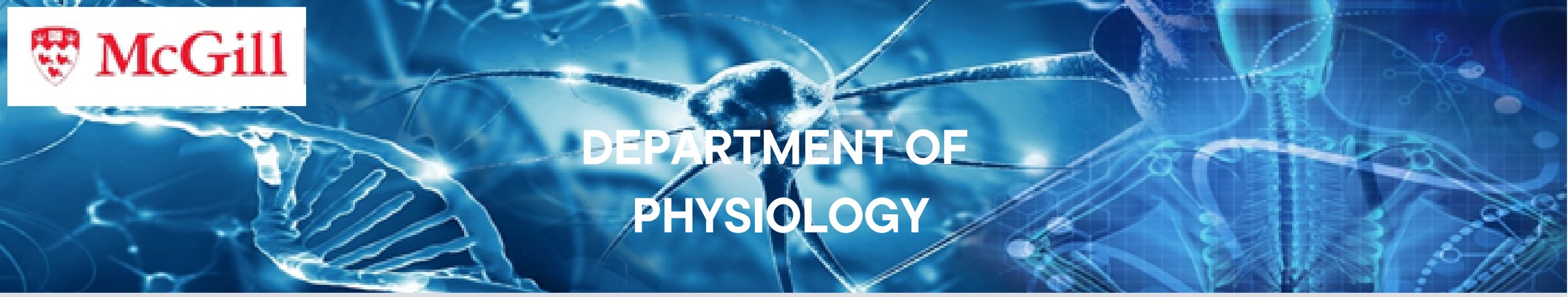

Dr. F.C. MacIntosh Lectureship Seminar

GUEST SPEAKER

Dr. Alexander Bershadsky

Professor and Senior Principal Research Scientist, Mechanobiology Institute, National University of Singapore

MONDAY, SEPTEMBER 18, 2023
11:00AM

MCINTYRE MEDICAL SCIENCES BUILDING
ROOM 208/209

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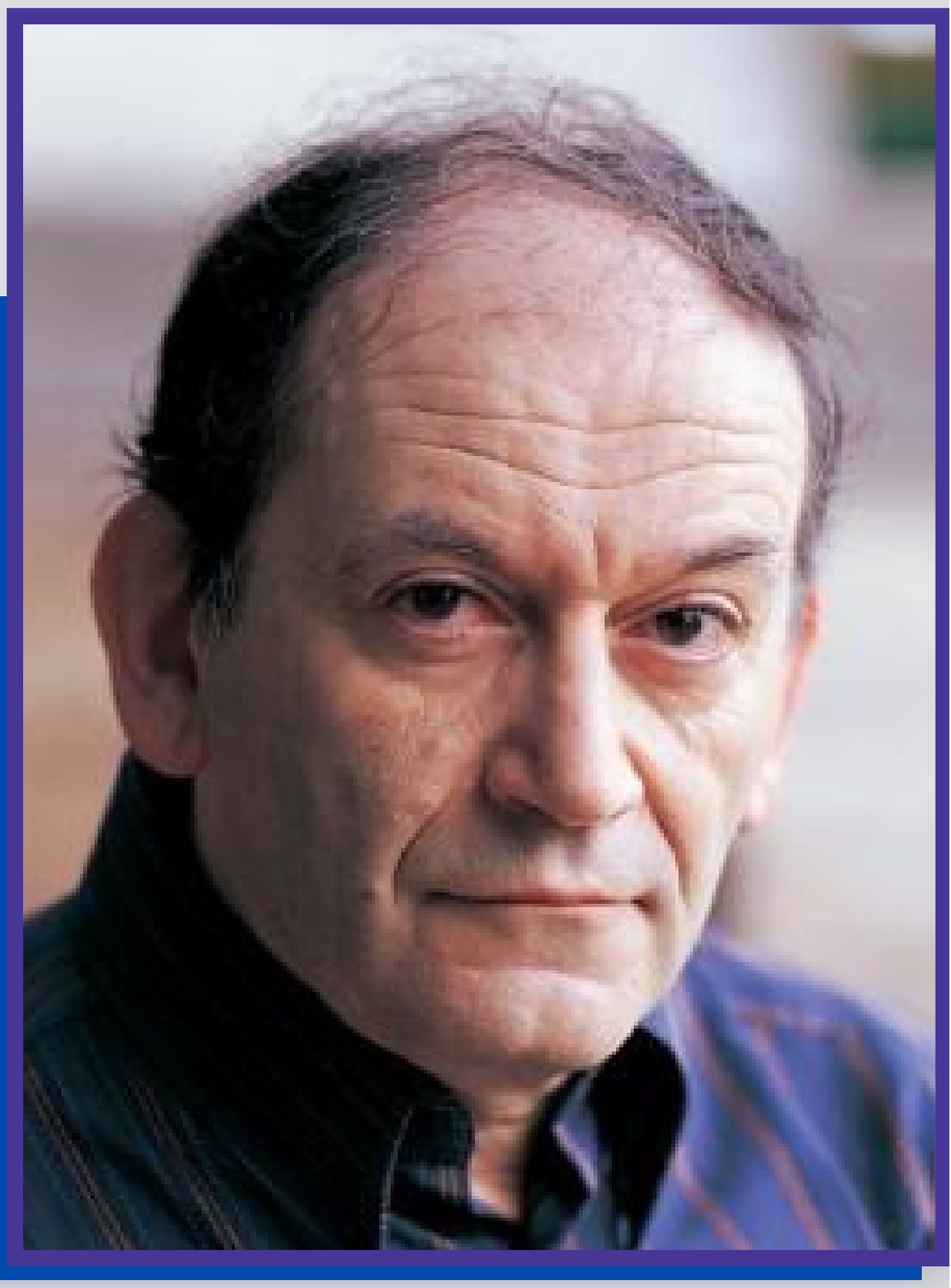
PASSCODE: 013531



Integrin-mediated adhesions in a crosstalk with actomyosin cytoskeleton and microtubules

Integrin-based focal and fibrillar cell-extracellular matrix adhesions (FA and Fib) are critical for the matrix rigidity sensing and fibronectin fibrillogenesis, respectively. Besides the association with the actin cytoskeleton, they interact with microtubules through molecular complexes containing KANK family proteins. Here, we compare the mechanisms underlying the FA and Fib dynamics. Microtubule disassembly or uncoupling from the adhesions by disruption of KANK-mediated link results in augmentation of FA but elimination of Fib. Thus, microtubules negatively regulate FA and positively - Fib. The underlying mechanism in both cases is a release from adhesion-uncoupled microtubules of Rho activator GEF-H1, triggering Rho-ROCK-myosin-II signaling cascade. Consequent burst of actomyosin contractility promotes the growth of mechanosensory FA and the disassembly of Fib. The same mechanism, local GEF-H1-dependent myosin-II activation, is involved in the sliding and disruption of the individual FA upon microtubule targeting to FA by optogenetic activation of KANK1. Thus, microtubules function as sensory and regulatory elements, whose interactions with integrin adhesions locally control formation of myosin filaments, which in turn remodel adhesions. While both FA and Fib can be formed by cells on planar substrate, Fib formation is specifically activated (in a myosin-II independent manner) by physiologically relevant micropatterns – decellularized extracellular matrix, electrospun nanofibers, or edges of microfabricated ridges. Consistently, the treatments increasing membrane/cortical tension disassemble fibrillar adhesions, but not focal adhesions. Thus, selective sensitivity of fibrillar adhesions to microtubule uncoupling and subsequent local myosin II activation can be explained by the myosin II-driven increase of membrane/cortical tension.