

Poster Presentations

[MS5-P13] Structural and functional characterization of the two phosphoinositide binding sites of PROPPINs

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PROPPINs, a eukaryotic WD-40 motif containing protein family, bind the polyphosphoinositides PtdIns3P and PtdIns(3,5)P₂ using a conserved FRRG motif. PROPPINs play a key role in macroautophagy besides other functions. We determined the 3.0 Å crystal structure of *Kluyveromyces lactis* Hsv2, which shares significant sequence homologies with its three *S. cerevisiae* homologues Atg18, Atg21 and Hsv2 [1]. Hsv2 forms a seven bladed β -propeller. Remarkably, in the crystal structure the two arginines of the FRRG motif are part of two distinct basic pockets formed by a set of highly conserved residues. In comprehensive *in vivo* and *in vitro* studies of ScAtg18 and ScHsv2 we defined within the two pockets a novel set of conserved residues essential for normal membrane association, phosphoinositide binding and biological activities. Our experiments show that PROPPINs contain two individual phosphoinositide binding sites. Based on docking studies we propose a model for phosphoinositide binding of PROPPINs.

[1] Krick, R., Busse, R. A., Scacioc, A., Stephan, M., Janshoff, A., Thumm, M., and Kühnel, K. (2012) Structural and functional characterization of the two phosphoinositide binding sites of PROPPINs, a beta-propeller protein family, Proc Natl Acad Sci U S A 109, E2042-2049.

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