Abstract

Ubiquitin-like proteins (UBLs) control various cellular processes such as protein degradation, DNA repair, autophagy, transcription, RNA splicing, and immune responses. Hub1 is one such UBLs that have been reported to regulate pre-mRNA splicing. However, the function and the mechanism of Hub1 in intron-rich eukaryotes has not been studied yet. We aimed to understand the role of Hub1 in RNA splicing in an intron-rich unicellular eukaryote Schizosaccharomyces pombe, and a multicellular eukaryote, Caenorhabditis elegans. This study demonstrates a conserved genome-wide role of Hub1 in pre-mRNA splicing in S. pombe. Hub1 alters the protein composition of the spliceosome selectively. It promotes splicing of pre- mRNAs that are synthesized faster. It is likely that rapidly synthesizing transcripts require Hub1 to couple transcription with splicing. We identified a functionally conserved Hub1 surface centered at two positively charged residues critical for splicing in S. pombe. We also show that Hub1 directly binds to the Kreb's cycle enzyme, Fum1, through another surface. This Hub1 surface also regulates pre- mRNA splicing. Additionally, our study showed the potential role of Hub1 in trans- splicing in the multicellular C. elegans. In summary, Hub1 employs multiple surfaces to facilitate binding of specific factors for its function in pre-mRNA splicing. My findings are highly relevant not only for regulatory and tissue-specific gene expression, but also for understanding new mechanisms of alternative splicing.