**The Ampere prize 2016 for Young Investigators**

Prof. Dr. Enrica Bordignon has received the AMPERE prize for Young Investigators on the 3rd of July 2016, during the EUROMAR conference in Aarhus, Denmark. The prize was given "in recognition of her achievements using spin-label EPR for the characterization of large proteins".

The Italian chemist is since April 2016 Chair of Electron Spin Resonance Spectroscopy at the Ruhr-University Bochum in Germany, where she collaborates within the Cluster of Excellence RESOLV (Ruhr Explores SOLvation). PhD at the University of Padova, Italy, in 2003 she moved to Germany as post-doctoral fellow in the group of Prof. Dr. Steinhoff. From 2008 to 2013, she was senior scientist at ETH Zurich, in the group of Prof. Dr. Jeschke, and in 2013 she was appointed associate professor at the Free University of Berlin.

Introducing Bordignon to her talk at EUROMAR, Prof. Dr. Meier called her "an ambassador of the EPR technique in the field of structural biology". Bordignon investigates the conformational changes of membrane proteins by means of site-directed electron spin resonance spectroscopy, in particular with dipolar spectroscopy (DEER also known as PELDOR). She has been successfully collaborating with several groups, using EPR to investigate the structural dynamics of a series of protein complexes, e.g. the aspartate transporter (1), the muscle alpha-actinin (2), and recently she contributed to the discovery of the stoichiometry and structural organization of the Ton complex formed by a pentameric ExbB in complex with a dimeric ExbD and TonB (3). The two main focuses of her lab are: Understanding at molecular level the key interactions and conformational changes of Bcl-2 proteins at the onset of apoptosis, a form of programmed cell death (4); studying the structural dynamics of ABC transporters, which confer drug resistance to cancer cells or are involved in the immune systems (5). Within the cluster of excellence, RESOLV scientists investigate how solvents – water in particular- influence the properties of chemical and biological processes. Therefore, she will extend her EPR studies to changes in water accessibility accompanying the proteins' conformational transitions via dynamic nuclear polarization.

During her talk in Aarhus "ABC exporters: analogies and differences", Bordignon presented a comprehensive EPR study on three different ABC exporters, highlighting the species-specific response to nucleotides. ATP binding cassette (ABC) exporters are found in all phyla of life and play a key role in the transport of a variety of molecules across cell membranes. Around half of the forty human ABC exporters are heterodimers encompassing two functionally non-equivalent ATP binding sites, which include transporters of major clinical importance such as CFTR, SUR1 and TAP1/2. Scientists in the field agree that a typical ABC exporter adopts two principal states, namely an inward-facing (IF) state with NBDs fully or partially separated and an outward-facing (OF) state with nucleotides bound at the closed NBD dimer interface, which is coupled to substrate extrusion at the transmembrane domains. Yet, the molecular events leading an open NBD dimer to a closed one having two nucleotides sandwiched at the interface (the so-called power stroke event) are still under debate.

Understanding at the molecular level how ABC exporters perform their function and what is the power stroke for substrate release is of key relevance for both fundamental and applied research – i.e. pharmaceutical applications. The heterodimeric ABC exporter TM287/288 from the thermophilic bacterium *T. maritima* is currently the only heterodimeric ABC exporter encompassing a non-canonical nucleotide binding site for which two inward-facing crystal structures are available. In contrast to ABC exporters comprising two consensus sites, the NBDs of TM287/288 remain in contact

mainly via the degenerate site D-loop. In Aarhus, Bordignon showed a comprehensive site-directed spin labelling EPR study on TM287/288, and she compared the nucleotide response of this heterodimeric exporters with another heterodimeric exporter from a mesophilic organism (BmrCD) and a homodimeric ABC exporter (MsbA).

The molecular events discovered by EPR allowed to build a mechanistic model, which reconciles the data available for heterodimeric exporters and highlight species-specific differences (6).

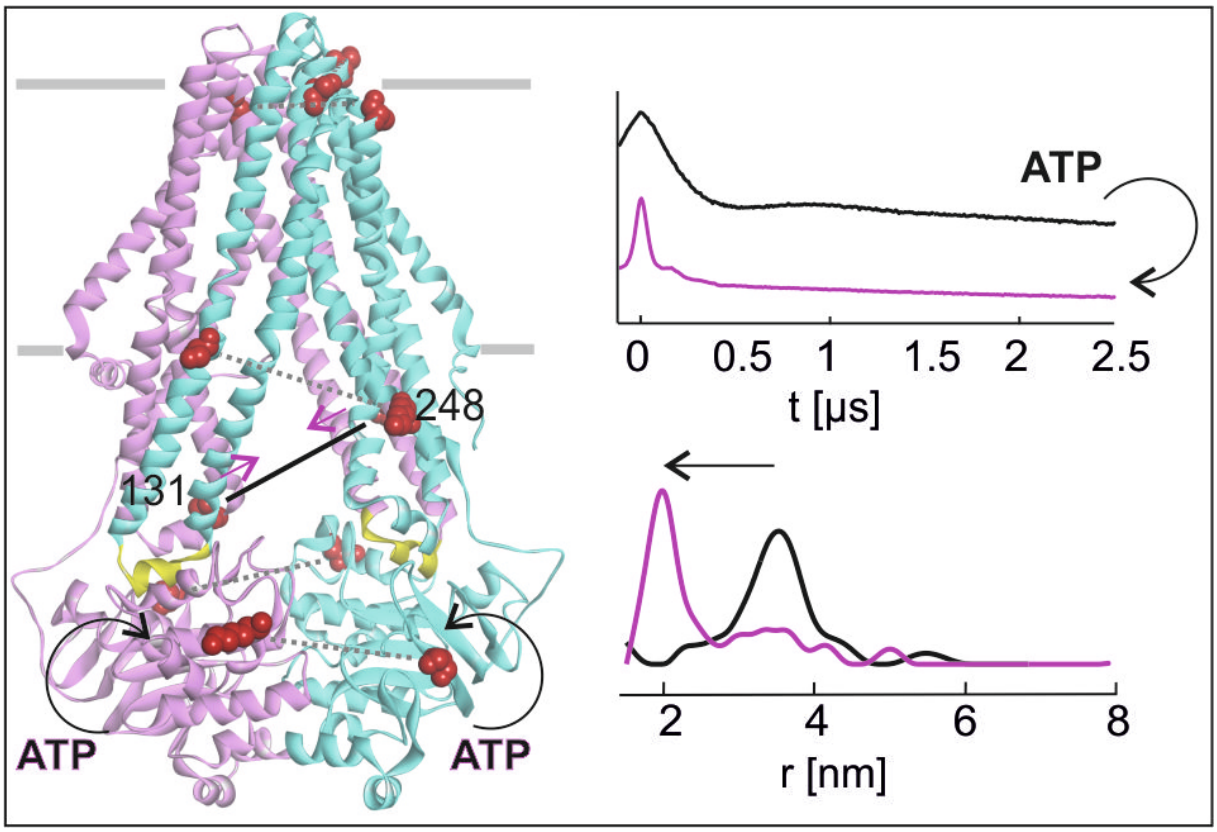


*Figure 1. The side chains in the TM287/288 ABC exporter which were mutated to cysteines and then spin labeled with MTSL are highlighted in the apo crystal structure (PDB 4Q4H). Example Q-band DEER traces and obtained distance distributions are shown on the right. The conformational change from an apo inward-facing structure to an ATP-bound outward-facing structure can be easily monitored by EPR.*


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