Conclusions Microarray analysis identified expression differences between troponin-positive and troponin-negative patients over time. Specific biological pathways possibly showing the late effects of acute events can be used to discover biomarkers of coronary heart disease.

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BAS/BSCR23 APOCYNIN TREATMENT REDUCES HIGH-FAT DIET-INDUCED OBESITY AND HYPERTENSION BUT HAS NO SIGNIFICANT EFFECT ON HYPERGLYCAEMIA

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Junjie Du, Jian-Mei Li. *Cardiovascular Research Team, Faculty of Health and Medical Sciences, University of Surrey, Guildford, Surrey, UK*

Dietary obesity is associated with insulin resistance and cardiovascular oxidative stress. Apocynin has traditionally been regarded as an inhibitor of NADPH oxidase but recently it was reported to be predominately an antioxidant in the vascular system. In this study we examined the antioxidative stress effect of apocynin on high-fat diet (HFD)-induced metabolic disorders and endothelium dysfunction. Mice (C57/BL6 at 6–7 month of age, n=7 per group) were fed with a HFD (44% fat) or normal chow diet (12% fat) for 15 weeks. The treatment group was supplied with apocynin (5 mM) dissolved in drinking water and the control group was supplied with vehicle. Compared with chow diet, a HFD significantly increased the body weight (~35%), the systolic blood pressure (BP, 13%) and the levels of fasting blood glucose (46%). Apocynin treatment significantly attenuated the HFD-induced obesity (44.1%±2.96 vs 37.5%±2.43 g) and the high BP (136.7%±7.9 vs 118.4%±5.3 mm Hg), but had no significant effect on blood glucose levels (8.74%±1.62 vs 8.13%±1.68 mmol/l). Compared with a chow diet, HFD significantly impaired the endothelium-dependent vessel relaxation to acetylcholine as examined by an organ bath, and this was reversed to control levels by adding tiron, which is a cell membrane permeable superoxide scavenger. Apocynin treatment preserved endothelium-dependent vessel relaxation to acetylcholine in the HFD group. In conclusion, antioxidant treatment with apocynin attenuated the HFD-induced increases in body weight; blood pressure and preserved the endothelium function. However, apocynin had no effect on HFD-induced increase in fasting blood glucose levels.

BAS/BSCR24 SPIRONOLACTONE REVERSES THE ADVERSE EFFECTS OF ALDOSTERONE AND HYPOXIA ON ADIPOSE TISSUE

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S Withers, C Agabiti-Rosei, D M Livingstone, R Aslam, R A Malik, A M Heagerty. *Cardiovascular Research Group, School of Biomedicine, University of Manchester, Manchester, UK*

We tested the hypothesis that aldosterone causes a loss of the normal anticontractile function of healthy fat via a hypoxia-related pathway, which can be rescued using spironolactone. Healthy rat mesenteric arteries (~250%μM diameter) and perivascular fat were investigated using wire myography and Perl's Prussian blue staining for activated macrophages. The effects of aldosterone%±spironolactone were assessed after incubation for 10 min and 3 h, and experimental hypoxia (95% N_2/5% CO_2) for 2.5 h. Contractile responses were calculated as a percentage of KCl contraction and expressed as mean±SEM. Macrophage activation was expressed semiquantitatively and expressed as macrophage abundance values (MAV). The anticontractile capacity of healthy fat was lost upon incubation with aldosterone (5 nM) (fat: 90±4% n=36, fat+10 min aldosterone: 165±5% n=25, fat+3 h aldosterone 172%±12% n=7) and was associated with an increase in activated macrophages (immediately fixed: 2.2±0.5% n=5 vs 10 min aldosterone: 3.8±0.4% n=5, p=NS; immediately fixed: 2.2±0.5% n=5 vs 3 h aldosterone: 4.7±0.3% n=5, p=0.0313). Spironolactone (10%μM) restored anticontractile activity after incubation for 3 h only (3 h:111±4% $p<0.05$, n=5) and caused a significant reduction in macrophage activation (3.0±1.0%, n=5). As for aldosterone, hypoxia caused an increase in contractility (149±17% n=15) and macrophage activation (5.5±0.5% n=5), which was reversed upon incubation with spironolactone (contractility: 120±12% n=5;MAV: 3.3±0.8%, n=3, p=0.500). Aldosterone ameliorates the anticontractile capacity of healthy fat by a common pathway to hypoxia, which correlates with an increase in the number of activated macrophages within adipose tissue. Spironolactone can restore the effect of hypoxia on contractility and macrophage activation in the absence of aldosterone.

BAS/BSCR25 IMPORTANCE OF INTERACTION BETWEEN PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-α AND NADPH OXIDASES IN CARDIAC HYPERTROPHY

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E Robinson, D J Grieve. *Centre for Vision and Vascular Science, Queen's University Belfast, UK*

Peroxisome proliferator-activated receptor-α (PPAR-α) and NADPH oxidases are known individually to have essential roles in left ventricular hypertrophy (LVH). However, the potential importance of interaction between the two in overall regulation of the hypertrophic phenotype is unclear. Here Nox2−/−, PPAR-α−/− and matched wild-type (WT) mice (n=8) underwent thoracic aortic constriction (TAC) or sham surgery and were studied 7 days later. No differences in basal contractile function (echocardiography) or LVH were observed. However, increased mRNA expression (real-time RT-PCR) of PPAR-α in Nox2−/− (1.49%±0.08 vs WT, 1.04%±0.11 arbitrary units; $p<0.05$) and of Nox2 in PPAR-α−/− mice (3.61%±1.21 vs WT, 0.95%±0.12 arbitrary units; $p<0.05$), together with increases in NADPH oxidase activity (lucigenin-enhanced chemiluminescence: PPAR-α−/−, 6.81%±0.94 vs WT, 3.49%±0.35 RLU; $p<0.05$), indicated co-regulation of myocardial Nox2/PPAR-α. As expected, TAC-induced LVH was significantly increased in PPAR-α−/− versus WT mice, but similar in Nox2−/− mice. Decreases in fractional shortening in WT mice (−16%±3%) were augmented in PPAR-α−/− and attenuated in Nox2−/− mice after TAC (−28%±4 and −10%±3; $p<0.05$ vs WT). PPAR-α mRNA expression was increased in WT, but not Nox2−/− mice (52%±11 vs −17%±11; $p<0.05$), while Nox2 mRNA expression remained elevated (1.33%±0.22 vs 0.69%±0.16 arbitrary units; $p<0.05$) in PPAR-α−/− versus WT mice after TAC. NADPH oxidase activity was significantly increased in TAC WT, but not PPAR-α−/− or Nox2−/− mice, although absolute levels in PPAR-α−/− remained elevated compared with WT sham. These data indicate co-dependence of PPAR-α and NADPH oxidases in the setting of pressure-overload LVH, although the underlying mechanisms are clearly complex.

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