A COMPARATIVE STUDY OF THE PRIMARY STRUCTURES OF PROTEIN AND SUGAR KINASES

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Kinases form an important and large group of enzymes, which play a key role in most metabolic processes and physiological control mechanisms. Phosporylation /dephosphorylation processes function in fundamental mechanisms of enzyme activation, active transport, molecular and cellular recognition and homeostatic control of organisms. Their ubiquity results in high diversity at all structural levels. Nevertheless, it is possible to define several separate groups characterized by a significant, internal level of homology. Our studies were conducted on kinases revealing significant similarity to human hexokinase (NP_277042, SwissProt database).

About 50 selected homologous sequences were aligned with the use of a genetic semihomology algorithm [1-3]. The multiple alignment outcome was verified both at the amino acid and nucleotide levels. Preliminary selection was checked using the BLAST program [4], and the multiple alignment evaluation was carried out with the use of the SEMIHOM (UWr), GEISHA (ICM UW), SH_Search (Fujitsu) and MultiAligner (Fujitsu) programs. Further studies refer to detailed analysis of a variability range and direction for each aligned sequence position.

A consensus tertiary structure, describing the variability range for selected domains, was constructed. As expected, the domain corresponding to the catalytic site shows the highest degree of conservativity. However, this region also contains an associated part of relatively high variability, which can be interpreted as due to the narrow specificity of each enzyme.

Genetic relationships for amino acids occupying corresponding positions were studied. Also examined was the correspondence between non-identical positions and predictions regarding evolutionary differentiation processes, including domination of a single transition/transversion mutational mechanism within this family.

Our studies also included analysis of intramolecular correlated mutations, and their effect on structure/function stabilization in the evolutionary process. Generally, the mutational correlation is consistent with the current hypothesis of mutational feedback [5].

For human hexokinases I-IV, a detailed multiple alignment, with complete information on genetic relationships between corresponding positions, is proposed. This alignment was used to construct a consensus sequence (program Consensus Constructor - ICM UW) characterizing this particular group of kinases.

Finally, a very useful method for secondary/supersecondary structure prediction was explored, based on a contact dot matrix, supported by the Weizmann database and its service of intramolecular contacts in proteins (http://bioinfo.weizmann.ac.il:8500/oca-bin/lpccsu).

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