Abstract: **551**

Notch signaling is differently altered in endothelial and smooth muscle cells of ascending aortic aneurysm patients

**Authors:**
DA Kostina¹, AS Kostina², VE Uspensky³, OM Moiseeva³, AA Kostareva³, AB Malashicheva³, ¹Peter the Great St. Petersburg Polytechnic University - Saint-Petersburg - Russian Federation, ²University of Verona - Verona - Italy, ³Almazov Federal Heart Centre - Saint Petersburg - Russian Federation,

**Topic(s):**
Signal transduction - Vascular

**Citation:**
Cardiovascular Research Supplements (2016) 111 (S1), S99

Purpose: Thoracic aortic aneurysm develops as a result of complex series of events that alter the cellular structure of the aortic wall. It has been shown in our and other previous studies, that patients with defects of left ventricular outflow tract may have mutations in NOTCH1 gene. Notch signaling between endothelial and smooth muscle cells plays an important role for smooth muscle differentiation, which is altered in patients with ascending aortic aneurysm (AoA). The aim of this study was to assess the expression level of Notch signaling components in endothelial and smooth muscle cells derived from aneurysms in patients with bicuspid aortic valve (BAV) and tricuspid aortic valve (TAV).

Methods: Human aortic endothelial cells (HAECs) and smooth muscle cells (SMC) were isolated from tissue fragments of BAV- and TAV-associated thoracic aortic aneurysm patients and from healthy donors used as controls. The baseline level of Notch receptors, ligands and target genes was estimated by qPCR.

Results: Endothelial cells of AoA patients had significantly lower mRNA levels of NOTCH1, NOTCH2, NOTCH4 and DLL4 comparing to controls. However the mRNA level of direct Notch target HEY1 was higher in HAEC of AoA patients. On the contrary, SMC of the patients had significantly higher mRNA levels of Notch receptors: NOTCH1, NOTCH2, NOTCH3 comparing to controls, while levels of direct Notch target genes, such as HEY1, HES1, was not changed in SMC of the patients.

Conclusions: Expression level of Notch receptors, ligands and effectors is altered in HAEC of AoA patients. In contrast, in SMC of the patients the level of Notch receptors is changed comparing to controls, but not the level of Notch effector genes such as HEY1 and HES1. Our results show that Notch signaling is differently altered in endothelial and smooth muscle cells of AoA patients. This corresponds to the hypothesis that Notch-dependent differentiation of SMC is governed by endothelial cells. We suppose that alterations of key Notch pathway elements in HAEC population may cause an impairment of SMC differentiation in patients with thoracic aortic aneurysm.