6A, 18B/1999G101

Structural basis for the ADP-specificity of a novel glucokinase from a hyperthermophilic archaeon

Sohei Ito[1], Shinya Fushinobu[1], Issei Yoshioka[2], Shinji Koga[2], Hiroshi Matsuzawa[3], Takayoshi Wakagi[1*]

[1]Department of Biotechnology, The University of Tokyo, 1-1-1 Yayoi, Bunkyo-Ku, Tokyo 113-8657, Japan. [2]Diagnostics Research & Development Department, Asahi Chemical Industry, 632-1 Mifuku, Ohito-cho, Tagata-gun, Shizuoka 410-2321, Japan. [3]Department of Bioscience and Biotechnology, Aomori University, 2-3-1 Koubata, Aomori-shi, Aomori 030-0943, Japan

Background

ATP is the most common phosphoryl group donor for kinases. However, certain hyperthermophilic archaea such as *Thermococcus litoralis* and *Pyrococcus furiosus* utilize unusual ADP-dependent glucokinases and phosphofructokinases in their glycolytic pathways. These ADP-dependent kinases are similar to each other, but show no sequence similarity to any of the hitherto known ATP-dependent enzymes.

Results

We solved the crystal structure at 2.3 Å resolution of an ADP-dependent glucokinase from *Thermococcus litoralis* (tlGK) complexed with ADP [1]. The overall structure can be divided into large and small α/β-domains and the ADP molecule is buried in a shallow pocket in the large domain. Unexpectedly, the structure was similar to those of two ATP-dependent kinases, ribokinase and adenosine kinase. Comparison based on three-dimensional structure revealed that several motifs important both in structure and function are conserved and that the recognition of the α- and β-phosphate of the ADP in the tlGK was almost identical with the recognition of the β- and γ-phosphate of ATP in these ATP-dependent kinases.

Conclusions

Noticeable points of our study are: 1) the first reported structure of ADP-dependent kinase, 2) the structural similarity to ATP-dependent ribokinase family, 3) its rare nucleotide specificity caused from a shift in nucleotide binding position by one phosphate unit, and 4) identification of the residues that discriminate ADP- and ATP-dependence. The strict conservation of the binding site for the terminal and adjacent phosphate moieties suggests a common ancestral origin of both the ATP- and ADP-dependent kinases.

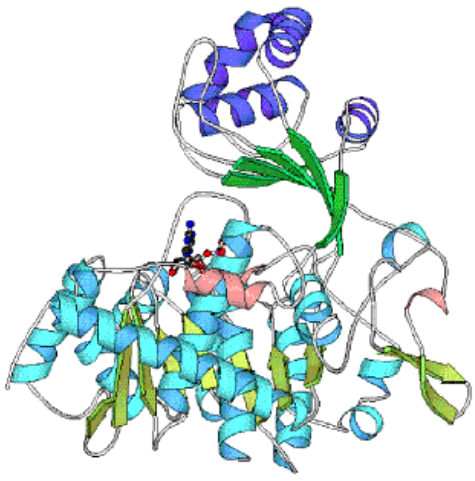

Figure 1 Ribbon diagram of tlGK including an ADP molecule.

Reference

[1] S. Ito *et al.*, (2001) *Structure* **9**, 205-214.

* atwakag@mail.ecc.u-tokyo.ac.jp