**Mechanical forces in endothelial function: exercise with moderation!**

**Speaker** Prof. Konstantin G. Birukov, MD, PhD  
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**Biosketch**  
Konstantin G. Birukov is Endowed Professor of Anesthesiology in Department of Anesthesiology, School of Medicine, University of Maryland, Baltimore, MD. In addition, he is Associate Chair for Basic Research and Director of UMSOM Lung Biology Program in School of Medicine, University of Maryland. He studied medicine in Moscow Medical School, Moscow, Russia and did his PhD in National Cardiology Research Center, Moscow, Russia. His research interests cover several areas of lung pathobiology including signal transduction and cytoskeletal basis of vascular endothelial permeability and inflammation; control of endothelial function by mechanical forces; role of oxidized phospholipids in lung pathobiology. The studies by his group led to a significant progress in understanding of autoregulatory cascades providing recovery and resolution of ALI.

**Abstract**  
Factors of endothelial cell (EC) mechanical microenvironment such as shear stress, mechanical strain or extracellular matrix stiffness, play essential role in the control of endothelial permeability and inflammation. Accumulating evidence suggests that vascular ECs contain mechanosensory complexes, which rapidly react to changes in mechanical loading, and develop context-specific adaptive responses to rebalance the cell homeostatic state. Pathologic high magnitude cyclic stretch (CS) causes rapid increase in EC permeability and augments barrier-disruptive effects of vasoactive agonists. Interestingly, pre- or post-conditioning at physiologically-relevant magnitudes of cyclic stretch (CS) promotes resealing of cell junctions disrupted by pathologic, CS magnitudes or barrier disruptive agonists. In turn, substrate stiffening causes endothelial barrier disruption and renders EC more susceptible to agonist-induced cytoskeletal rearrangement and inflammation. Further in vivo studies provide direct evidence that proinflammatory stimuli increase lung microvascular stiffness which in turn exacerbates endothelial permeability and inflammation and perpetuates a vicious circle of lung inflammation. How physiologically and pathologically relevant magnitudes of mechanical loading lead to differential activation of EC protective or disruptive cell signaling remains a standing question that requires further clarification. The results from our group and others suggest a role for physiologically relevant mechanical forces as an active barrier-protective and anti-inflammatory regulator of cellular signaling, rather than passive bystander, and suggest a key role for RhoA, Rac1 and Rap1 signaling GTPases mechanically regulated in a magnitude-dependent manner in propagation of ALI recovery and restoration of lung endothelial barrier.

Prof. Konstantin G. Birukov has been invited by Prof. Olivier Guenat, ARTORG Center, University of Bern.

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**June 3, 2019**  
“New insights in the pathogenesis of sepsis and a sneak preview to future therapy!” Prof. Tom van der Poll, Amsterdam University Medical Centers, Academic Medical Center, University of Amsterdam, NL

The DBMR Research Conference takes place from 5 pm – 6 pm and will be followed by an apéro.