The dynamic chaperone network in the endoplasmic reticulum

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Efficient ER functioning relies on a network of chaperones, calcium level and redox state, whereas variation in these cellular parameters can lead to ER stress and diseases. Here, we present structural and functional studies to resolve key mechanisms underlying the dynamic chaperone network at atomic resolution. In a first step, in cyclo NMR resolve the complete functional cycle of the ATP-driven Hsp70 chaperone BiP at atomic level. In a second step, we characterize the disulfide isomerase PDIA6. We find that PDIA6 forms biomolecular condensates, both in vitro and in the ER lumen during protein folding homeostasis. PDIA6 condensates recruit Hsp70 BiP and a number of further chaperones specifically into the condensates to form functional “folding factories” inside the ER. Together, our data establish the existence of a functional chaperone condensate that subcompartmentalizes the ER.

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東北大学
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