Structure studies of IMP-specific phosphatase ISN1 from Saccharomyces cerevisiae

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Nucleotide metabolism involves purine nucleotide degradation and produces urate via formation of the nucleobase xanthine. The end product, nitrogen-rich urate, is excreted by human and primates, but is fully catabolized to glyoxylate, carbon dioxide, and ammonia by the ureide pathway, which is conserved in plants, many bacteria, and fungi. Inosine 5'- monophosphate (IMP) is an intermediate in the catabolism. In parallel to the catabolic fate of IMP, IMP production from inosine by the salvage reaction was identified in Escherichia coli and A. thaliana. Accordingly, an interconversion between IMP and inosine might be metabolic process involved in the regulation of nucleotide metabolism. Currently, IMP- specific phosphatases, which are responsible for inosine production in catabolism, are unknown, except for IMP-specific 5'-nucleotidase 1 (ISN1). ISN1 from Saccharomyces cerevisiae (ScISN1) catalyzes the dephosphorylation of IMP to inosine. In this presentation, we will report our progresses on the structural and biochemical studies of ScISN1. These regulatory and catalytic features of ScISN1 are unusual, mainly due to sequence and structural variations. Our findings provide structural and biochemical insight into the allosteric regulation of enzymes of the ISN1 family.