Abstract: P575

Regulation of purinergic signaling in response to arterial injury

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Introduction
Cell damage causes the release of a significant amount of ATP and subsequent activation of purinergic system. Purinergic signaling is involved in the regulation of a variety of physiological processes, including inflammation, cell proliferation and migration. A specific set of activated pathways is mainly determined by the expression of target receptors and ectonucleotidases, which regulate levels of extracellular ATP and its metabolic products, primarily adenosine. Clarification of the role of purinergic signaling in the vascular wall response to injury is important for understanding of the fine mechanisms of atherosclerotic plaque formation and restenosis development.

Purpose
The aim of the study was to determine temporal expression profiles of genes involved in purinergic signaling during the healing response to arterial injury in rat.

Methods
Total RNA was isolated from the rat carotid arteries at seven timepoints ranging from 2 hours to 12 weeks after balloon injury. Transcriptome profiling was performed using microarrays.

Results
Several ectonucleotidases, participating in the balance of extracellular ATP and its metabolic products, showed differential expression. In particular, CD39 catabolizing pro-inflammatory ATP to ADP and AMP, decreased from 20 hours of observation. CD73, which metabolizes AMP to anti-inflammatory adenosine, and adenosine deaminase, which destructs extracellular adenosine, increased at 20 hours and remain upregulated until day 2 and day 5, respectively. Several purinergic receptors of ATP and ADP from P2X and P2Y families demonstrate differential expression. Specifically, P2X1, known as regulator of vSMC contractile phenotype, decreased from 20 hours of observation, while P2Y2 and P2Y6, known as regulators of vSMC synthetic phenotype, upregulated immediately after injury. Low-affinity adenosine receptors A2b and A3 were upregulated from day 2 to day 5. Several downstream targets of purinergic signaling also showed differential expression. Among them protein kinase A, involved in vSMC proliferation, and genes associated with inflammatory response - NLRP3 subunit of inflammasome and its targets IL1b and IL18, as well as adhesion molecules ICAM1 and VCAM1.

Conclusions
Analysis of time-course expression profiles demonstrated that purinergic signaling pathways are dynamically controlled at mRNA level in rat carotid artery balloon injury model. This indicates the potential involvement of purinergic signaling in the regulation of local inflammation and vSMC phenotype during response to vascular injury.