BP 2: Cytoskeleton

Time: Monday 11:30–12:45 Location: H1

Invited Talk BP 2.1 Mon 11:30 H1

PINCH-1 promotes migration in extracellular matrices and influences the mechano-phenotype — •Claudia Tanja Mierke — University of Leipzig, Biological Physics, Leipzig, Germany

Cell migration performs a critical function in numerous physiological processes, including tissue homeostasis or wound healing, and pathological processes that include malignant cancer progression. The efficiency of migration appears to be based on the mechano-phenotype of the cytoskeleton. Cytoskeletal properties depend on intercellular and environmental factors. Thus, connections between the cell and its microenvironment are established by cell-matrix adhesion receptors. Upon activation, focal adhesion proteins such as PINCH-1 are recruited to sites where focal adhesions form. PINCH-1 specifically couples through interactions with ILK, which binds to cell-matrix receptors and the actomyosin cytoskeleton. However, the role of PINCH-1 in cell mechanics regulating cellular motility in 3D-collagen matrices is elusive. PINCH-1 is thought to facilitate 3D-motility by regulating cellular mechanical properties, such as stiffness. Therefore, PINCH-1 wild-type and knock-out cells were examined for their ability to migrate in dense extracellular 3D-matrices and cellular deformability. PINCH-1 wild-type cells migrated more numerous and deeper in 3D-matrices. PINCH-1 wild-type cells are less deformable (stiffer) compared to PINCH-1 knock-out cells. Migration and deformability were reduced by drug-dependent inhibition of Arp2/3 complex or actin polymerization. Finally, PINCH-1 appears to be essential for providing cellular mechanical stiffness, which regulates 3D motility.

BP 2.2 Mon 12:00 H1

A novel second PI(4,5)P_2 binding site determines PI(4,5)P_2 sensitivity of the tubby domain — Veronika Thallmair[1], Lea Schultz[1], Wencai Zhao[1], Siewert J. Marrink[2], Dominik Oliver[1], and •Sebastian Thallmair[2,3] — [1]Philipps-University Marburg, Germany — [2]University of Groningen, The Netherlands — [3]Frankfurt Institute for Advanced Studies, Frankfurt am Main, Germany

Phosphoinositides (PIs) are important signaling lipids multitasking in diverse cellular signaling pathways. They operate by recruiting proteins to the membrane surface by means of PI recognition domains. One of the recognition domains for PI(4,5)P_2 lipids, which is the major PI species in the plasma membrane, is the tubby domain. It is conserved in the tubby-like protein (TULP) family and plays an important role in targeting proteins into cilia.

We used coarse-grained (CG) molecular dynamics (MD) simulations with the re-parametrized Martini 3 force field to explore the PI(4,5)P_2 affinity of the C-terminal tubby domain (tubbyCT). Our CG MD simulations revealed a novel second binding site consisting of a conserved cationic cluster at the protein-membrane interface. The simulations together with mutation experiments in living cells showed that the second binding site substantially contributes to the fine-tuned PI(4,5)P_2 affinity of tubbyCT. We will discuss the computational and experimental characterization of the novel binding site, its importance for the membrane targeting properties of tubbyCT, and for its ability to recognize distinct PI(4,5)P_2 pools in the plasma membrane.

BP 2.3 Mon 12:15 H1

Motor proteins generate the curved shape of the mitotic spindle — •Arian Ivec[1], Maja Novak[1], Nenad Pavin[1], and Iva Tolić[2] — [1]Department of Physics, Faculty of Science, University of Zagreb, Bijenička cesta 32, 10000 Zagreb, Croatia — [2]Division of Molecular Biology, Ruder Bošković Institute, Bijenička cesta 54, 10000 Zagreb, Croatia

The mitotic spindle is a complex micro-machine made up of microtubules and associated proteins that are highly ordered in space and time to ensure its proper biological functioning. A functional spindle has a characteristic shape, which includes curved bundles of microtubules that are twisted around the pole-to-pole axis. An in-depth understanding of both how the linear and rotational forces define the overall shape of the mitotic spindle and how the twisted shapes arise as a result of interactions between microtubules and motor proteins is still unclear. To answer this, we introduce a model in which motor proteins generate forces at the poles and along the microtubule bundles, thereby regulating the shapes of microtubule bundles. The model provides predictions for forces in the spindle, including that the shape of the entire spindle is predominately determined by rotational forces, and that a difference in bending forces explains the disparity in the shapes of inner and outer bundles.

BP 2.4 Mon 12:30 H1

Bottom-up assembly of functional DNA-based cytoskeletons for synthetic cells — •Kevin Jahnke[1,2], Pengfei Zhan[3,4], Na Liu[3,4], and Kerstin Göpfrich[1,2] — [1]Max Planck Institute for Medical Research, Heidelberg, Germany — [2]Heidelberg University, Heidelberg, Germany — [3]Stuttgart University, Stuttgart, Germany — [4]Max Planck Institute for Solid State Research, Stuttgart, Germany

Bottom-up synthetic biology aims at reconstructing a cell from biomolecular constituents. However, the combination of multiple elements and functions remained elusive, which stimulates endeavors to explore entirely synthetic bio-inspired solutions towards engineering life. To this end, DNA nanotechnology represents one of the most promising routes, given the inherent sequence specificity, addressability, and programmability of DNA. Here, we demonstrate functional DNA-based cytoskeletons operating in microfluidic cell-sized compartments and lipid vesicles. The synthetic cytoskeletons consist of DNA tiles self-assembled into filament networks. These filaments can be rationally designed and controlled to imitate features of natural cytoskeletons, including dynamic instability, ATP-triggered polymerization, and vesicle transport in cell-sized confinement. Also, they possess engineerable characteristics, including assembly and disassembly powered by DNA hybridization or aptamer-target interactions and autonomous transport of gold nanoparticles. This work underpins DNA nanotechnology as a key player in building synthetic cells.