Identification of potential phosphodiesterase essential for U6 snRNA stability

Joanna Krwawicz1,3, Jan Kutner1, Andrzej Dziembowski2,3 and Krzysztof Ginals1

1Interdisciplinary Centre for Mathematical and Computational Modelling, University of Warsaw, Warsaw, Poland
2Institute of Genetics and Biotechnology, University of Warsaw, Warsaw, Poland
3Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland

Pre-mRNA splicing is mediated by 5 small nuclear ribonucleoparticles (snRNAs) and associated factors. Among snRNPs, the U6 possesses unique biogenesis pathway and the most striking feature of mammalian U6 snRNA is presence of 2′,3′-cyclic phosphate at its 3′ end. In yeast U6 snRNA is also modified at 3′ end but the exact chemical nature of this modification is not well defined. Through advanced bioinformatics searches, we identified new potential phosphodiesterase belonging to 2H superfamily and encoded by essential but so far uncharacterized gene. Depletion of this protein causes U6 snRNA instability and impairment of pre-mRNA splicing. The growth defect of the essential gene depletion is suppressed by U6 snRNA overexpression from plasmid. Therefore the protein was named USP1 for U Six Phosphodiesterase 1. Further experimental studies to clarify the structure of U6 3′ end and the detailed role of USP1 are in progress.