Abstract: P562

Expression profiling of complicated and uncomplicated atherosclerotic plaques of the lower extremities

Authors:
A Fedorov¹, A Razuvaev², B Kox¹, E Ignatieva¹, J Roy², L Perisic Matic², U Hedin², A Kostareva¹, ¹Federal Almazov Medical Research Centre, Institute of molecular biology and genetics - Saint-Petersburg - Russian Federation, ²Karolinska Institute - Stockholm - Sweden,

Topic(s):
Atherosclerosis, Cerebrovascular Diseases, Aneurysm, Restenosis

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S138

Introduction
Despite progress in the development of vascular interventions, long-term patency after surgical treatment of atherosclerosis is still jeopardized by restenosis and occlusion of the reconstructed vessel segment. The mechanisms behind restenosis have been scrutinized mainly for the coronary vessels and can not be directly translated to the peripheral arterial bed.

Purpose
The aim of the study was to determine gene expression profiles associated with development of restenosis in the ilio-femoral arterial segment.

Methods
Patients undergoing open surgery for occlusive ilio-femoral atherosclerosis were included in the study. Primary atherosclerotic plaques (n = 9) were compared with restenotic lesions (n = 7) using global gene expression analysis and morphological evaluation. Differentially expressed genes were determined followed by enrichment analysis and functional characterization.

Results
70 genes were shown to be differentially expressed (P<0.01, fold change >1.2). About one third of differentially expressed genes encoded for noncoding RNAs (ncRNAs). Enrichment analysis demonstrated that cell survival, cell cycle progression and response to stress were predominant pathways associated with differentially expressed genes. Several transcription factors associated with early response to stress were upregulated in restenotic lesions compared to primary atherosclerotic plaques. In particular, subunits of the transcription factor AP1, factors of the nuclear receptor family (subfamily 4, group A), as well as their upstream regulators - members of EGR family of transcription factors were found overexpressed in secondary lesions.

Conclusions
Major changes in gene expression profiles in restenotic ilio-femoral lesions were characterized by upregulation of transcription factors involved in cell cycle control and early response to stress. The results of the study provide information about potential biomarkers and therapeutic targets for prevention of restenosis after vascular reconstructions.