

Finding novel pyrophosphate-dependent kinases based on their donor selectivity determinants revealed by crystal structures

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Almost all kinases use ATP as their phosphate donor, while a few kinases utilize inorganic pyrophosphate (PPi) instead. PPi-dependent kinases are often homologous to their ATP-dependent counterparts, but determinants of their different donor specificities remain unclear. We identify a PPi-dependent member of the ribokinase family. Determination of its crystal structures complexed with PPi analogs elucidates the PPi-binding mode of this enzyme. Structural comparison and sequence alignment reveal five important residues: three basic residues specifically recognizing PPi and two large hydrophobic residues occupying a part of the ATP-binding pocket. Two of the three basic residues adapt a conserved motif of the ribokinase family for the PPi binding. Using these five key residues collectively as a signature pattern, we discover novel PPi-specific members of the ribokinase family. Introduction of these residues may enable transformation of ATP-dependent ribokinase family members into PPi-dependent enzymes.

Reference

1. Nagata, R., Fujihashi, M., Sato, T., Atomi, H. & Miki, K. *Nat. Commun.* accepted.