**NOTCH1 variants in children with aortic coarctation**

**Authors:** T. Tatarinova¹, N. Alexseeva¹, E. Grekhov¹, O. Freylikhman¹, A. Kostareva¹, O. Moiseeva¹. 
Federal North-West Medical Research Center - Saint-Petersburg - Russian Federation

**Objectives:** To investigate the contribution of the genetic component in the COA development by analyzing the family histories and searching mutations in NOTCH1.

**Methods:** We collected 68 unrelated children with COA, diagnosed by echocardiography, cardiac catheterization, and or surgical observation. Echocardiographic data were obtained for the relatives when available. The genetic study included 51 patients with CAO. We applied a strategy of targeted mutation screening for 10 out of 34 exons of the NOTCH1 gene by direct sequencing. Control DNA was obtained from 200 healthy donors.

**Results:** The age of patients at the time of the study was 11.2±1.2. The sex distribution was 47 males and 21 females. The mean pressure gradient in the coarctation of the aorta was 45.7±2.6 mm Hg. COA was combined with BAV in 55.9% cases, with hypoplasia of the aortic arch 32.4% or descending aorta 13.2%; 2.9% patients had complete interruption of the aortic arch and 2.9% had subaortic stenosis. Mitral valve pathology was observed in 13.2% cases. Combinations of COA with other forms of CHD were identified in 26.5% of the cases (12 PDA, 9 VSD, 6 ASD, 1 TGA). Echocardiography data was available for 82.4% mothers and 30.9% fathers. CHD were noted in 13 parents (7 BAV, 1 VSD, 4 ASD, 1 PVS).
**NOTCH1 variants in children with aortic coarctation**

**Authors:** T. Tatarinova¹, N. Alexseeva¹, E. Grekhov¹, O. Freylikhman¹, A. Kostareva¹, O. Moiseeva¹.

Federal North-West Medical Research Center - Saint-Petersburg - Russian Federation

**Results 2:** 29 variants of the *NOTCH1* gene were identified. Four of them led to amino acid exchange, but only R1279H was observed in patients 7/51 and controls 4/200 (p=0.00026). Exon substitutions were more representative for children with COA. For example, at least one variant in exons 12 (g.30469C/T, g.30445C/T), 23 (g.39006G/A), 34 (g.48696G/A, g.48901G/A, g. 48930G/A) was identified in 25.5% of patients and 4.0% of the controls. Intron substitutions, on the contrary, frequently observed in the controls: variant intron 29 (g.43831T/C) in the control and study groups was identified in 75.5% and 21.6% (p=6 × 10⁻¹³), intron 12 (g.30591C/T) - in 70.0% and 15.7% (p=1 × 10⁻¹²).

**Conclusions:** Statistical analysis showed, that the weighted combination of substitutions gene *NOTCH1* will concern this observation as favorable in 82.5% of cases in healthy donors and in 96% of patients will indicate a risk of COA.