Poster

Structure and allosteric regulation of the inosine 5'-monophosphate-specific phosphatase from *Saccharomyces cerevisiae*

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Nucleotide metabolism is intricately regulated by a variety of enzymatic reactions. In purine catabolism, the dephosphorylation of inosine monophosphate (IMP) produces inosine [1,2], the primary intermediate. The reaction is catalyzed by IMP-specific 5'-nucleotidase 1 (ISN1) which is present in many but not all eukaryotic organisms [3].

ISN1 plays a role in IMP catabolism in the metabolic transition of yeast from respiratory to fermentative growth, but details of ISN1 regulation are unknown. We characterized the crystal structure and kinetic features of ISN1 from S. cerevisiae (ScISN1). Structural and kinetic analyses revealed that tetrameric ScISN1 is a substrate IMP-dependent allosteric enzyme and negatively regulated by inosine and adenosine triphosphate (ATP). The regulation involves an allosteric site for inosine-binding in the vicinity of the active site, along with IMP-induced local and global conformational changes in the monomer and a tetrameric arrangement, respectively.

In this presentation, we will report the details of structural and biochemical studies of ScISN1. These regulatory and catalytic features of ScISN1 are different to those of the homologous enzyme from plasmodia, mainly due to sequence and structural variations. Our findings provide valuable insights into the allosteric regulation of enzymes within the ISN1 family.

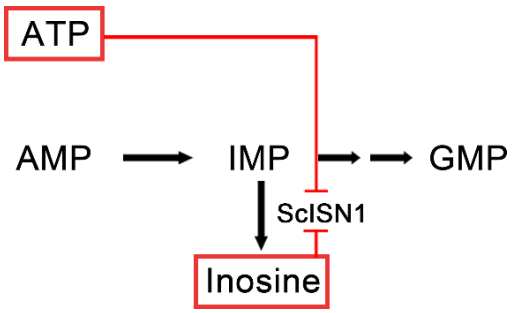

Figure 1. Scheme of Inosine/IMP homeostasis.

[1] Pedley, A.M. and Benkovic, S.J. (2017) A New View into the Regulation of Purine Metabolism: The Purinosome. Trends Biochem. Sci. 42, 141- 154.

[2] Smith, P.M. and Atkins, C.A. (2002) Purine biosynthesis. Big in cell division, even bigger in nitrogen assimilation. Plant Physiol. 128, 793-802.

[3] Carrique, L., Ballut, L., Shukla, A., Varma, N., Ravi, R., Violot, S., Srinivasan, B., Ganeshappa, U.T., Kulkarni, S. and Balaram, H. (2020) Structure and catalytic regulation of Plasmodium falciparum IMP specific nucleotidase. Nat. Commun. 11, 3228.

[4] Walther, T., Novo, M., Rössger, K., Létisse, F., Loret, M.O., Portais, J.C. and François, J.M. (2010) Control of ATP homeostasis during the respirofermentative transition in yeast. Mol. Syst. Biol. 6, 344