Methods: DNA extracted from explanted DCM hearts (n=17, 1 female; 49±13 years; LVEF: 18±5%) were investigated for cloning of the TCR-β gene. Non-DCM hearts (ischaemic cardiomyopathy: n=2; valvular heart disease: n=2; donor hearts: n=3) served as controls. PCR-products analyzed by high-resolution fragment analysis (GeneScan), displayed a Gaussian-like distribution profiles in polyclonal and single dominant peaks in mononuclear T-cell populations. Clonal TCR-β PCR-products were directly sequenced.

Results: The GeneScan analysis of the TCR-β PCR-products demonstrated a clonal T-cell population in 18/19 (95%) of the DCM hearts. In contrast, exclusively polyclonal composition of the TCR-β PCR-products were obtained from the non-DCM hearts. Sequence analysis of the clonal TCR-β PCR-products from the n=9 DCM hearts determined Vβ19.01 (1039-67) to be the predominant TCR-β chain, which confirms the autoimmune hypothesis of DCM. Our results, demonstrating a clear predominance of Vβ19.01 T-cell clones in DCM, warrant the molecular analysis of the respective immunoregulatory sequences and eventually a TCR-biased immunotherapy in DCM (e.g. with DNA vaccines).

1039-04
Prenatal Naltrexone Exposure Adversely Affects Postnatal Cardiac Development: A Model for Dilated Cardiomyopathy

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Background: Opioid Growth Factor (OGF) is an inhibitory peristatine that interacts with its receptor (OGFr) to target cell proliferation and DNA synthesis. Previous studies have shown that deletion or disruption of the OGF/OGFr interaction by naltrexone (NTX) had a stimulatory effect on myocardial development. We hypothesized that in utero exposure to NTX alters postnatal cardiac development.

Methods: Time-mated Sprague-Dawley rats received injections of 30 mg/kg of NTX or 0.3 ml saline twice a day throughout gestation. Offspring were cross-fostered to non-injected, lactating females. Left ventricle (LV) size and function were evaluated by echocardiography in postnatal day (PND) 26, 55 and 110 Ntx exposed and control rats. In six to eight male and female offspring of each group were studied for LV diastolic dimension, LV thickness, shortening fraction (SF) and heart rate.

Results: PD 26 male and female and PD55 female offspring exposed to NTX had significant increases in LV size and dysfunction compared to controls (p<0.01). PD110 NTX exposed rats had increased thickness of the LV free wall (p=0.05), but no changes occurred earlier. SF was significantly decreased (p<0.01) relative to controls in all Ntx exposed rats at all ages studied. SF decreases in the Ntx group ranged from 12-19%. Heart rate was significantly decreased in the NTX exposed rats compared to controls (p<0.05).

Conclusions: NTX exposing demonstrated significant changes in ventricular size, systolic function and heart rate. The NTX rats had dilated left ventricles at earlier ages. After PND 26, the NTX treated rats had decreased ventricular systolic function and decreased heart rates at all ages studied. This data suggests that in utero blockade of OGF activity by NTX leads to significant ventricular dilation and impaired systolic function. This information may provide a unique model that will allow for further study of dilated cardiomyopathies.