## SEMINAR SERIES



Sonja Lorenz
Rudolf-Virchow-Zentrum
für Experimentelle Biomedizin,
Universität Würzburg

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## Understanding structural principles regulating the ubiquitin system

The ubiquitin system is central to eukaryotic cell and tissue homeostasis. Driven by  $\sim 1000$  enzymes in human cells, ubiquitin modifies over 50.000 protein target sites in dozens of structurally distinct ways, thereby controlling protein lifetimes, levels, localization, conformational dynamics, interactions, and activities. A major challenge in understanding and therapeutically exploiting this crucial signaling system thus lies in defining the determinants of its specificity. To address this challenge my laboratory investigates the mechanistic principles of the ubiquitination machinery by structural, chemical biological, and cell-based approaches.

In this talk, I will review our major accomplishments in revealing paradigms of (i) linkage specificity in ubiquitin chain formation, as mediated by E2/RING-type ligase systems, (ii) regulation in E2 enzymes and HECT-type ligases, and (iii) substrate recognition by HECT-type ligases. I will also touch on our preliminary work exploring specialized ubiquitin ligases in the human pathogen Leishmania with key roles in infectivity.

**Host: Marina Rodnina** 



