SFB 1078

Protonation Dynamics in Protein Function

Mon, **Nov. 25**, 2019

15:15 – 16:15

Freie Universität Berlin
Physics Department
Lecture Hall B

(Arnimallee 14, 14195 Berlin-Dahlem)

Colloquium

Prof. Volodymyr Korkhov – Department of Biology, ETH Zürich, Switzerland

Structures of a membrane adenylyl cyclase-G protein complex reveal a novel mechanism of cAMP signaling pathway regulation

Membrane adenylyl cyclases (ACs) are the key enzymes in mammalian signal transduction. The ACs convert ATP to cyclic adenosine monophosphate (cAMP), thus regulating a plethora of cellular responses to a variety of extra- and intra-cellular stimuli, such as hormones, drugs, changes in intracellular Ca^{2+}, etc. I will present the cryo-EM structure of a mammalian membrane AC bound to an activated G protein subunit, AC9-Gs, at a resolution of 3.4 Å. The structure reveals the architecture of a complete membrane AC. Furthermore, comparisons of several structures of the AC-Gs complex in different conformations, in the absence and presence of the activator and/or substrate analogue, reveal a novel auto-inhibited conformation of the AC9, the “occluded state”. Our structural and biochemical analysis of the AC9-Gs complex suggests a novel auto-regulatory mechanism of cAMP-based signal transduction.

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