Binding properties of SUMO-interacting motifs

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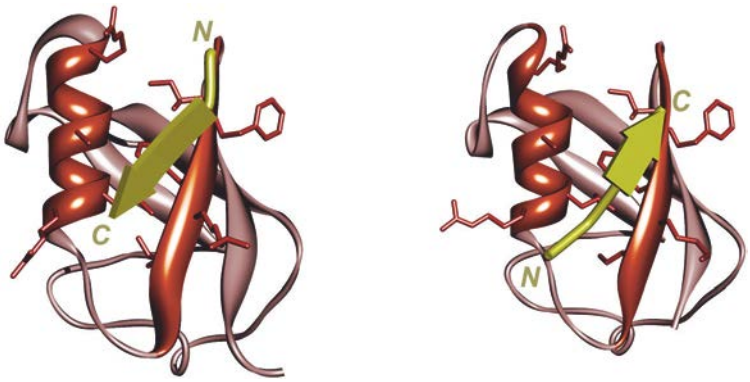
A large number of yeast proteins is known to interact non-covalently with Small Ubiquitin-like Modifiers (SUMO) via short SUMO-interacting Motifs (SIMs), but the structural details of this interaction were poorly characterized. The sequence analysis of a large dataset of 148 yeast SIMs [1] revealed the existence of a hydrophobic core binding motif and a preference for acidic residues either within or adjacent to the core motif. Thus the sequence properties of yeast SIMs are highly similar to those described for human. We performed Molecular dynamics simulations to investigate the binding preferences for four representative SIM peptides differing in the number and distribution of acidic residues and assessed the relative stability of the two observed alternative binding orientations (parallel, antiparallel).



Structure of ySUMO in complex with different ligands. Left: detailed view of the Srs-2 SIM (yellow) bound to the ySUMO (red) in a parallel orientation [2]. Right: detailed view of the Fibronectin III-derived monobody SIM (yellow) bound antiparallel to ySUMO (red) [3]. The SUMO structural elements involved in SIM binding are highlighted in darker color

For all SIMs investigated, the antiparallel binding mode remained stable in the simulations and the SIMs were tightly bound via their hydrophobic core residues supplemented by polar interactions of the acidic residues. In contrary, the stability of the parallel binding mode is more dependent on the sequence features of the SIM motif like the number and position of acidic residues or the presence of additional adjacent interaction motifs. This information should be helpful to enhance the prediction of SIMs and their binding properties in different organisms to facilitate the reconstruction of the SUMO interactome.

[1] T. Srikumar et al., *Mol Syst Biol*, **2013**, *9*, 6.
[2] A. Armstrong et al., *Nature*, **2012**, *483*, 59-63.
[3] R. Gilbert et al., *Proc Natl acad Sci USA*, **2011**, *108*, 7751-7756