International Lecture Series
Disease Biology and Molecular Medicine

ALL WELCOME!

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19:00 h

Historischer Saal
Stadtmuseum Halle
im
Christian-Wolff-Haus
Große Märkerstr. 10
(ca. 100 m vom
Marktplatz)

"Targeting the ubiquitin system in cancer - novel therapeutic windows revealed by chemoproteomics"

Regulation of the protein lifespan is key for most biological processes. When proteins reach the end of their lifetime, most of them get modified by the attachment of ubiquitin (Ub). This has been implicated in the elimination of damaged proteins, but also in physiological proteolytic control of processes such as transcription, signal transduction, and cell cycle transitions. So far, the analyses have focused on Ub attachment, with several hundred Ub conjugating enzymes characterized to date. Much less is known about enzymes that remove Ub from substrate proteins, yet around a hundred genes have been identified, sharing consensus motifs for deubiquitylating enzymes (DUBs). Such diversity is inconsistent with a simple recycling function and strongly suggests a range of specific (but currently largely undiscovered) biological functions. Members of the DUB family are already known to contribute to neoplastic transformation and are implicated in neurodegenerative diseases, making them attractive targets for drug design.
We are analyzing a particular subset of the deubiquitylating enzyme family, containing an ovarian tumor (OTU) domain. This conserved motif encodes for a potential cysteine protease, conserved throughout evolution. The function of this class of proteins is largely unknown. We employ a tandem affinity purification method to determine protein interaction partners and a proteomics screen for protease substrate discovery will identify substrates and provide entry points for genetic and biochemical analyses of their function. Our studies indicate a central role for OTUs, in particular OTUB1, in regulating cell invasion and morphology by modulating the stability of small GTPases. The impact of these molecular interactions are studied within the context of host-pathogen interactions and tumourigenesis.

Selected publications
Wijnhoven et al. 2015, **Molecular Cell** 60, 362. Zauri et al. 2015, **Nature** 524, 114.
Welker et al. 2015, **Nature** 522, 81. Blackledge et al. 2014, **Cell** 157, 1445.
Kessler 2013, **Curr Opin Chem Biol** 17, 59. Khoronenkova et al. 2012, **Mol Cell** 45, 801.
Chauhan et al. 2012, **Cancer Cell** 22, 345. Parsons et al. 2011, **Mol Cell** 41, 609.

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