Open PhD position in the Ulrich lab

Prof. Dr. Kathrin Ulrich, Molecular and Cell Biology, Saarland University



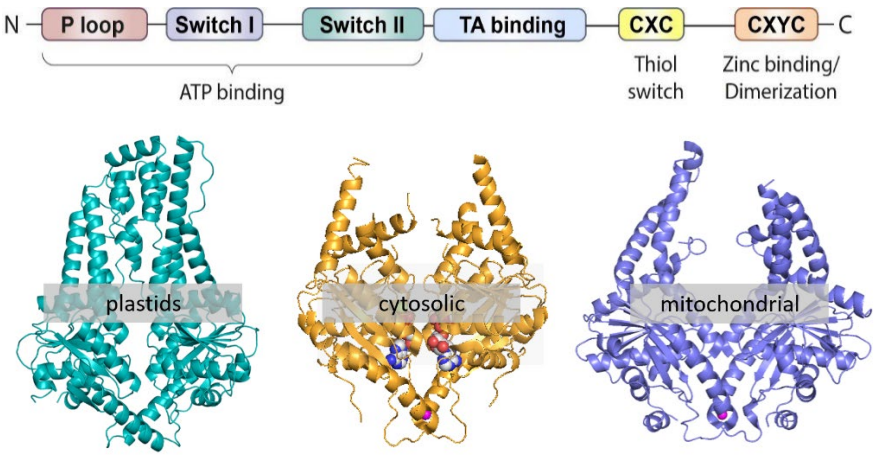
Research interest:

The Ulrich lab studies the cellular function and regulatory mechanisms of redox-regulated chaperones. We aim to understand the interplay between redox and protein homeostasis in maintaining a healthy proteome during stress conditions and aging.

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PROJECT: Evolutionary conservation of stress-sensing chaperones

Background and Significance: Stress-sensing chaperones are fast-acting, dynamic components of the proteostasis network to prevent protein aggregation upon sudden environmental changes [1,2]. The cytosolic yeast protein Get3 (ASNA1/TRC40 in human) functions as a redox-regulated, ATP-independent chaperone that protects cells against oxidative stress and starvation [3,4]. Under non-stress conditions, it mediates the ATP-dependent targeting of tail-anchored (TA) proteins to the ER membrane [5]. The switch into the chaperone-active state is induced by reversible thiol oxidation of a conserved CXC motif which is under direct control of Get3's nucleotide-binding state, making it an ideal sensor of ATP-depleting, oxidative stress [6].



Research Plan: The goal is to explore the evolutionary conservation of the chaperone function of Get3-like proteins found among all phyla – from bacteria to human. We aim to investigate Get3-like proteins in organelles and elucidate their role as sensors of endogenous and environmental stresses, protecting cellular proteostasis against redox imbalances.

The project focuses on structural and functional characterization of recombinant Get3-like proteins from various organisms and aims to elucidate the molecular mechanism, evolved to regulate the stress-specific chaperone activation. Complementation studies in yeast or human cells will reveal the physiological role of the ancient chaperone function and serve to explore the crosstalk between redox and protein homeostasis.

Position: Fully funded T-VL E13, 65% at Saarland University, Campus Saarbrücken. The UdS has an international focus and strong research profile in Natural Sciences and Technology. Saarbrücken and surroundings are beautiful and affordable areas to work and live.

[1] **Ulrich** (2023) *Biochem Soc Trans* 51: 1169-1177; [2] Reichmann et al. (2018) *Mol Cell* 69: 203-213; [3] Powis et al. (2013) *J Cell Sci* 126: 473-483; [4] Voth et al. (2014) *Mol Cell* 56: 116-127; [5] Schuldiner et al. (2008) *Cell* 134: 634-645; [6] **Ulrich**, et al. (2022) *Mol Cell* 82: 3226-3238 e3227