Structural Modeling of Trehalose Synthases in Pathogenic Organisms

Gonçalves, L.M; Rebello, A.N; De Mesquita, J.F.

Federal University of Rio de Janeiro State, Bioinformatics and Computational Biology Group, RJ, Brazil

INTRODUCTION. Trehalose is a disaccharide present in bacteria, fungi, insects, yeasts, plants and invertebrates. This sugar plays a very important role during stress, such as dehydration, starvation and heat shock, which leads to its accumulation. The presence of this sugar in certain human pathogens acts as a stress protector and also as a virulence factor. Trehalose-6-phosphate synthase (TPS1) is the first enzyme of trehalose synthesis pathway responsible for the reaction of UDP-glucose with glucose 6-phosphate to form trehalose-6-phosphate and UDP. **OBJECTIVE:** In the present study, we aim to determine if the binding residues of the TPS1 are sequentially and structurally conserved in organisms with pharmacological interest. **MATERIAL AND METHODS:** To obtain the TPS1 sequences from Escherichia coli, Candida, Mycobacterium and Saccharomyces cerevisiae we performed data mining in the UniProt database. The multiple sequence alignment was performed using Clustal Omega and the binding site highlighted. Structural theoretical models were created through comparative modeling (Mholline). Structural alignments were performed using TM-align of each model with experimentally determined TPS1 structures available in the Protein Data Bank and RMSD values generated. The binding sites of the models and the determined TPS1 were highlighted with PyMol. **DISCUSSION AND RESULTS**: The multiple sequence alignment showed that the binding sites are conserved in the different organisms, but only the last binding site is not conserved. The RMSD values from the alignment between the Protein Data Bank TPS1 structure and the generated models varied from 0.16 to 1.05, indicating that the generated models are reliable. The structural alignments showed that the binding site is also structurally conserved. **CONCLUSION:** This study suggests that different organisms have the binding site of TPS1 conserved, which is important for the same enzyme activity and is important for future drugs development.

Key words: Trehalose, TPS1, binding site.
Supported by: CNPq, UNIRIO