MINI-SYMPOSIUM

25 November 2021 from 11:00 - 12:00
Dept. Mathematics, aud. D1 (1531-113)

From 11:00-11:30   Prof. Dr. Lutz Schmitt
Dept. of Biochemistry, Heinrich-Heine-Universität Düsseldorf, Germany
Structure and efflux mechanism of the yeast pleiotropic drug resistance transporter Pdr5

From 11:30-12:00   Prof. Christian A. Olsen
Center for Biopharmaceuticals and Dept. Drug Design and Pharmacology
Faculty of Health and Medical Sciences, University of Copenhagen, Denmark
Chemical Tools for Investigating Histone Deacetylase (HDAC) Enzymes

See seminar abstracts on page 2-3 of this announcement

Everyone interested is welcome to attend.
25. November 2021, 11.00-11.30
Dept. of Mathematics, aud. D1 (1531-113)

Prof. Dr. Lutz Schmitt
Dept. of Biochemistry, Heinrich-Heine-Universität Düsseldorf, Germany

**Structure and efflux mechanism of the yeast pleiotropic drug resistance transporter Pdr5**

The ABC transporter Pdr5 of *S. cerevisiae* is a key player of the pleiotropic drug resistance (PDR) network that works as a first line of defense against a wide range of xenobiotic compounds. As the first discovered member of the family of asymmetric PDR ABC transporters, extensive studies have been carried out to elucidate the molecular mechanism of drug efflux and the details of the catalytic cycle. PDR5 turned out to be an excellent model system to study functional and structural characteristics of asymmetric, uncoupled ABC transporters. In this context, asymmetry refers to the fact that one of the two nucleotide binding sites (NBS) deviates from the canonical architecture, which as a consequence impairs ATP hydrolysis at this NBS. Pdr5 is one of the most extreme asymmetric or degenerated ABC transporters as all catalytic relevant amino acids of NBS1 are exchanged to non-active residues. Only, recently a protocol to purify Pdr5 in a functional state was established and allowed the first in vitro studies that also resulted in a structural analysis of Pdr5 by single particle cryo-EM. These structures revealed details of an ATP-driven conformational cycle, which mechanically drives drug translocation through an amphipathic channel, and a clamping switch within a conserved linker loop that acts as a nucleotide sensor. The conformation of one half of the transporter remains nearly invariant throughout the cycle, while its partner domain undergoes changes that are transmitted across inter-domain interfaces to support a peristaltic motion that displaces transport substrate.

All welcome
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