Poster I-34

Structural Analysis of proplasmepsin from the human malarial pathogen plasmodium vivax

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Short Abstract: We have concentrated our effort in understanding some crucial features of the protein plasmepsin from the human malarial pathogen plasmodium vivax. The analysis for identification and alignment of homologous sequences for proteins with decided structure was led with the Star Sting Suite.

Long Abstract:
The malarial is one of the main illnesses that afflict the populations of tropics countries, become infected 300 million people more than annually and causing the death of about 1,1 million of them. The discovery of new antimalarial drugs is of vital importance for the tropical countries, and this challenge must be adequately responded by those countries (NOTEBERG, et al.,2003).
The plasmepsin of the human malarial pathogen plasmodium vivax is an endo peptidase. The plasmopepsin is responsible for the digestion of the human hemoglobin which occurs during the phase of incubation of the Plasmodium vivax in the interior of the hemácias. This process turned into the object of research with the goal to obtain the medicine that has inhibiting action on plasmopepsin. The crystal structure of proplasmepsin from the human malarial pathogen Plasmodium vivax was deciphered by X-Ray diffraction and the data are deposited in the PDB file 1miq. This enzyme belongs to the functional class Hydrolase, superfamily: acid proteases, family: pepsin-like, class: mainly beta, and architecture: barrel.
In order to design a new drug, the knowledge of the structural properties of the molecule is necessary and the relationship between its chemical structure and function is fundamental. Upon identification and posterior alignment of homologous sequences, for the proteins with solved structure the structure / sequence / function relationship was analyzed with the Star Sting Suite.
We have concentrated our effort in understanding some crucial features of the plasmopepsin protein. Analysis of the 1miq.pdb file by using Sting indicates that the structure has some amino acids yielding the energy of intramolecular contacts above the average. Those residues can have an important role in the stability of this protein when cross-referenced with the residues showing order of cross presence and cross link above the expected – average

values.
In this work we focused on those residues: 47, 52, 164, 249, 285 (chains A and B), with the highest energy of internal contacts found. Only the residue 215 (chains A and B) satisfies the condition of having a very high order of cross presence. Only the amino acids 34, 35, 37, 125, 171, 214, 216, 302 (chains A and B), are identified as very conserved (having 90% reliability) - occupying the very same position with identical residues in all homologous proteins.
These three ensembles (energy of internal contacts, order of cross presence, and preserved positions) of amino acids are our primary targets in terms of studying and affecting this particular protein stability and functionality. All the three ensembles were obtained using the Star STING environment, in particular the module: Java Protein Dossier and its “Select” feature, where we were able to pick some parameters and their intervals and end up with a focused view on amino acids of interest.

References:

BERNSTEIN, N.K., CHERNEY, M.M., YOWELL, C.A., DAME, J.B., JAMES, M.N. Structural Insights into the Activation of P. vivax Plasmepsin J.Mol.Biol. v329 pp.505-524 , 2003.
NOTEBERG, D. et al. Hignh-Speed Optimization of inhibitors of the malarial proteases Plasmepsin I and II. J.Combinatorial Chemistry. Vol.5, n.4, p.456-464, 2003.
MATTIUZ, A. R.; COSTA, I. C.; ALMEIDA, C.L. de; SOUZA, S.; BAUDET, C.; HIGA, R. H. STING Millennium: a Web based suite of programs for comprehensive and simultaneous analysis of protein structure and sequence. Nucleic Acids Research, v.31, n. 13, p. 3386-3392, 2003.