

## THEORETICAL STUDIES ON SUGAR AND PROTEIN KINASES: STRUCTURAL AND MUTATIONAL VARIABILITY

JACEK KUŚKA<sup>1</sup> and JACEK LELUK<sup>2</sup>

<sup>1</sup>Institute of Biochemistry and Molecular Biology, University of Wrocław,  
Tamka 2, 50-137 Wrocław, Poland, <sup>2</sup>Interdisciplinary Centre for Mathematical  
and Computational Modelling, Warsaw University, Pawińskiego 5A,  
02-106 Warsaw, Poland

Homologous sequences of sugar and protein kinases were the subject of a comparative analysis. The analyzed sequences were taken from the SWISS-PROT database. A sequence multiple alignment procedure was carried out and verified with the use of a genetic semihomology algorithm [1-3]. Identification of residues which are in close contact was carried out using data from the Weizmann Institute database (*Ligand-Protein Contact and Contacts of Structural Units*, <http://bioinfo.weizmann.ac.il:8500/oca-bin/lpccsu>). Analysis and visualization of variability was acquired with the aid of a human hexokinase (NP\_277042) 3D model from the Protein Data Bank.

Results are the following:

- corresponding positions are occupied by 1 to 12 residues,
- in particular, residues involved in the formation of the catalytic site are conservative, however, positions surrounding this site reveal some variability,
- the leader peptide is very mutable,
- residues involved in contacts between kinase domains are conservative,
- residues which are in close contact are characterized by identical or very similar levels of variability.

This analysis confirms a hypothesis [4] concerning a high mutual correlation of residues which are in close contact. It is probably required by the structural and functional stability of the proteins.

### REFERENCES

1. Leluk, J. A new algorithm for analysis of the homology in protein primary structure. **Computers Chem.** 22 (1998) 123-131.
2. Leluk, J. A non-statistical approach to protein mutational variability. **BioSystems** 56 (2000) 83-93.
3. Leluk, J. Regularities in mutational variability in selected protein families and the Markovian model of amino acid replacement. **Computers Chem.** 24 (2000) 659-672.
4. Neher, E. How frequent are correlated changes in families of protein sequences? **Proc. Natl. Acad. Sci. USA** 91 (1994) 98-102.