1181-144 Assesement of the Myocardial Transcriptome in Heart Failure Using Redundant Cross-Species Oligonucleotide Arrays

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Background: Although myocyte hypertrophy is a characteristic feature of congestive heart failure, the specific transcriptional changes and their mediators are complex and redundant. In order to fully understand heart failure pathogenesis, multiple pathways must be studied simultaneously. Oligonucleotide array technology provides a platform for these experiments, but it is limited to only a few species. Here we report the cross-species use of human, muscle-specific oligonucleotide arrays to elucidate transcriptional changes associated with heart failure in canine pacing-induced cardiomyopathy.

Methods: Heart failure was induced in male mongrel dogs by ventricular pacing (210 bpm) for 12 weeks. RNA was isolated from left ventricular free wall myocardium obtained from paced and control un-paced dogs (n=3 each, each, excluding chloride gradient method). Within each group, samples were combined in equimolar amounts resulting in single tailing and control RNA pools. Duplicate in vitro transcriptions were performed on each pool from 2 tailing and 2 control cRNA probes that were hybridized to a custom human Affymetrix oligo array (4601 probe sets, 32.96 oligo 3s or 2-3 probe sets /gene). Over- and under-expressed genes were selected using GenChip software.

Results: 500 (~25%) of the ~2000 genes were detected. Of these 500 genes, 10 were over-expressed and 3 were under-expressed in heart failure. While many of the upregulated genes were novel, most belonged to established metabolic pathways: signal transduction (G protein c-s2, caviolin-3), calcium handling (calumenin) and remodeling (prepro32), collagen, connective tissue growth factor); energy metabolism (brain creatine kinase, aconitase 2) and oxidative stress (diaphorase).

Conclusions: Pacing-induced heart failure is accompanied by large transcriptional changes in genes related to calcium handling, receptor-mediated signal transduction, energy metabolism, and oxidative stress, as well as several novel genes. These results validate the cross-species use of oligo-nucleotide arrays, and provide novel targets for further studies of heart failure pathogenesis.

1181-145 Hemodynamic Assessment of Septic Mice Deficient in Inducible Nitric Oxide Synthase Demonstrates Improved Myocardial Performance

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Introduction: Vasodilation and myocardial depression characteristic of septic shock may result from overproduction of nitric oxide, and can lead to pressor-refractory hypotension. Vasodilation and myocardial depression characteristic of septic shock may result from overproduction of nitric oxide, and can lead to pressor-refractory hypotension. Introduction: Vasodilation and myocardial depression characteristic of septic shock may result from overproduction of nitric oxide, and can lead to pressor-refractory hypotension. Introduction: Vasodilation and myocardial depression characteristic of septic shock may result from overproduction of nitric oxide, and can lead to pressor-refractory hypotension. Introduction: Vasodilation and myocardial depression characteristic of septic shock may result from overproduction of nitric oxide, and can lead to pressor-refractory hypotension. Introduction: Vasodilation and myocardial depression characteristic of septic shock may result from overproduction of nitric oxide, and can lead to pressor-refractory hypotension. Introduction: Vasodilation and myocardial depression characteristic of septic shock may result from overproduction of nitric oxide, and can lead to pressor-refractory hypotension.

Methods: Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study.

Results: Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study. Septic mice deficient in inducible nitric oxide synthase were generated and used for this study.

Conclusions: These results support the hypothesis that overproduction of nitric oxide contributes to the pathogenesis of septic shock. These results support the hypothesis that overproduction of nitric oxide contributes to the pathogenesis of septic shock. These results support the hypothesis that overproduction of nitric oxide contributes to the pathogenesis of septic shock. These results support the hypothesis that overproduction of nitric oxide contributes to the pathogenesis of septic shock. These results support the hypothesis that overproduction of nitric oxide contributes to the pathogenesis of septic shock. These results support the hypothesis that overproduction of nitric oxide contributes to the pathogenesis of septic shock.

1181-153 Detection of Myocardial Infarction in Heart Failure Patients With Severe Left Ventricular Systolic Dysfunction by Contrast Enhanced MRI

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Background: Contrast-enhanced Magnetic Resonance Imaging (CE-MRI) can visualize both transmural and subendocardial myocardial infarction. Most clinical trials classified cardiomyopathy as ischemic (ICM) based on one or more of the four following criteria: history or clinical evidence of prior myocardial infarction (MI), significant coronary stenosis on coronary angiography, prior revascularization, or an abnormal functional stress test. Patients who do not meet these criteria are classified as nonischemic (NICM). This study investigated the use of CE-MRI to identify evidence of prior myocardial infarction in patients with severe left ventricular dysfunction of mixed etiologies.

Methods: Ols and CE-MRI were performed on 43 patients with severe left ventricular dysfunction. 27 (63%) were classified as ICM (LVEF≤30%) and 16 (37%) as NICM (LVEF>32%). Wall motion and the transmural extent of hyperenhancement (He) representing prior infarction were scored by two blinded observers using a 2 segment model. Results: Inducible nitric oxide synthase was over-expressed and 3 were under-expressed in heart failure. While many of the upregulated genes were novel, most belonged to established metabolic pathways: signal transduction (G protein c-s2, caviolin-3), calcium handling (calumenin); and remodeling (prepro32), collagen, connective tissue growth factor); energy metabolism (brain creatine kinase, aconitase 2) and oxidative stress (diaphorase). In heart failure, 100% of patients with severe left ventricular dysfunction satisfying criteria for ICM have evidence of prior MI as identified by contrast-enhanced MRI, whereas only 50% of such pts have a history or clinical evidence of prior MI. In addition, 13% of pts with non-ischemic cardiomyopathy have evidence or prior MI.

Conclusions: In patients with severe left ventricular dysfunction, CE-MRI can detect prior MI in those pts with a history or clinical evidence of prior MI.