

Oral session 8

Poster session 2

Name of presenter: Alex Ali Sayour

### Abstract # 53

#### Comparison of the anti-remodeling effect of pressure unloading and chronic soluble guanylate cyclase activation in rats with left ventricular myocardial hypertrophy

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**Background:** Pressure unloading induces the regression of left ventricular (LV) myocardial hypertrophy (LVH). Recent findings suggest that chronic pharmacological activation of the soluble guanylate cyclase (sGC) - cyclic guanosine monophosphate (cGMP) pathway also promotes anti-remodeling in LVH. Our aim was to investigate the effects of the sGC activator cinaciguat in a rat model of LVH and compare it to pressure unloading therapy.

**Methods and results:** Abdominal aortic banding was performed in rats for 6 or 12 weeks. Sham operated animals served as controls. Pressure unloading was induced by removing the aortic constriction after week 6. The animals were treated from week 7 to 12, with p. o. cinaciguat (10 mg/kg/day) or placebo. Cardiac function and morphology were assessed by left ventricular pressure-volume analysis and echocardiography. In addition, markers of myocardial hypertrophy, fibrosis, nitro-oxidative stress, apoptosis and cGMP signaling were analyzed.

Pressure unloading effectively reversed LVH, decreased collagen accumulation and provided protection against oxidative stress and apoptosis. Regression of LVH was also associated with a full recovery of cardiac function. In contrast, chronic sGC activation had only a minor effect on the extent of pre-established hypertrophy. However, the increased cGMP signaling significantly decreased the extent of myocardial fibrosis, nitro-oxidative stress and cardiomyocyte apoptosis. The inhibition of pathological processes resulted in preserved systolic and diastolic function.

**Conclusion:** Our results indicate that both chronic sGC activation and pressure unloading exert anti-remodeling effects and improved LV function in LVH, however, in a different way.

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Oral session 13

Poster session 2

Name of presenter: Natalie Savage

### Abstract # 54

#### The role of cardiomyocyte Nox4D, a redox-active splice variant of NADPH oxidase-4

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**Background:** NADPH oxidase-4 (Nox4) is a reactive oxygen species (ROS)-generating enzyme that has protective effects in the heart through several redox-mediated signalling pathways. We previously identified that a splice variant of Nox4, Nox4D, is nuclear-localised, capable of ROS production, and is expressed in cardiomyocytes. The aim of this project was to investigate the effects of Nox4D in cardiomyocytes in vivo.

**Methods and results:** We generated mice with inducible cardiomyocyte-specific overexpression of Nox4D (icsNox4D). After tamoxifen induction in adult mice, icsNox4D showed a 10-fold increase in Nox4D protein level in the heart compared to controls, whilst echocardiography revealed similar cardiac structure and function. In vitro overexpression of Nox4D increased proliferation of neonatal rat cardiomyocytes but this was unchanged in adult hearts, as assessed by EdU incorporation and the expression of cell cycle genes. The impact of icsNox4D on the response to MI induced by permanent left anterior descending coronary artery (LAD) ligation was next determined. There were no differences between icsNox4D and control mice in infarct size, LV function or LV remodelling 4 weeks post-MI. Furthermore, this correlated with no differences in the gene expression of hypertrophy or cell cycle markers in icsNox4D in either the infarct border zone or remote zone. Ongoing work is investigating the effects of Nox4D overexpression in cultured adult cardiomyocytes.

**Conclusion:** Cardiomyocyte-specific overexpression of Nox4D in the adult mouse heart is well tolerated and appears not to induce an obvious detrimental phenotype. The responses of these mice to other stresses should be investigated.

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Poster session 2

Name of presenter: Monika Bartekova

### Abstract # 55

#### Cardioprotective effects of acute and chronic treatment with flavonoid quercetin against ischemia/reperfusion injury in isolated rat hearts: focus on the role of age in the efficiency of treatment

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**Background:** Quercetin is a plant flavonoid with potential beneficial effects in cardiovascular system. The aim of the present study was to explore the ability of quercetin to prevent ischemia/reperfusion (I/R) injury of the heart in its acute and chronic administration.

**Methods and results:** In the chronic treatment, impact of age on the efficiency of quercetin in preventing I/R injury was also analyzed. Quercetin was applied either directly to perfusion solution before or after ischemia (acute treatment; 15µmol/L), or orally to the rats before the hearts were excised and perfused (chronic treatment; 20mg/kg/day for 4 weeks). In the chronic treatment, effects of quercetin were tested in juvenile (4-weeks old) and adult (12-weeks old) rats.

The results demonstrated that quercetin exerts cardioprotective effects against I/R injury in both acute and chronic settings; however, in chronic administration its effects depends on the age of the treated