Cardiac Hypertrophy / Cardiomyopathy 1 (M)

PE5

March 19 (Sat)

Poster Presentation Area (Exhibition Hall A+B+C)

9 : 55—10 : 40

PE-025

Functional and Morphological Characteristic of Myocardial Hypertrophy Regression and Apoptosis

Galina A. Drozdova
Anotoliyi V. Pasechnik, Michail L. Blagonravov, Victor A. Frolov
Russian Peoples Friendship University, Moscow, Russia

Rabbits with vasorenal hypertension (12 weeks) were treated with verapamil, lotensin and lopressor in mild therapeutic dosages for 6 weeks. After treatment blood pressure in a.carotis and intraventricular pressure were measured by invasive methods. After killing myocardial morphological investigation was carried out. Markers of apoptosis included oligonucleosomal DNA fragmentation in the extracted cardiac DNA and morphologically the nucleus quantity and their fragments, lying free in the intracellular area. All the drugs reduced blood pressure, real cardiac workload and myocardial mass: most of all lotensin > 40 % and least of all lopressor > 24%. In hypertrophy regression caused by lotensin interrelation of cardiac structural elements remains similar as the one in myocardial hypertrophy: capillary and mitochondria lowering as well as collagen hyperplasia were observed. Myocardial mass reduction after the use of verapamil is accompanied by increase in the quantity of blood vessels per unit myocardial mass. Treatment with lopressor caused the normalization of myocardial structures. Hypertrophy regression was accompanied >120 % increase in DNA fragmentation; the quantity of free nucleus also increased > 85 %. Thus, regression of myocardial hypertrophy, caused by different drugs, is not always absolutely identical. The increase of apoptosis can be one of possible mechanism of decrease of myocardium mass in drug-induced hypertrophy regression.

PE-026

SPRR1A is a gp130 Pathway and Stress Inducible Gene that Prevents Myocardial Injury during Ischemia

[1]Hideo Yasukawa
[2]Sylvain Pradervand, [3]Tomoyuki Nakamura, [4]Yusuke Sugi, [4]Takahiro Mori, [4]Hiroshi Kudoh, [4]Kiyoko Takemiya, [4]Nobuhiro Tahara, [4]Hisashi Kai, [2]Chien Kenneth, [1]Tsutomu Imaizumi
[1]Cardiovascular Research Institute, Kurume University, Kurume, [2]Institute of Molecular Medicine, University of California, San Diego, San Diego, USA, [3]Horizontal Medical Research Organization, Kyoto University, Kyoto, [4]Department of Internal Medicine (III), Kurume University, Kurume

The interleukin-6 cytokines, acting via gp130 receptor pathways, play a pivotal role in the reduction of cardiac injury induced by mechanical stress or ischemia and in promoting subsequent adaptive remodeling of the heart. In this study, a combinatorial strategy based on microarray and SAGE analyses have identified the small proline rich repeat protein 1A (SPRR1A) is downstream target of gp130 signaling, that are strongly induced in cardiomyocytes responding to mechanical stress or ischemia. Up-regulation of SPRR1A was markedly reduced in the gp130 cardiomyocyte restricted knockout mice. In cardiomyocytes, MEK1/2 inhibitors prevented SPRR1A induction by gp130 cytokines. Furthermore, binding of NF-IL6 (C/EBPbeta) and c-Jun to the SPRR1A promoter was observed after cardiotrophin1 stimulation in cardiomyocytes, suggesting that MAP kinase-induced activation of NF-IL6 and c-jun is important for SPRR1A induction. Interestingly, immunohistochemical analysis revealed that SPRR1A induction after mechanical stress of pressure overload was restricted in myocytes surrounding piecemeal necrotic lesions. A similar expression pattern of SPRR1A was found in post-infarcted rat hearts. Both in vitro and in vivo ectopic expression of SPRR1A protected cardiomyocytes against ischemic injury. Thus, this study identifies SPRR1A as a novel stress-inducible downstream mediator of gp130 cytokines in cardiomyocytes and demonstrates its cardio-protective effect against ischemic stress.

PE-027

Beneficial Effects of Non-Fat Diet on Lipotoxic Cardiomyopathy Due to Systemic Carnitine Deficiency

Toru Asai
Ryotaro Takahashi, Hisashi Murakami, Ryuichiro Murakami, Toshihisa Hirai, Yasushi Numaguchi, Hideo Matsui, Kenji Okumura, Toyoaki Murohara
Department of Cardiology, Nagoya University Graduate School of Medicine, Nagoya

Recent studies suggest that excess lipid accumulation in cardiomyocytes due to imbalance between fatty acid uptake and utilization promote lipotoxic cardiomyopathy. We investigated the effect of dietary lipid cessation on a murine model of systemic carnitine deficiency (SCD), juvenile visceral steatosis (JVS) mouse, which develops pathological cardiac hypertrophy with lipid accumulation due to depressed fatty acid utilization. Both wild-type mice and JVS mice were fed a non-fat diet or a normal diet from 4 weeks of age. At 8 weeks of age, non-fat diet attenuated the cardiac hypertrophy and LV dilatation with improvement of LV fractional shortening and survival in JVS mice. These results suggest that excess myocardial lipid accumulation due to depressed fatty acid utilization may play a crucial role in the development of lipotoxic cardiomyopathy in SCD.

	Wild-type mice		JVS mice	
	Normal diet	Non-fat diet	Normal diet	Non-fat diet
Ventricular weight/body weight (mg/g)	3.60±0.04	3.75±0.05	9.49±0.20*	6.68±0.16*,†
LV fractional shortening (%)	53.2±0.7	52.8±0.5	28.0±2.0*	41.3±1.3*,†
LV end-diastolic dimension (mm)	2.27±0.08	2.37±0.03	3.36±0.13*	2.63±0.06†
Survival rate at 16weeks of age (%)	100	100	10.3*	77.3†

Mean±SEM, *p<0.001 vs Wild-type, †p<0.001 vs JVS mice treated with normal diet.

PE-028

Erythropoietin Improves Cardiac Function of Doxorubicin-induced Cardiomyopathy

[1]Longhu Li
[1]Genzou Takemura, [1]Shusaku Miyata, [1]Masayasu Esaki, [1]Hideshi Okada, [1]Yiwen Li, [1]Hiromitsu Kanamori, [1]Rumi Maruyama, [1]Shinya Minatoguchi, [2]Takako Fujiwara, [1]Hisayoshi Fujiwara
[1]Department of Cardiology, Gifu University Graduate School of Medicine, Gifu, [2]Department of Food Science, Kyoto Women's University, kyoto

Doxorubicin(DOX)-induced cardiomyopathy accompanying heart failure limits the therapeutic use of DOX for patients with malignant diseases. In the present study, we examined possible beneficial effects of erythropoietin(EPO), which was reported to be protective against ischemic cadiac diseases, to DOX-induced cardiomyopathy. DOX-induced cardiomyopathy was generated in mice by a single intraperitoneal injection of DOX(15 mg/kg). EPO(5000 IU/kg/time) was then intraperitoneally injected to mice three times; the same volume of saline was used for the control group. Mice were examined 2 weeks later. In the control mice, left ventricular dilatation and dysfunction were apparent according to echocardiography and cardiac catheterization, which were found significantly improved in the mice treated with EPO. Left ventricular cavity was less dilated at autopsy and cardiac fibrosis and CD45-positive leukocyte infiltration were less significant in the EPO-treated hearts. Western blot analysis revealed that EPO significantly restored myocardial Akt that was down-regulated in DOX-induced cardiomyopathy. Electron microscopy revealed that degenerative changes of cardiac myocytes showing non-apoptotic structure were apparently mitigated in the EPO-treated group, compared with the control group. These findings suggest that cardioprotective effects of EPO on DOX-induced cardiomyopathy may be related with anti-fibrosis, anti-inflammation, Akt restoration, and cardiomyocyte protection via not anti-apoptotic mechanism. The present study provides the first evidence of efficacy of EPO against DOX-induced cardiomyopathy.