Title:	In silico molecular modelling of MTHFR protein across eukaryotic species
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Abstract:	Methylenetetrahydrofolate reductase (MTHFR) is a key regulatory enzyme involves in folate and methionine cycle which are important for the biosynthesis of nucleotide, lipid, and amino acids. Deficiency and mutations in MTHFR lead to hyperhomocysteinemia, vascular diseases, neural tube diseases, diabetes, and various cancer diseases in humans. In other eukaryotes like in plants, it has role in photorespiration, germination, root development, and lignification. In mice, MTHFR accelerates aggregation of unmodified keratin in mice hair, in this way MTHFR retains its core function in various eukaryotes. To study the various pathophysiological role of MTHFR in various species, complete 3D structures of different diverged species were modeled using template-based modelling. As loops play a major role in protein, problematic loops were refined and validated using several tools. Impact of experimentally determined mutations analysed on these models, docking of FAD and SAM to get insight into possible binding modes and how they interact with the enzyme. As identification of SNPs in the human genome growing nowadays, damaging SNPs in human MTHFR gene were analysed using SIFT, PROVEAN, PolyPhen2, Mutpred. Total of 14 SNPs were identified which affect the structure and dynamics of human MTHFR protein. As these mutations occur in the course of evolution these deleterious SNPs may having impact on other eukaryotes also.
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