STRUCTURAL ALIGNMENT: A CLUE FOR ENZYME FUNCTION?

Guelfi, A[1]; Molina, SMG[2]; Neshich, G[3]
[1]Bolsista CNPq, aluna doutorado Depto. Genética, Esalq/USP, Piracicaba, SP, Brasil. [2]Profª. Drª. Depto. Genética, Esalq/USP, Piracicaba, SP, Brasil. [3]Pesquisador da Embrapa Informática na Agropecuária, Núcleo de Bioinformática – Líder do grupo. Campinas, SP, Brasil.
neshich@cbi.cnptia.embrapa.br
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GSTs (glutathione S-transferases) are ubiquitous enzymes essential in cellular detoxification. They catalyse the addition of glutathione to hydrophobic xenobiotic compounds (p.e. herbicides). They also catalyse the reduction of hydrogen peroxide to water, like glutathione peroxidase. The most important family of GSTs is found in cytosol and in a dimeric form, but there are also microsomal trimeric forms. The purpose of this work is to verify the relation between structure and function of GSTs. Seventeen structures were selected for analysis and the criteria to choose them to be further aligned were: 1) no mutations in the sequence, 2) resolution 2.3 ? or better, 3) non redundant sequences. The sequence alignment of these selected structures was done using ClustalX and was visualized using TreeView. Later, the structural alignment was done with PrISM (Protein Information System for Modeling). Complete sequences were considered for the alignments and the results showed three different groups. The first group includes sigma, pi, mu and alpha classes of GSTs. The second group of GSTs is composed by theta, beta, tau, omega and zeta (1fw1) classes. The third has phi and zeta (1e6b) classes. The first group shows the least phylogenetics divergence, with sequence identities (seqID) varying from 85.1% (2gss and 1glp) to 29.8% (2gss and 2gsq), and rmsd (root mean square deviation) varying from 0.4 ? (2gss and 1glp) to 2.1 ? (2gss and 2gsq). The second group has more phylogenetics distance with values of seqID and rmsd varying from 22.7% and 2.2 ? (1jlv and 1gwc) to 19.5% and 2.7 ? (1fw1 and 1f2e), respectively. The third group has two pdbs from phi class (1gnw and 1aw9) with 2.1 ? rmsd and 46.6% seqID, and 1e6b from zeta class (2.6 ? rmsd and 25.3% seqID compared with 1gnw). It is interesting to note that 1fw1 and 1e6b were classified in different groups despite their 48.1% seqID. Another point is the relatively high seqID between pdbs 1gnw and 1aw9 (46.6%) that have poor rmsd (2.1 ?) compared with 2gss and 2gsq that showed the same rmsd but only 29.8% seqID. These data corroborate with the fact that analyses based only on amino acid sequences do not give enough information about enzymes' structures. This can lead us to think that without structural information little we can know about enzymes' function. Further analyses are being done to understand the main question: what is the relation between structure and function of GSTs.