocarditis is an important cause of acute and chronic heart failure with no good therapy to reduce/prevent disease. We wanted to determine whether purified exosome product (PEP) could improve and/or prevent myocarditis using a preclinical mouse model of myocarditis. Because estrogen protects women from myocarditis and heart failure we also tested premenopausal PEP (pmPEP).

**Method:** To determine the appropriate dose of PEP/pmPEP, we administered PEP and pmPEP vs. PBS ip to male BALB/c mice at day -1, 0 and +1 with virus inoculation on day 0 to induce myocarditis, and harvested mice at day 10 post infection (pi) during the peak of acute myocarditis. Next we treated male BALB/c mice with PEP, pmPEP or PBS ip on day 8, 9 and 10 pi (a clinically relevant timepoint) and harvested on day 11 pi during acute myocarditis. **Results:** We found that the dose and exposure route were successful. pmPEP, but not PEP, significantly decreased acute myocarditis based on histology (ANOVA *p*=0.0009) and decreased total immune cells (CD45 *p*=0.008), macrophages, neutrophils and mast cells (CD11b *p*=0.04), macrophages (F4/80 *p*=0.009), and T cells (CD3 *p*=0.02, CD4 *p*=0.01) but no other immune cell populations in the heart. Markers for both M1 and M2 macrophages were also significantly decreased with pmPEP treatment indicating a “global” decrease in inflammation. Importantly, CR1, the central inhibitor of the complement cascade, was significantly increased by pmPEP but not PEP (*p*=0.004). We found that either PEP or pmPEP treatment given during myocarditis significantly reduced inflammation compared to PBS (ANOVA PEP *p*=0.006, pmPEP *p*= 0.005).

**Conclusion:**These findings suggest that PEP/pmPEP could be administered to patients who present with acute onset myocarditis to decrease the severity of disease and potentially prevent sudden death.