BDR SEMINAR (Kobe/online hybrid)

Mechanobiology Seminar Series presents

Alexander D. Bershadsky

Mechanobiology Institute, National University of Singapore &
Department of Molecular Cell Biology, Weizmann Institute of Science, Israel

Monday, January 23, 2023

11:00-12:00

1F Auditorium, DB Building C, Kobe / Broadcast online via Zoom
Zoom meeting URL will be announced on the event day by e-mail.
※This seminar is open only to BDR members.

A trialogue between integrin adhesions, actomyosin cytoskeleton, and microtubules

Integrin-based adhesions – focal adhesions, fibrillar adhesions and podosomes – mediate interactions of cells with the extracellular matrix critical for the processes of mechano-transduction/mechano-sensing, formation of fibronectin fibrils, and metalloproteinase-dependent matrix degradation, respectively. Besides the association with the actin cytoskeleton, integrin adhesions continuously interact with dynamic microtubules through the molecular complexes containing KANK family proteins. Here we show that breaking these interactions results in release of microtubule-associated Rho activator GEF-H1 from microtubules, which triggers activation of Rho-ROCK signalling cascade and the assembly of myosin IIA filaments. The burst of myosin IIA filament formation differentially remodels the integrin adhesions, promoting disassembly of the podosomes and fibrillar adhesions, but augmenting assembly and growth of the focal adhesions. At the same time, inspiring the interactions between microtubules and focal adhesions by local optogenetic activation of KANK1 protein triggers sliding of focal adhesion and their disassembly. Remarkably, GEF-H1-dependent Rho-ROCK-myosin II activation is required not only for the focal adhesion growth upon uncoupling from microtubules, but also for the focal adhesion disassembly induced by the optogenetic targeting of microtubules. Molecules involved in this process include, besides GEF-H1, kinases FAK and PAK, tubulin acetylase ATAT1, microtubule motor kinesin-1 and microtubule-associated actin polymerisation activator APC. Thus, microtubules function as sensory and regulatory elements, whose interactions with integrin adhesions locally control formation of myosin filaments, which in turn remodel adhesions. Evidence is presented of this pathway's involvement in angiogenic sprouting.

Host: Li-Kun Phng
Laboratory for Vascular Morphogenesis, BDR
Contact: likun.phng@riken.jp

RIKEN BDR
RIKEN Center for Biosystems Dynamics Research (BDR)