

## MS03-P107 - LATE | KEEPING MUSCLE PROTEINS IN SHAPE – UCS-PROTEINS ACTING AS MYOSIN-SPECIFIC QUALITY CONTROL FACTORS

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The broad variety of movement-based organismal functions - ranging from muscle contraction to cytokinesis and endocytosis - rely on the motor protein myosin. Given the intricate fold, myosin family members require help of several chaperones to attain their native conformation. Interestingly, the chaperone UCS (UNC45/CRO1/SHE4) has been additionally shown to facilitate degradation of misfolded myosin by acting as an adaptor for UFD2-mediated ubiquitination [1, 2].

The aim of this study is to unravel how myosin interacts with UCS-proteins and how this is connected to protein quality control. Initially, we investigated interaction motifs of the fungal UCS-protein SHE4 with myosin and determined a co-crystal structure with the respective peptide. Subsequently, focusing on myosin interactions with the more complex, metazoan UCS-protein UNC45, we demonstrated that within the interaction motif a strictly conserved tyrosine residue is critical for chaperone engagement. Guided by crosslinking mass spectrometry, we obtained a model of full-length UNC45-myosin interactions, suggesting that the identified chaperone recognition motif can flip to recruit UNC45.

Our work provides molecular insight into how UCS-proteins bind to myosin and is fundamental for subsequent studies addressing the regulated formation of the myosin-chaperone complexes and their role in muscle myosin proteostasis.

[1] D. Hellerschmied, M. Roessler, A. Lehner, L. Gazda, K. Stejskal, R. Imre, K. Mechtler, A. Dammermann, T. Clausen, *Nature Communications*, 9, (2018), 484

[2] D. Hellerschmied, T. Clausen, *Current Opinion in Structural Biology*, 25, (2014), 9