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Title: Study of the ubiquitin-like fold in Sde2

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Abstract:

Post translational modification by ubiquitin is one of the most studied form of protein modification in eukaryotes. Ubiquitin and ubiquitin like proteins/modifiers (UBL/ULMs) regulate various biological processes by covalently conjugating to proteins. Majority of UBLs have been attributed as a protein modifier like ubiquitin, there are notable exceptions to it as well. Hub1, a ubiquitin like protein regulates RNA splicing but is not involved in protein modification. Another example of ubiquitin like domain protein (UDP) is Sde2, which regulates intron specific pre-mRNA splicing in Schizosaccharomyces pombe. Previously it has been shown that Sde2 has a ubiquitin fold at its Nterminus and a predicted C-terminus rich in helices. Two deubiquitinating enzymes (DUBs) Ubp5 and Ubp15 cleave Sde2 at a conserved GG KGG motif to generate Sde2 UBL and Sde2-C. Despite having low sequence similarity with ubiquitin, Sde2 N-terminus attains a ubiquitin fold and still gets recognized by Ubp5 and Ubp15. This lead to the first part of the study, where we tried to find out the specificity of this DUBs-Sde2 interaction, it seems that the whole UBL fold is necessary for its recognition by Ubp5 and Ubp15 and results in ubiquitin-like processing. Recent reports have elucidated the function of Sde2-C in regulation of RNA splicing in fission yeast and replication stress release factor in mammalian cells; but no significant function has been attributed to Sde2 UBL . We sought to find out the function of Sde2 UBL; from our experiment we could see some higher molecular adducts Sde2 UBL suggesting a possible role in protein conjugation. Lastly, we hypothesized that presence of UBL fold in Sde2 could regulate its incorporation in the spliceosome but not for other splicing factors like Hub1.

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