

The structural impact of the N-terminal peptide fragment in retinal IMPDH I, 603 variant, while exposed to purine nucleotides regulation

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Abstract

Inosine monophosphate dehydrogenase (IMPDH), catalyzes the rate-limiting step in the GMP biosynthetic pathway, via oxidation of IMP to XMP. There are two isozymes for IMPDH in mammals, IMPDH I and IMPDH II, each with 514 amino acids and with %84 sequence homology. The mouse retinal tissue contain mainly IMPDH I which exist in three isomeric forms: IMPDH I (514), IMPDH I (546) and IMPDH I (603). Purine nucleotides play important roles in enzyme activity regulation and maintaining homeostasis of purin nucleotides within the cell via unknown mechanism. In this study, we are aimed to evaluate the possibility of the structural variation of the major mouse retinal isoform, IMPDH I (603), with respect to the canonical variant, while undergoing allosteric regulation by the purine nucleotides. Our results indicated that regulation of IMPDH I occurs mainly via different macromolecular clusture of the tetrameric enzyme.

Key words: IMPDH, retina, GTP, allosteric regulation