sfb 635
posttranslational control of protein function

IGS DHD

Seminars in Genetics and Molecular Cell Biology

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Chemical ubiquitination

Although 8 ubiquitin chain topoisomers are found in nature, we can enzymatically generate and study only few of them. The same holds true for ubiquitinated or ubiquitin-like modified polypeptides. Only for few polypeptide sequences and proteins the ligase combinations are known and can be isolated, needed for ubiquitin or ubiquitin-like modification in vitro. We have developed chemical strategies that allow the construction of virtually any ubiquitin or ubiquitin-like conjugate. This technology has made custom ubiquitination services reality and the basics of this technology will be explained in detail. In addition, a series of novel ubiquitin-based probes will be discussed that have been designed to study the activity of deubiquitinating enzymes (DUBs). These probes are based on the ubiquitin structure and are equipped with a reactive moiety that allows covalent inhibition of DUBs through reaction with their active site cysteine nucleophiles. This strategy allows for example the identification of novel DUBs and the simultaneous activity measurement of multiple cysteine-dependent DUBs present in a given example. We recently discovered by serendipity DUB probes based on alkynes as a reactive moiety. Interestingly, these alkynes have so far been considered to be unreactive but it appears that DUBs can trigger a chemical reaction not yet known. The discovery and implications of this unexpected alkyne reactivity will be discussed. Alkyne-based DUB probes react with a wider range of DUBs compared to other probes previously developed while they seem inert to reactions other than reactions with active site cysteine residues in deubiquitinating enzymes.

Tuesday, April 1, 2014 at 12.15 p.m.

Institute for Genetics,
Zülpicher Str. 47 a, Lecture hall, 4th floor

Host: Kay Hofmann, Institute for Genetics,
University of Cologne

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