0434

Evaluation of ROS generation and mitochondrial respiration in atrial samples from diabetic and non-diabetic coronary patients

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Abnormalities in redox balance together with mitochondria dysfunction are currently recognized as major pathomechanisms that underlie the progression of chronic cardiovascular diseases and diabetes mellitus (DM). In particular, the generation of reactive oxygen species (ROS) has been systematically reported to increase during the evolution of DM.

The aim of the present study was to assess the impact of diabetes on ROS production and mitochondrial respiratory function in myocardium of diabetic and non-diabetic patients with coronary heart disease (CHD) with preserved ejection fraction. Patients that underwent non-emergency cardiac surgery were randomized in 3 groups: (1) Control group – valvular patients with no documented coronary heart disease, (2) CHD group – patients with documented CHD without DM, and (3) CHD + DM group – patients with documented CHD and DM. Generation of superoxide anion was assessed by laser scanning confocal microscopy in frozen sections of right atrial appendages using the dihydroethidium staining. Mitochondrial oxygen consumption was measured in permeabilized atrial fibers by high resolution respirometry.

Our data showed a significant decrease in complex I-supported respiration for coronary patients with and without diabetes whereas complex II-supported respiration was found to be impaired only in the diabetic group. No significant differences could be detected with respect to superoxide production between CHD and CHD + DM groups.

0155

Selenoprotein T attenuates the development of left ventricular dysfunction after myocardial infarction in rats

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Selenoproteins are mediators of the essential micronutrient selenium, but their biological effects are not yet fully understood. Selenoprotein T (SelT), a recently discovered thioredoxin-like selenoprotein, is abundant during embryonic development but declines during adulthood. Bioinformatical studies suggested that SelT had antioxidant properties but its role has not already been established in vivo. Preliminary data obtained in our laboratory showed that myocardial infarction increases SelT protein expression in mouse heart as revealed by Western blotting analysis, suggesting that SelT may play a yet unexplored role in the cardiovascular system. Thus, we sought to investigate SelT’s role in myocardial infarction. Male Wistar rats were subjected to either cardiac ischemia (45 min) followed by reperfusion (IR) or sham surgery. Five days before IR, SelT (15 μg/kg/day, IP) or saline infusion was started by osmotic minipump. Eight days after myocardial infarction, left ventricular (LV) function was assessed by echocardiography, MRI and LV hemodynamics (pressure-volume loops). IR resulted in a significant increase of LV systolic and diastolic diameters, in a decrease of cardiac output and fractional shortening. This was associated with a decrease of LV end-systolic pressure and an increase of LV end-diastolic pressure. SelT restored cardiac output and LV fractional shortening (+26% and +52%, respectively in comparison with I/R) associated with an improvement of LV end-diastolic/end-systolic pressures and LV tissue perfusion (–61%, +54% and +30%, respectively in comparison with I/R). Furthermore, SelT did not modify LV infarct size. SelT, administered before IR, preserves LV function and perfuses in a rat model of myocardial infarction and might be a new therapeutic target in the treatment of this disease.

0217

Antioxidant and protective effects of a pu-erh tea extract (camellia sinensis) on primary cultured rat cells

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Oxidative stress is recognized to be implicated in the pathogenesis of cardiovascular and non-alcoholic fatty liver diseases. It is well known that tea is a rich source of phenolic compounds known for their antioxidant activity. Consequently, the antioxidant and protective effects of phenolic compounds from a pu-erh tea extract (PTE) were evaluated on primary culture of rat hepatocytes (PTE was quantified in its composition in catechins and polyphenol content by HPLC analysis. The antioxidant capacity of tea products was determined using TAC and DPPH assay methods. Then, antioxidant and hepatoprotective effects were determined by pretreating hepatocytes during 4h with various concentrations of PTE (25, 50 and 100μg/ml), epigallocatechin-3-galate (EGCG) as major catechin of PTE (12μM corresponding to 100μg/ml) and N-acetylcystein (NAC) (0.1 and 1mM) as an antioxidant reference. Then, cells were stressed for 1h with 150μM tert-Butyl hydroperoxide (TBHP). Viability was determined by real time cellular impedance and MTT assays. Oxidative stress was measured by CellRox, MitoSox and TMRE stainings and evaluated by fluorescence microscopy on an ArrayScanXTI high Content Analysis Platform (Cellomics Inc.). We found that TBHP induced oxidative stress (+1.5 fold increase vs control) was prevented by PTE pretreatment (+1.07 fold increase vs control) and EGCG (+1.1 fold increase vs ctrl). We also demonstrated that PTE pretreatment protected rat hepatocytes (~28% mortality relative to TBHP) against TBHP induced mortality (+23% mortality relative to ctrl). However, EGCG did not prevent death in the same proportion that PTE (~9% mortality relative to TBHP). In this study, we reported that PTE pre-exposure prevented oxidative stress and mortality induced by TBHP. Moreover, we reported here that PTE has higher antioxidative and protective effects than EGCG alone, well known for its antioxidative effects, which means that EGCG may act in synergy with other PTE components.

0294

PTP1B endothelial gene deletion limits cardiovascular dysfunction and mortality during experimental septic shock

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Sepsis-associated myocardial and vascular dysfunction is one of the main causes of mortality in critically ill patients, for which no efficacious therapies exist. We recently showed that PTP1B gene deletion affords myocardial protection in experimental heart failure. However, whether PTP1B inactivation opposes sepsis-associated myocardial dysfunction is unknown. Thus, we assessed the effect of endothelial PTP1B gene specific deletion on left ventricular (LV) function and inflammation in mice with endotoxemic shock. We used endoPTP1B−/− mice obtained with classical Cre-loxP system. To obtain endoPTP1B−/−, we crossed Tie2-Cre (endothelial-specific promoter) with PTP1B-floxed (floxed). Septic shock is induced by intraperitoneal injection of lipopolysaccharide (LPS) followed by a subcutaneous fluid resuscitation at 1 and 5 hours after LPS injection. Differents studies were realized at 8 hours after LPS injection. LV function was evaluated by echocardiography. Vascular function was evaluated by arteriography. Plasma samples were collected to measure the production of inflammatory cytokines by Elisa multiplex assay.

Plasmatic levels of TNF-α and IL-6 are increased 8 hours after LPS injection showing a systemic inflammatory response with no significant difference between