

Extracellular purines in vascular endothelial barrier preservation

Alexander D Verin

Georgia Regents University, USA

Endothelial cells (EC) form a semi-permeable barrier between the interior space of blood vessels and the underlying tissues. In lung injury the EC barrier is weakened leading to increased vascular permeability. Little is known about the processes that determine EC barrier preservation. Recently, attention has been given to the therapeutic potential of purinergic agonists in the treatment of cardiovascular diseases. Our data indicate that ATP and its degradation product adenosine are able to protect EC barrier in vitro and in vivo. We show that adenosine induces rapid increases in cAMP level and activation of protein kinase A (PKA) /myosin light chain (MLC) phosphatase (MLCP) cascade and this correlates with a significant attenuation of endotoxin (LPS)-induced EC permeability. In contrast, we demonstrate that ATP induced PKA/MLCP activation and EC barrier enhancement without increase in cAMP. We also have recently shown the involvement of P2Y receptors coupled to Gi2 or Gq (for ATP) and P1 A2a receptors coupled to Gs (for adenosine) in purine-induced EC barrier enhancement. In addition, our data indicate that the inhibition of phosphatase 1 (such as 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. Collectively, our data strongly suggest that EC barrier preservation induced by extracellular purines is dependent upon activation of specific purinergic receptor/G-protein complexes. Further, purine-induced EC barrier preservation requires the coordinated activation of PKA signaling and MLCP activation leading to EC cytoskeletal changes.

Biography

Verin has completed his Ph.D. at the age of 29 from Moscow State University School of Biology and postdoctoral studies from Indiana University School of Medicine. He is Professor of Medicine and Vascular Biology at Georgia Regents University. He has published more than 120 papers in reputed journals and has been serving as an editorial board member of American Journal of Physiology and member of NIH and AHA study sections. Currently he is the academic editor of Cardiology and Angiology and editorial board member of Cardiovascular Pharmacology, Tissue Barriers and World Journal of Respiriology.

AVERIN@gru.edu