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An unique metabolism of pyrimidine nucleosides in *Thermus thermophilus* HB8.

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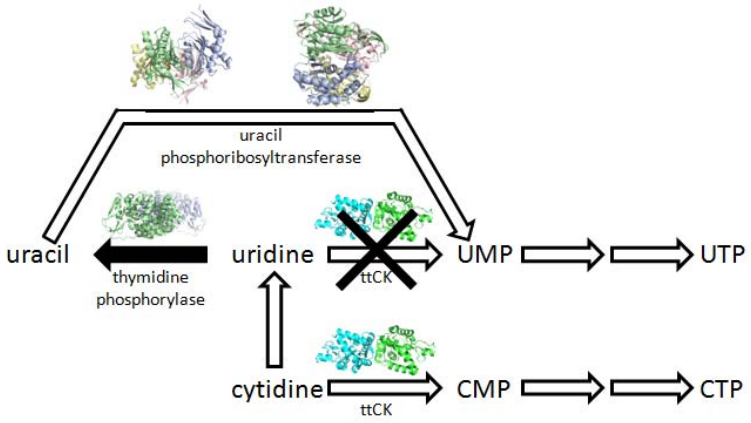
Nucleosides are one of the most important molecules and are used for producing nucleotides in the salvage pathway. Because the salvage pathway requires less molecules and energy for producing nucleotides than *de novo* pathway, the salvage pathway plays an important role in the organisms. However, enzymes involved in this pathway are diverse among species. Therefore, it is necessary to study the pathway in a single organism. In this study, we studied enzymes in the salvage pathway of pyrimidine nucleosides in *Thermus thermophilus* HB8. First, we studied the catalytic specificity of uridine kinase (ttCK). ttCK had substrate specificity towards only cytidine, which was in contrast to other uridine kinase homologues with specificity towards both uridine and cytidine. To our knowledge, there has been no report about cytidine-specific uridine kinase. To elucidate this unique specificity, we determined the X-ray crystal structure of ttCK-CMP complex. In the determined structure, N4 atom in the base of CMP was located near Tyr93. Tye93 equivalent residue is histidine in homologues with dual activity for uridine and cytidine. When Tyr93 was replaced by phenylalanine and leucine, no activity towards uridine was observed. However, when Tyr93 was replaced by histidine, the dual activity towards cytidine and uridine was observed. These indicated that only 93rd amino-acid residue determined the uridine specificity of uridine kinase. The genomic annotation predicted that ttCK is the sole enzyme that reacts with uridine. Thus, this work raised the possibility that there was an unidentified enzyme metabolizing uridine in *T. thermophilus* HB8. Based on the *in vitro* assay, we found that thymidine phosphorylase catalyzed phosphorolysis of uridine as well as thymidine. Because *T. thermophilus* HB8 has the uracil phosphoribosyltransferase, which produces UMP from uracil and phosphoribosyl pyrophosphate, uridine may be recycled via uracil in this bacterium. Separation of cytidine and uridine salvage pathways my provide a survival advantage *T. thermophilus* HB8 with the GC-rich genome..



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