

4th International Conference and Exhibition on

Lung & Respiratory Care

August 01-02, 2016 Manchester, UK

Adenosine in lung endothelial barrier strengthening: Role of Rac1 and MLCP signaling

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Endothelial cells (EC) form a semi-permeable barrier between the interior space of blood vessels and the underlying tissues. In acute lung injury (ALI) the EC barrier is weakened leading to increased permeability. The mechanisms that govern the highly clinically relevant process of increased EC permeability are under intense investigation. Little is known about the processes that determine barrier preservation/enhancement. Our data indicate that extracellular adenosine is able to protect and restore EC barrier *in vitro* and *in vivo*. We also demonstrated that adenosine induces activation of small GTPase, Rac 1 and this correlates with a significant attenuation of lipopolysaccharide (LPS)-induced EC permeability increase. Conversely, introduction of active Rac1 into EC strengthen EC barrier. In parallel, adenosine induces activation of myosin light chain (MLC) phosphatase (MLCP) and this also correlates with attenuation of LPS-induced EC permeability. In addition, we have shown that inhibition of MLCP leads to the phosphorylation of several cytoskeletal targets, which correlates with permeability increase suggesting that dephosphorylation of these proteins may be involved in the barrier-enhancing effect. Further, introduction of active MLCP subunits into the lung endothelium reduces LPS-induced lung inflammation strongly supporting the positive role of MLCP activity in EC barrier preservation against ALI in murine model. Therefore, the ability of adenosine to strengthen EC barrier appears to be dependent on Rac1 and MLCP activation. We speculate that adenosine-induced EC barrier preservation requires the coordinated activation of Rac1 and MLCP leading to EC cytoskeletal changes.

Biography

Alexander D Verin has completed his PhD from Moscow State University, Moscow Russia and Post-doctoral studies from University of Indiana. Currently he is a Professor at Vascular Biology Center and Pulmonary Division at Augusta University, Augusta, GA. He has published more than 135 papers in reputed journals and serving as an Academic Editor of *British Journal of Medicine and Medical Research and Cardiology and Angiology*, and an Editorial Board Member in several other journals in the field of pulmonary/cardiovascular research such as *Cardiovascular Pharmacology*, *Journal of Multidisciplinary Pathology*, *Tissue Barriers* and *World Journal of Respiriology*.

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