



Life Sciences Seminar

Integrated structure/dynamics/function studies of large protein complexes by NMR

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Host: Leonid Sazanov

Integrated structure/dynamics/function studies of large protein complexes by NMR & co: from the structural basis of membrane-protein import into mitochondria to dynamic mechanisms of a 0.5 MDa enzyme. Integrated structure/dynamics/function studies of large protein complexes by NMR & co: from the structural basis of membrane-protein import into mitochondria to dynamic mechanisms of a 0.5 MDa enzyme. Proteins are highly dynamic entities. Processes such as enzymatic turnover or chaperoning are intimately linked to their ability to sample multiple conformations. Such complex problems are best tackled by an integrated approach, combining NMR spectroscopy - which gives direct access to dynamics with crystal structures, MD simulations, SAXS and other biophysical methods. In my presentation I will highlight two recent examples of integrated structural biology approaches from my group. The first part will focus on an important biological question of mitochondrial biogenesis: how are the highly aggregation-prone membrane proteins, synthesized far from their final destination, transported to their respective membranes? We will show the structural basis of the mode of action of the mitochondrial chaperone TIM910, while it carries mitochondrial membrane proteins. Our NMR/MD/SAXS/in-vivo approach reveals a highly dynamic chaperone machinery and provides a rationale for dysfunction and disease related to this chaperone system. In the second part I will present our recent results on the 0.5 MDa-large aminopeptidase enzyme machinery TET2. We show how one can combine medium-resolution EM data with NMR data to obtain a high-resolution structure de novo. Furthermore, we reveal how dynamic parts of the protein are at the heart of enzymatic function -- including parts that are even missing in crystal structures, and how NMR deciphers details of substrate trafficking and active-site binding. Taken together, I will provide an overview ranging from methodological advances, including the integrated use of multiple structural/biological techniques, to challenging biological questions and how structural biology can resolve mechanistic questions.

Thursday, September 6, 2018 02:00pm - 03:00pm

Mondi Seminar Room 2, Central Building



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