Solution structure of the yeast URN1 splicing factor FF domain:

FFs and SURPs, two domains with a similar fold

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FF domains were first identified as repeat sequences of about 60 amino acids found in the murine splicing factor FBP11 (Formin Binding Protein 11). They are present in three protein families: the splicing factors FBP11, Prp40 and URN1, the transcription factors CA150, and the p190RhoGTPase-related proteins[1]. The first binding site mapped for a FF domain was that of FBP11FF1 domain. It corresponded to the interaction with a phosphorylated sequence[2]. According to this, FF domains were defined as phoshphoserine binding domains. However, the group of ligands FF domains can bind to form, at best, a motley crew with binding reports pointing also to negative/aromatic sequences[3], the tetratricopeptide repeat (TPR)[4], the transcription factor TFII-I [5] and even to RNA.

To expand our knowledge on the FF domain, we selected the FF domain present in the URN1 yeast splicing factor as the subject for structural studies. The URN1 protein is one of the two known proteins containing only one FF domain, making it the most simplified representative of FF domain-containing splicing factors. The solution structure reveals that the domain adopts the classical FF fold, with a distinctive negatively charged patch on its surface. All available FF structures have a well-conserved fold but variable electrostatic patches on their surfaces. These patches are unconserved, even for domains with similar pKas.

We performed structural comparisons of the FF domains to other proteins with similar folds. In addition to the structures detected by SCOP we included SURP domains, which also adopt the $\alpha1$-$\alpha2$-3_{10}-$\alpha3$ architecture[6]. We observed that the main difference between all these structures resides in the orientation of the second helix. Remarkably, in DEK, SURP and Prp40FF1 structures (the exception is the FBP11FF1 domain), this second helix participates in ligand recognition.[4,6,7]

[1] Bedford M.T., Leder P. *Trends Biochem. Sci.* 1999, 24, 7
[2] Allen M., Friedler A., Schon O., Bycroft M. *J.Mol.Biol*. 2002, 323, 3
[3] Smith M. J., Kulkarni S., Pawson T. *Mol. Cell. Biol.* 2004, 24
[4] Gasch A., Wiesner S., Macias MJ. *J.Biol.Chem.* 2006, 281,1
[5] Jiang W., Sordella R., Settleman J., *Mol. Cell.* 2005, 17, 1
[6] Kuwasako K., He F., Yokoyama S., *Structure* 2006, 14, 11
[7] Devany M., Kotharu N.P., Matsuo H., *Protein Sci* 2004, 13, 8

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