

Specificity evolution of the ADP-dependent sugar kinase family - in silico studies of the glucokinase/phosphofructokinase bifunctional enzyme from *Methanocaldococcus jannaschii*

Merino, Felipe

Guixé, Victoria

In several archaea of the Euryarchaeota, the glycolytic flux proceeds through a modified version of the Embden-Meyerhof pathway, where the phosphofructokinase and glucokinase enzymes use ADP as the phosphoryl donor. These enzymes are homologous to each other. In the hyperthermophilic methanogenic archaeon *Methanocaldococcus jannaschii*, it has been possible to identify only one homolog for these enzymes, which shows both ADP-dependent glucokinase and phosphofructokinase activity. This enzyme has been proposed as an ancestral form in this family. In this work we studied the evolution of this protein family using the Bayesian method of phylogenetic inference and real value evolutionary trace in order to test the ancestral character of the bifunctional enzyme. Additionally, to search for specificity determinants of these two functions, we have modeled the bifunctional protein and its interactions with both sugar substrates using protein-ligand docking and restricted molecular dynamics. The