Gene signature of patients with acute coronary syndrome is characterized by upregulation of IL-17 gene pathway

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Objective. Inflammatory pathways play an important role for both the development and the complications of atherosclerotic plaques. A complex interplay between innate and adaptive immune cells, via different cytokine production, accounts for plaque rupture with the consequent clinical manifestation of an acute coronary syndrome (ACS). To date, the complex network of inflammatory pathways at the gene expression profile generated during ACS is still largely unknown. In the present study we used a genome-wide microarray approach to detect changes in gene expression induced by plasma sampled from the coronary circulation of patients with ACS.
Approach and Results. Human coronary artery endothelial cells (ECs) were stimulated in vitro for 12 hours with plasma obtained from the coronary sinus (CS) and the aorta (Ao) of patients with ACS; patients with stable angina served as controls. Gene expression profiles were generated by microarray studying endothelial cells stimulated with plasma obtained from CS and compared to gene expression induced by plasma sampled from Ao. Only genes with >2-fold increase or decrease were considered significant. Functional and network analyses of statistically significant genes were performed using Ingenuity Pathways Analysis 8.0 (IPA). IPA analysis showed that the up-regulated genes [Chemokine (C-C motif) ligand 2 (CCL2), Chemokine (C-X-C motif) ligand 1 (CXCL1), Interleukine 8 (IL8), Janus kinase 1 (JAK1), v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS), muscle RAS oncogene homolog (MRAS), prostaglandin-endoperoxide synthase 2, prostaglandin G/H synthase and cyclooxygenase (PTGS2)] were mainly associated to pathways of IL-17 signaling; the results were validated by real time PCR.
Conclusions. In patients with ACS a significant intracoronary production of selected cytokines/chemokines occurs; this leads to the up-regulation of several genes involved in different inflammatory responses. However, the IL-17 pathway seems to play a crucial role the pathophysiology of ACS and lays the basis for further development of new biological markers predictive of ACS.

Ross R, Glomset JA. "The pathogenesis of atherosclerosis I". New England Journal of Medicine, 1976; 295: 369-77.
Libby P. "Inflammation in atherosclerosis ". Nature, 2002; 420: 868-874.
Stumhofer Jason S, Laurence Arian, Wilson Emma H, et al. Interleukin 27 negatively regulates the development of interleukin 17–producing T helper cells during chronic inflammation of the central nervous system. Nature Immunology. 2006; 7: 937–945.