BIOMATERIALS

Forces in Biomolecular Systems SFB 863

The mechanism of ATP-dependent chromatin remodeling

Felix Müller-Planitz

Medical Faculty, Adolf Butenandt Institute, Molecular Biology,

Ludwig-Maximilians-Universität, München

Abstract:

ATP-dependent chromatin remodeling machines move nucleosomes along DNA in all eukaryotic cells. They thereby directly regulate fundamental biological processes such as transcription, replication and DNA repair. Some remodeling enzymes, such as the ISWI class of remodeling factors, not only reposition nucleosomes but also establish a regular spacing between neighboring nucleosomes, which is a hallmark of chromatin. How remodelers are able to reposition and regularly space nucleosomes has remained elusive both mechanistically and structurally. I will report results from direct tests of prominent models for the mechanism of nucleosome repositioning and spacing. Contrary to long-held beliefs, build-up of mechanical tension inside the nucleosome is not necessary to reposition nucleosomes. Instead, all data are consistent with a mechanism that resembles catalysis by protein chaperones. Spacing of nucleosomes is accomplished by moving one nucleosome along DNA until a neighboring one is encountered at a characteristic distance. The neighboring nucleosomes then lock together, a phenomenon we termed nucleosome clamping. We complement these functional dissections of the remodeling reaction with structural approaches, and I will present our latest efforts to reconstruct the structural architecture of ISWI remodelers using protein crosslinking coupled to mass spectrometry.

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Room PH 127

Contact: Ulrich Gerland, gerland@tum.de, phone: 089-289-12394