**Abstract: P301**

**Inflammatory signaling is activated in association with differential expression of lncRNAs in heart failure with preserved systolic function**

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**Introduction/ Background**

Chronic inflammation of the myocardium is focused as the crucial mechanism of the cardiac remodeling. Long noncoding RNAs (lncRNAs) have been demonstrated to play a pivotal role in the pathogenesis of cardiac hypertrophy and failure, but the mechanism of their contribution is still unclear.

**Purpose**
We investigated the changes in the pro- and anti-inflammatory gene expression and tried to identify the associating lncRNAs in the process of cardiac remodeling.

**Methods**
Dahl salt-sensitive rats (n=21, 6 week-old) were divided to two groups. Group 1 (n=9) was fed with diet containing 0.3%NaCl and group 2 (n=12) with 8%NaCl. Echocardiography was performed every one week. Three rats of each group were sacrificed every one week after 12 week-old for histological examination and investigation of total RNA of the heart. Microarray profiling and real-time PCR analysis of mRNA and lncRNA was performed.

**Results**
The hearts of group 2 showed preserved left ventricular ejection fraction (EF) with significant increase in wall thickness and myocardial cell hypertrophy by 14 week-old. After then EF progressively decreased leading to sudden death. Group 2 were again divided to two groups according to EF at the time of sacrifice. Three rats showed preserved EF (70±8%, group 2) and another three showed significantly decreased EF (38±9%, group 3). Microarray profiling analysis following confirmation with real-time PCR of the myocardial mRNA revealed significant up-regulation of coding genes related to inflammation in addition to ANF, BNP and embryonic type of contractile proteins. They were interferon lambda3, interleukin 1 beta, interleukin 1 receptor kinase 3, TNF receptor superfamily 1b 11b 12a, Relt, and complement components 1qa, 1qb, 1qc 1s, 2, 3, 4a. In PPAR axis Ppara and Pparg1a were down- and Pparg and Pparg1b were up-regulated. Anti-inflammatory genes Sirt1, 4 and 5 were down-regulated. 13,611 lncRNAs were detected among which 344 significantly up- or down-regulated. 43 lncRNAs were significantly up-regulated and 31 down-regulated, and each had one to five near-by coding genes. The lncRNA overlapping with the exon of Sirt4 was down-regulated. Six of those 43 lncRNAs once significantly up-regulated (Figure 1: group 2 vs group 1) were on the contrary down-regulated in group 3 compared with group 2 (Figure 2). The most significantly enriched GOS targeted by up-regulated lncRNAs was associated with immune system process and down-regulated was with single-organism metabolic process.

**Conclusion**
Pro-inflammatory genes were up-regulated and sirtuins were down-regulated during hypertrophic remodeling.
LncRNAs related to immune and inflammatory systems were up-regulated. Furthermore, the expression of several lncRNAs was suppressed as the systolic function deteriorated.

Differential expression of lncRNAs

Six lncRNAs once up-regulated in group 2 (Fig 1) were on the contrary down-regulated in group 3 (Fig 2)