Background: In severe aortic stenosis remodelling of the left ventricle takes place due to pressure overload, with development of concentric myocardial hypertrophy and fibrosis. Severe myocardial remodelling induces diastolic dysfunction. There may be complete reverse remodelling of the myocardium after surgery for aortic stenosis. Mediators regulating reverse myocardial remodelling are poorly described.

Aim: To establish a mouse model of reversible pressure overload of the left ventricle, and to investigate if specific cytokines actively reverse myocardial remodelling.

Methods: C57Bl mice, seven weeks old, were subjected to banding of the ascending aorta. The constriction resulted in pressure overload and left ventricular hypertrophy. Four weeks later the constriction was removed in a debanding operation. Animals were euthanized three days after debanding. Degree of stenosis, left ventricular mass and signs of pulmonary congestion were evaluated with ultrasound. Gene expression in the left ventricle was analyzed with microarray from Affymetrix and compared with hearts from animals euthanized before debanding (AB) and sham operated animals (SDB).

Results: Expression of 401 of 45049 genes was increased after debanding versus AB and 537 versus SDB. A series of enzymes, genes encoding collagens, growth factors and mediators with pro-hypertrophic effect were downregulated after debanding. An active mediator for reverse remodelling would be expected to be overexpressed both versus AB and SDB. This was the case with 101 genes, mainly enzymes and transcription factors. Only one cytokine, visfatin, was upregulated versus both AB and SDB. We will now validate this observation and investigate the effect of visfatin on myocardial remodelling. Visfatin is an adipocytokine with an insulin-mimetic effect, and is associated with higher diastolic BP in obese children.