changes in response to coronary ESC perfusion, including declines in CF, HR, LVP, /dP/
max, and /dP/dtmax, with increased ESC perfusion rates. However, the magnitude of
these parameters differed between the two model strains. At less than 10 cells/mm², the
percent decline of these parameters in wild type hearts appeared significantly greater
(p<0.05) than those of apoE-/-: CF 15.2±1% in wild type vs. 10% in apoE-/-, HR 19% vs.
7%, LVP 9% vs. 6%, /dP/dtmax 11% vs. 8%, and /dP/dtmax 24% vs. 11%. Increasing the
endothelial density to 101±10 cells/mm² led to further deterioration of the heart func-
tions but the apoE-/- hearts remained lower levels of the parameter declines. Histopatho-
logical analysis showed the presence of numerous ESC in microcirculation as well as in the
extravascular tissue.

Conclusions: Perfusion with ESC through coronary arteries causes concentration-
dependent changes in heart function. Compared to wild type controls, the hearts of
apoE-/- mice which underwent atherosclerosis-related chronic ischemia appeared to be
better tolerant to high ESC perfusion.

T011-T110

The Mitochondrial Metabolic Phenotype and Mouse Strain Influence Isoproterenol-Induced Cardiac Hypertrophy

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Introduction We previously described a novel model of isoproterenol (ISO)-induced
hypertrophy in which A/JU mice exhibit greater cardiac hypertrophy than B6 mice. The
objective of this study was to determine the relation between this variable hypertrophic
response and the mitochondrial metabolic phenotype.
Methods 39 male mice (19 AJU, 20 B6) received randomly either ISO (100 mg/kg, sc) or vehicle
daily for five days. Hearts were assayed for response to stimulation of the geno-
merically expressed mitochondrial enzymes pyruvate dehydrogenase (PDH), medium chain acyl-CoA dehydrogenase (MCAD), carnitine palmitoyl transferase I (CPT-I) and citrate synthase activities. Nine
consomic B6.AM mice (B6 containing mitochondrial DNA from AJU) were also studied. Results ISO-treated AJU mice displayed a greater increase in gramicidin heart
weight (vs. vehicle) than ISO-treated B6 (24% vs. 3%, respectively, p<0.001). Enzyme
activities were greater in vehicle-treated B6 than AJU mice (Table). ISO administration reduced active PDH activity (PDHA) in B6 mice by 47% (p<0.001), with no significant change in AJU. The hypertrophic response and basal and stimulated enzyme activities were similar in B6 and AJU mice.

Conclusions 1) Compared to AJU, B6 mice demonstrate less ISO-induced cardiac hyper-
trophy, but greater activity of fatty acid and carbohydrate oxidative enzymes. 2) ISO-
induced hypertrophy reduces myocardial PDH in a strain-dependent manner. 3) These
mitochondrial enzyme activities are not influenced by mitochondrial DNA.

Data are mean ± SEM. * p<0.01 B6 vs. AJU by ANOVA. † p<0.01 ISO vs.
vehicle by t-test.

<table>
<thead>
<tr>
<th>A/J vehicle</th>
<th>B6 vehicle</th>
<th>A/J ISO</th>
<th>B6 ISO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrate synthase (µmol/min/gww)</td>
<td>59 ± 4</td>
<td>171 ± 5 *</td>
<td>56 ± 3</td>
</tr>
<tr>
<td>MCAD (µmol/min/gww)</td>
<td>10.4 ± 1.1</td>
<td>11.7 ± 0.9 *</td>
<td>8.9 ± 0.9</td>
</tr>
<tr>
<td>CPT-I (µmol/min/gww)</td>
<td>1.7 ± 0.1</td>
<td>2.4 ± 0.2 *</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td>PDH active (U/gww)</td>
<td>2.2 ± 0.4</td>
<td>4.8 ± 0.5 *</td>
<td>1.9 ± 0.3</td>
</tr>
</tbody>
</table>

T011-T111

Homocysteine Promotes Ventricular Remodeling by Induction of Apoptosis of Rabbit Cardiomyocytes and Priming the Mast Cells to Induce interleukin-6, With Significant Inhibition by Troglitazone

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Background: Homocysteine (Hcy) has been linked to the pathophysiology of atherosclerosis, on the other hand, it has been linked to ventricular remodeling and heart failure through pro-
flammatory causes. This may occur due to direct effects on the cardiomyocytes or indi-
rectly by involving other cells like macrophages, fibroblasts and mast cells.

Methods: After isolating rabbit cardiomyocytes (CMs) using the standard perfusion method, we have given d,l Hcy (1x10-4 M) to the cells and at three hours we quantitated the apop-
totic cells using Flow Cytometry. We used Annexin V (FITC +) - Propidium iodide method for apoptosis detection. Apoptotic cells manifest as Annexin V - FITC positive and Propid-
ium iodide negative, while necrotic cells manifest as Annexin V - FITC positive and PI
positive. We have also given d,l Hcy to Human Leukemic Mast Cells (HMC-1) with 1 ng/
ML of Interleukin 1 beta (IL1b) in a dose dependent manner (10, 50, 100 x 10-6 M). We added the Peroxisome Proliferator Activator Receptors (PPAR) gamma agonist (Troglita-
zone) to the cells as well (10 x 10-6 M). We used ELISA technique to quantitate the amount of Interleukin 6 (IL 6 ) in the supernatants after 24 hours of incubation.

Results: We found that d,l Hcy induces apoptosis of CMs in the Hcy group (3.0% versus 1.0 %
control , p = 0.02 ). On the other hand, we noticed a dose dependent increase in IL 6 concentration in the group treated with HMC1 cell line with a small fixed dose of IL1b and increasing doses of d,l Hcy ( 35 pg/mL versus 75 pg/mL, for IL1b alone versus IL1b + Hcy 100x10-6, p< 0.004). Surprisingly, adding Troglitazone to the Hcy - IL1b - HMC-1 solution blunted the stimulatory response ( 35 pg/mL versus 15 pg/mL, p =0.045 ) . Low concentration Troglitazone in a separate study did not kill HMC-1 cell line per flow cytom-
etry and viability methods.

Conclusions: Hcy induces apoptosis of rabbit cardiomyocytes, and according to our knowledge this is the first experiment that documents this finding. Moreover, Hcy primes the mast cells to the effects of IL1b to produce IL6, this was blunted by PPAR inhibition. Apoptosis and IL6 are involved in ventricular remodeling and heart failure. Further testing is warranted to study the various effects of Hcy on cardiomyocytes.

T011-T112

Use of Abciximab Prior to Primary Angioplasty in ST-
Segment Elevation Myocardial Infarction Results in Early Recanalization of the Infarct-Related Artery: Results of the Multicenter Randomized ReoPro-
BRIDGING Study

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Background. The ReoPro-BRIDGING Austrian multicenter randomized study investi-
gated the effect of Abciximab (ReoPro) on infarct-related artery (IRA) patency and early
reperfusion prior to primary coronary intervention (pPCI). Methods. Thirty-eight patients with ST-segment elevation AMI were treated with ReoPro 0.25 mg/kg bolus followed by 10 μg/min infusion and randomized either to start ReoPro during the organization time (66±33 min) for pPCI (Group 1, n=16) or immediately after pPCI (Group 2, n=20). Serial measurements of creatine kinase (CK), CKMB, myoglobin, and 12-lead ECG were performed at baseline as well as 2, 4, 6, 8, 10, 12, 24 and 48 h thereafter. Results. A trend to a more rapid and higher release of cardiac enzymes was observed in patients of Group 1: rate of rise of CK 164±203 vs 127±170 U/min; CKmax: 92±85 vs 77±62 U/L, CKMBmax: 20±12 vs 105±85 U/L and myoglobin max. 239±43 vs 859±243 ng/ml (P<0.01). SC-segment resolution >50% occurred in 12 patients (67%) in Group 1 and 6 patients (30%) in Group 2 (p=0.024) before pPCI. TIMI flow 0 was observed in 6 (33%) vs 11 patients (50%) of Group 1 vs 2 (p=0.3). Corrected TIMI flow count was significantly lower (57±33 vs 76±22 frames, p=0.034) and angiographic mini-
lum diameter was larger (0.70±0.76 vs 0.29±0.39 mm, p=0.020). Before PCI, 10 patients (30%) in Group 2 (p=0.024) before pPCI, 7 (21%) of 33 patients in Group 1 (p=0.025) in Group 2 (p=0.025) before pPCI. TIMI flow 0 was observed in 6 (33%) vs 11 patients (50%) of Group 1 vs 2 (p=0.3). Corrected TIMI flow count was significantly lower (57±33 vs 76±22 frames, p=0.034) and angiographic minim-
lum diameter was larger (0.70±0.76 vs 0.29±0.39 mm, p=0.020) in Group 2 patients.

Conclusions. Use of ReoPro in the organization phase for pPCI results in early and bet-
ter recanalization of the infarct-related artery prior to pPCI with a consecutive rapid release of cardiac enzymes.

T011-T113

The HNO/Nitric Oxide Donor Angel's Snow Enhances Myocyte Contractility in a PKA-Dependant Manner

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Background: Nitroxy anion (HNO/NO-) donors exert similar positive inotropic/lusitropic
effects in normal and failing hearts but the apoE-/- hearts remained lower levels of the parameter declines. Histopatho-
logical analysis showed the presence of numerous ESC in microcirculation as well as in the
extravascular tissue.

Conclusions: Perfusion with ESC through coronary arteries causes concentration-
dependent changes in heart function. Compared to wild type controls, the hearts of
apoE-/- mice which underwent atherosclerosis-related chronic ischemia appeared to be
better tolerant to high ESC perfusion.