Universität Basel

Research Project

Watching the Nanomachinery of the Nuclear Pore Complex At Work by High Speed-AFM

Third-party funded project

Project title Watching the Nanomachinery of the Nuclear Pore Complex At Work by High Speed-AFM
Principal Investigator(s) Lim, Roderick ;
Co-Investigator(s) Gerber, Christoph ;
Organisation / Research unit
Departement Biozentrum / Nanobiology Argovia (Lim)
Department
Project start 01.04.2014
Probable end 31.03.2018
Status Completed

Nuclear pore complexes (NPCs) form the sole passageways between the nucleus and cytoplasm in eukaryotic cells. The functional role of each 100 nm-diameter NPC is to ensure that only specific molecules (i.e., cargo) gain access to the nucleus. To do so, the NPC *a priori* inhibits macromolecules above 40 kDa from traversing its channel. Presently, the NPC mechanism remains unresolved although it is likely based on biochemical recognition and not size exclusion *per se*. Exclusive access is given to specific cargoes that are accompanied by transport receptor proteins (i.e., karyopherins or Kaps) that interact with the NPC nanomachinery. These consist of 200 intrinsically disordered proteins (i.e., resembling random coils; known as phenylalanine-glycine (FG)-repeat nucleoporins or FG Nups) that collectively form a barrier within the central NPC channel. Given that structural analysis (i.e., electron microscopy, X-ray diffraction, etc) remains formidable (due to their lack of structure), FG Nup studeis have been restricted to *in vitro* biophysical or biochemical analyses. Not surprisingly, inherent differences in experimental approach and length-scale have resulted in contrasting views on the selective barrier mechanism. In this work, we want to validate the underlying molecular mechanism of the NPC by obtaining a real time view of FG Nup dynamics and cargo translocation at the single NPC level *in situ.* **We therefore propose to apply high speed-AFM (HS-AFM) as the only possible means to watch the nanomachinery of the NPC at work.**

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