% WOMEN IN POSTGRADUATE TRAINING (1992-2001) (rate of change)

Field	Minimum % women	Maximum % women	r (linear regression)	Slope	P value Cardiol vs others (P<0.05=sig)
Cardiol	9.76	15.50	0.94	0.608	----
Ob-Gyn	48.10	71.40	0.99	2.36	<0.001
Pediatrics	56.50	65.80	0.98	0.856	0.01
Familiy practice	36.20	49.10	0.99	1.23	<0.001
Surgery-General	14.80	23.70	0.99	0.835	0.024
Neurology	25.60	38.20	0.97	1.34	<0.001
All disciplines	28.10	35.62	0.95	0.656	0.608

FEATURED POSTER

1116

Tuesday Featured Poster Presentations

Tuesday, March 09, 2004, 9:00 a.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: Noon-1:00 p.m.

Noon

1116-1 Preconditioning of the Diabetic Myocardium With Acute Metformin Treatment

Aman K. Kakkar, James J. Greer, William H. Bestermann, David J. Lefer, Louisiana State University Health Sciences Center, Shreveport, LA

Metformin is a widely used drug for the treatment of type 2 diabetes mellitus. Metformin activates AMP-activated protein kinase and suppresses lipogenic transcription factors such as sterol regulatory element binding protein-1 (SREBP-1). We investigated the effects of acute metformin treatment on the severity of acute myocardial infarction in both nondiabetic and diabetic mice.

Mice were subjected to left anterior descending coronary artery occlusion (MI) for 30 min. followed by 24 hr. of reperfusion (R). Myocardial area-at-risk (AAR) was determined with *in vivo* Evans Blue dye injection and myocardial infarct size (INF) was measured using TTC staining. db/db diabetic mice and nondiabetic mice (10 weeks of age) were injected (i.p.) with metformin (0.25 mg/Kg) 18 hours before the onset of MI.

Serum glucose levels were 94±6 mg/dL in nondiabetic mice and 323±16 mg/dL in db/db diabetic mice ($p<0.01$ between groups). Metformin treatment did not alter serum glucose levels at the time of MI. Data for myocardial infarct size in nondiabetic mice are shown in Figure 1. Acute treatment with metformin significantly ($p<0.001$) reduced INF/AAR in nondiabetic mice. Data for myocardial infarct size in db/db diabetic mice treated with metformin are shown in Figure 2. Metformin therapy also significantly ($p<0.05$) attenuated the extent of myocardial infarction in the db/db diabetic mouse heart.

We conclude that acute metformin treatment protects against myocardial infarction in both nondiabetic and diabetic mice.

Figure 1

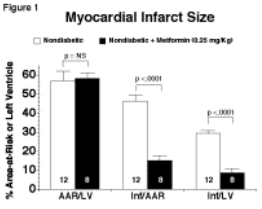
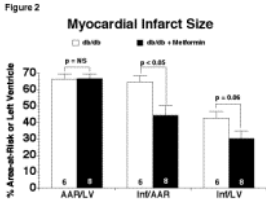


Figure 2



Noon

1116-2 Delivery of Human Myoblasts Transduced With a Novel Bicistronic Vector Carrying Human Vascular Endothelial Growth Factor $_{165}$ and Angiopoietin-I Forms Mature Blood Vessel in the Heart

Lei Ye, Husnain Kh Haider, Ruowen Ge, Peter K. Law, Terrance Chua, Salim Aziz, Eugene KW Sim, National University of Singapore, Singapore, Singapore, National University Medical Institute, Singapore, Singapore

Backgrounds

We hypothesized that synergy between $VEGF_{165}$ and angiopoietin-1 (Ang-1) by using a novel bicistronic vector encoding for two growth factors may lead to better prognosis when delivered using human myoblasts.

Methods

Human myoblasts carrying *lac-z* reporter gene were transduced with adenovirus carrying bicistronic vector encoding for human $VEGF_{165}$ and Ang-1. The transduced myoblasts were functionally assessed by immunostaining and RT-PCR. Myocardial infarction model was created in 17 female swines by coronary artery ligation and grouped as DMEM injected (group-1 n= 6), myoblast transplanted (group-2 n= 5), and myoblast carrying bicistronic vector (group-3 n=6). Three weeks later, 5 ml basal DMEM with $3x10^8$ cells or without cells was injected intramyocardially in and around the infarct and immunosuppressed for six weeks using 5mg /kg cyclosporine. The animal was euthanized and the heart was explanted at 6-12 weeks post cell transplantation and processed for histological studies.

Results

High transduction efficiency of myoblasts (>98%) was achieved by multiple transduction procedure. Myobalsts efficiently secreted $VEGF_{165}$ and Ang-1 simultaneously as revealed by dual fluorescent immunostaining and RT-PCR. Extensive survival of the *lac-z* positive myoblasts was observed in and around the infarct. Average vascular density at low power field (x100) by double immunofluorescence staining for vWFactor-VIII and smooth muscle actin in group-3 (25.07±3.54; 23.71±3.15) was significantly higher than group-1 (16.0±2.56 *p<0.01*; 7.87±1.46 *p<0.01*), group-2 (16.22±3.15 *p<0.01;* 11.89±3.06 *p<0.01*) respectively at 6 weeks post treatment. The mature blood vessels count in group-3 was the highest (94.6%). Regional blood flow (ml/min/g) at 6 weeks improved in group-3 (3.00± 0.37) significantly as compared to group-1 (1.22± 0.45 *p<0.01*) and group-2 (1.12± 0.14 *p<0.01*). The Ejection fraction in bicistronic group-3 was 43.0 ±10.4% which was significantly higher than the control group-1 (34.67±15.37, $p<0.05$).

Conclusion

Multiple growth factor gene delivery using myoblast as a carrier leads to angiomyogenesis with higher percentage of mature blood vessel formation.

Noon

1116-3 Regulation of Intercellular Adhesion Molecule-1 Transcription in Ischemic-Reperfused Myocardium Through STAT3 Activation

Xiao Ping Yang, Anthony DiPaula, Jr., Lewis C. Becker, Johns Hopkins University School of Medicine, Baltimore, MD

Intercellular adhesion molecule-1 (ICAM-1) is rapidly upregulated on endothelial cells (ECs) during ischemia-reperfusion (I-R) and mediates tissue leukocyte accumulation and subsequent cell injury. Different from other adhesion molecules, the ICAM-1 proximal promoter contains a STAT1/STAT3 motif (GAS sequence). Because this motif flanks an SP1 binding site which is very close to the TATA box, it may be important for regulation of ICAM-1 transcription. To study the role of STAT after myocardial I-R, open chest anesthetized rats underwent anterior descending coronary artery occlusion for 35 min and reperfusion (R) for 0, 15, 30, 60, 120, or 240 min. Myocardial samples were rapidly frozen and analyzed for STAT activation (gel shift and immunoprecipitation), ICAM-1 mRNA level (real-time R-T PCR) and tissue cytokines (multiplexed sandwich ELISA). STAT was activated by 15 min R and peaked at 60 min R. Gel supershift assay identified the activated STAT isoform as STAT3 without STAT1. ICAM-1 mRNA level increased rapidly at 30 min R, and remained increased through 120 min R. Coimmunoprecipitation of nuclear extract indicated that STAT3 was bound to SP1, suggesting possible transcriptional cooperativity. Cytokine assay showed an increase in myocardial IL-6 during I-R. To determine whether activated STAT3 could regulate ICAM-1 transcription in ECs, cultured human cardiac microvascular endothelial cells were exposed to IL-6, 40 ng/ml. Phosphorylated STAT3 was identified by immunoprecipitation within 15 min, and ICAM-1 mRNA increased shortly afterwards at 30 min after IL-6 exposure. Transfection of a GAS decoy oligonucleotide to inhibit STAT3 partially blocked IL6-induced ICAM-1 mRNA expression. The results indicate that STAT3 is activated very quickly in the myocardium following I-R, interacts with SP1 in the nucleus, and is responsible for rapid upregulation of ICAM-1 transcription.

Noon

1116-4 Consequences of Hemodynamic Instability After Carotid Artery Stenting

Alex Abou-Chebl, Rishi Gupta, Christopher T. Bajzer, H. Christian Schumacher, Jay S. Yadav, The Cleveland Clinic Foundation, Cleveland, OH

Purpose: To determine if hemodynamic instability (HI) during extracranial carotid artery stenting (CAS) increases the risk of adverse events.

Background: CAS has been utilized in patients considered at high risk for carotid endarterectomy (CEA). HI is a known side effect of carotid sinus stimulation induced by CEA and CAS. Recent literature suggests that the presence of HI may increase the risk of adverse cardiovascular events following CEA, however the frequency and consequences of HI have not been systematically evaluated in a large population of patients undergoing CAS.

Methods: Patients with HI were identified from the carotid stent registry maintained at The Cleveland Clinic Foundation. This is a prospectively collected database of all patients undergoing extracranial CAS for atherosclerotic lesions between 1999-2002. In addition, the medical records of all CAS patients were retrospectively reviewed to identify patients with peri-procedural HI who may have been missed by the database. HI was defined as symptomatic or asymptomatic hypotension (systolic blood pressure < 90) or braycardia (heart rate < 60). The use of vasopressors or atropine and all peri-procedural adverse events were study endpoints.

Results: A total of 404 consecutive patients with a mean age of 70.5 ± 9.8 yrs were studied. Sixty four percent were men. The mean stenosis severity was 85.6 ± 10.1%. Peri-procedural hypotension occurred in 113 (28%) patients and required vasopressors in 85