Structural adaptation of serine hydroxymethyltransferase to extreme environments

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Serine hydroxymethyltransferase (SHMT) catalyzes the reversible cleavage of serine to form glycine and monocarbonic groups, essential in several biosynthetic pathways. Recently, the crystallographic structures of SHMT from four mesophilic organisms were solved. The availability of information produced by the genomic projects, prompted the analysis of the structural adaptation of SHMT to “extreme” environments, such as high temperatures and ionic strenghts, by exploitation of structural data from extremophilic organisms. The sequences of 11 extremophilic SHMTs obtained from the databanks were multiply aligned to 53 homologs from mesophilic organisms and analyzed to detect the net flow of preferred amino acid exchanges in the direction mesophile to extremophile. The structural basis of the observed exchanges was further investigated through the systematic application of homology modelling to 11 extremophilic SHMTs, using the structures of SHMT from E. coli, man and rabbit as templates. The results of the study suggest that, in thermophilic SHMT, thermal stability can be achieved through three main strategies: i) an increased number of charged residues at the protein surface; ii) an increased hydrophobicity of the protein core; iii) substitution of thermolabile amino acids exposed to the solvent.
Adaptation of SHMT from the halophilic Halobacterium NRC-1 was analysed with a similar approach. The results suggest that, in this case, stability was achieved through mechanisms aimed at harnessing the high ionic concentration, such as: i) a significant excess of acidic residues and alanine, over glutamine and, particularly, lysine, at the protein surface; ii) a smaller population of isoleucine, due to an increase of valine residues, occurring at buried b-strands of the enzyme, which could lead to an increased flexibility of the halophilic protein, preventing the enzyme from salting out effects.
The analysis reported here can be applied to other enzyme systems for which suitable structural information is available.