and mid-myocardial sonomicrometry crystals for LV volume determination. Pneumatic assessment in conscious state. CHF (20-30% reduction in dP/dt and LV end diastolic volume/volume ratio 0.7±0.3 vs 6.2±0.3 mg/ml, volume 8.2±0.3 ml/m2, systolic diameter (1.4±0.5 cm) and increased SF (5.6±17 in KO mice compared to untreated group (p<0.01). Sim did not alter LV function in WT mice. eNOS expression was preserved in KO mice. Phospho-eNOS expression was lower in KO mice compared to WT and KO mice. Conclusions: Disruption of the BZ results in reduced eNOS activation and progressive cardiac remodeling and dysfunction. Sim reduces contractile dysfunction and remodeling by increasing AKT-mediated eNOS phosphorylation. Since BSR and eNOS expression is reduced in human heart failure, this novel effect of Sim may be potentially beneficial in the treatment of heart failure.

Results

Phospho-Akt, which phosphorylates eNOS, was also increased in KO vs WT mice. Phospho-eNOS expression was lower in KO mice compared to WT and KO mice. Conclusions: ASMT provided mild improvements in hemodynamics and LV function in conscious dogs with chronic heart failure.

1135-85

Cellular Cardiomyoplasty With Bone Marrow Cells Improves Cardiac Performance in Heart Failure Induced by Healed Infract in Rats

Emerson Oliveira, V. Pinho-Ribeiro, J. P. Saar Zwerneck, R. C. Santos Goldenberg, Elizabeth Mattos, Dilne P. Dohmann, Massa O. Masuda, Antonio C. Campos de Carvalho, Instuto de Biotitica Carlos Chagas Filho, UFRJ, Rio de Janeiro, Brazil, Instituto de Medicina do Rio de Janeiro, Brazil, Background: Post-infarction congestive heart failure is a leading cause of death in developed and developing countries. The heart failure results from the extensive cell death and the remodelling process may cause a decrease in myocardial function. Severe cardiovascular diseases can result in chronic heart failure. The heart failure results from the extensive cell death and the remodelling process may cause a decrease in myocardial function. Severe cardiovascular diseases can result in chronic heart failure.

1135-86

Selective Ablation of Insulin Receptor Substrate-1 Decreases Cardiac Contractility In Vivo Without Attenuating PAI-1 Expression or Perivascular Fibrosis

Satoshi Fuji, Tomoko Furumoto, Hisako Onozuka, Taisel Mikami, Daisuke Goto, Tarikuzan Zaman, Taiko Sugawara, Yashuo Terasuchi, Takashi Kadowaki, Burton E. Sobel, Akira Kitabata, Hokkaido University, Sapporo, Japan, We have previously shown that coronary perivascular fibrosis is augmented by increased expression of insulin receptor substrate-1 (IRS-1)-mediated signaling. Insulin injected, IRS-1 knock-out (KO) mice lack 175-kDa tyrosine-phosphorylated protein (IRS-1) pivotal in many processes involved in remodeling of the extracellular matrix. IRS-1 KO mice exhibit normal glucose tolerance. We investigated the potential role of insulin receptor substrate-1 (IRS-1)-mediated signaling. Insulin injected, IRS-1 knock-out (KO) mice lack 175-kDa tyrosine-phosphorylated protein (IRS-1) pivotal in many processes involved in remodeling of the extracellular matrix. IRS-1 KO mice exhibit normal glucose tolerance. We investigated the potential role of insulin receptor substrate-1 (IRS-1)-mediated signaling.

Impact of Autologous Skeletal Myoblast Transplantation on Hemodynamics and LV Function in Repeated Coronary Microembolization-Induced Heart Failure in Awake Dogs

Kurahara M., Hua Zhou, Geng-Hua Yi, Eva M. Becker, Warren Smecker, An-Usuo Gu, Jack Harvey, Rance Kao, Ge-Ping Zhang, Satoshi Mihry, Myung J. Lee, Jie Wang, Daniel Burkoff, Mount Sinai School of Medicine, New York, New York, NY, Background: Previous studies suggested that autologous skeletal myoblast transplantation (ASMT) improves left ventricular (LV) function in small animals following myocardial infarction. We tested the effects of ASMT on hemodynamics and LV function in repeated coronary microembolization-induced chronic heart failure (CHF) in conscious dogs. Methods: 13 dogs were chronically instrumented with LV and aortic pressure sensors and LV cavity, BZ, apex, and mid-myocardial sonomicrometry crystals for LV volume determination. Pneumatic cuff was placed to perform inferior vena cava occlusion. Each dog underwent baseline assessment in conscious state. CHF (20-30% reduction in dP/dtmax and LV diastolic pressure) was induced by daily coronary microembolizations via a chronically implanted coronary catheter. A skeletal muscle biopsy was performed and myoblasts were isolated and expanded. 2.8X10^7-7.6X10^7 myoblasts were injected into the infracted region of 8 dogs after establishment of CHF. Saline injection (sham) was performed in 5 control dogs. Animals were evaluated every 2 weeks for up to 10 weeks. Hemodynamic measurement included LV systolic and diastolic pressure, LV outflow tract pressure, and mean arterial pressure. Ejection fraction was determined by echocardiography. Ees (LV contractility) and alpha (LV stiffness) were determined by pressure volume analysis. Results: Compared to saline injection, ASMT significantly increased dP/dtmax (15.0±4.3% vs 6.5±2.3%, P<0.05), mean arterial pressure (12.7±2.1% vs 6.2±1.9, P<0.05), and Ees (2.8±1.1% vs 4.8±1.4% after an average of 8+2 weeks follow-up (all the values are expressed as percent change from baseline CHF, P<0.05 for each comparison). LV end diastolic pressure (6.5±1.7% vs 3.5±1.1%, and alpha (4.2±2.5% vs 6.6±1.4% trended to decrease and ejection fraction trended to increase (3.3±3.4% vs 4.2±2.7% although these parameters did not reach significant difference. Conclusions: ASMT provided mild improvements in hemodynamics and LV function in conscious dogs with chronic heart failure.

1135-84

Selective Ablation of Insulin Receptor Substrate-1 Decreases Cardiac Contractility In Vivo Without Attenuating PAI-1 Expression or Perivascular Fibrosis

Satoshi Fuji, Tomoko Furumoto, Hisako Onozuka, Taisel Mikami, Daisuke Goto, Tarikuzan Zaman, Taiko Sugawara, Yashuo Terasuchi, Takashi Kadowaki, Burton E. Sobel, Akira Kitabata, Hokkaido University, Sapporo, Japan, We have previously shown that coronary perivascular fibrosis is augmented by increased expression of insulin receptor substrate-1 (IRS-1)-mediated signaling. Insulin injected, IRS-1 knock-out (KO) mice lack 175-kDa tyrosine-phosphorylated protein (IRS-1) pivotal in many processes involved in remodeling of the extracellular matrix. IRS-1 KO mice exhibit normal glucose tolerance. We investigated the potential role of insulin receptor substrate-1 (IRS-1)-mediated signaling. Insulin injected, IRS-1 knock-out (KO) mice lack 175-kDa tyrosine-phosphorylated protein (IRS-1) pivotal in many processes involved in remodeling of the extracellular matrix. IRS-1 KO mice exhibit normal glucose tolerance. We investigated the potential role of insulin receptor substrate-1 (IRS-1)-mediated signaling.