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STRUCTURAL PARAMETERS TO FILTER CRUCIAL CATALYTIC SITE AMINOACIDS FROM FRUCTOSE 1,6-BISPHOSPHATE ALDOLASE.

Authors:
MARCELO MENDES BRANDÃO (*Hemotherapy and Hematology Center - UNICAMP*)
PAULA R. KUSER (*Embrapa information technology*)
GORAN NESHICH (*Embrapa information technology*)

Short Abstract: In this work we demonstrate the minimum structural parameters needed to isolate the active site of the fructose 1,6-bisphosphate aldolase, using the Diamond STING suite. DSs is a web based set of programs for a comprehensive analysis of a relationship between protein sequence, structure, function, physical chemical characteristics and stability.

Long Abstract:
Aldolases are best know by their role in the glycolysis pathway where fructose 1,6-bisphosphate aldolase (EC 4.1.2.13) (FBPA) catalyze the reversible cleavage of fructose 1,6-bisphosphate (FBP) into glycerone phosphate and D-glyceraldehyde 3- phosphate. An important step in the catalytic mechanism of FBPA is the proton subtraction from the C4 hydroxyl of FBP, leading to breakage of the C3-C4 bond. The three residues, on human FBPA I, Asp33, Glu187, and Lys229 have all been suggested to be the general base for this step. All three aminoacids involved in the catalytic site of the FBPA I seem to be highly conserved through the evolution, but to answer to the main question of this work no conservation based parameter was used to force an only structural description of those residues The eukaryotes enzymes generally fall into Class I and are found as tetramers (approx.160KDa) of identical polypeptide chains. They occur in mammals as isoenzymes in different tissues. Recently aldolase was pointed as a common autoantigen in Alzheimer's disease, suggesting a new target for potential immune modulation. Further more, in a preliminary proteomic survey of rectus abdominus muscle from obese/overweight and morbidly obese women subjects it was detected a statistically significant increase in adenylate kinase AK1, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), and aldolase A. Diamond STING suite is a web based set of programs for a comprehensive analysis of a relationship between protein sequence, structure, function, physical chemical characteristics and stability based on a collection of publicly available (PDB, HSSP and Prosite) and own data, all stored in STING database (STING_DB) and accessed by the JavaProtein Dossier (JPD) module. In this work STING_DB and JPD were used to point out the minimum set of parameters which can define the catalytic site essential aminoacids of the FBPA I structures from H. sapiens, Plasmodium falciparum, Oryctolagus cuniculus, Leishmania mexicana, Trypanosoma brucei and D. melanogaster. All proteins were obtained on the Protein Data Bank (PDB) and the active sites for each structure were identified by searching on Catalytic Site Atlas (CSA). Even so all three aminoacids involved in the catalytic site of the FBPA I seem to be highly conserved through the evolution, to answer to the main question of this work no conservation based parameter was used forcing an only structural description of those residues. In conclusion, the identification of crucial aminoacids can help researchers to

target new approaches to enlighten the protein functionality, e.g. structural analysis can filter residues which can be used as a target for RNA interference technique or mutagenesis assays. With this information it is possible to reduce the experimental time and can save a lot of research budget.