Thymidine Kinase of Mycoplasmic Origin – an Enzyme with Lasso

Urszula Kosinska[a], Cecilia Carnrot[b], Liya Wang[b], Staffan Eriksson[b], Hans Eklund[a], [a]*Molecular Biology, SLU, Uppsala, Sweden.* [b]*Molecular Biosciences, SLU, Uppsala, Sweden.* E-mail: urszula@xray.bmc.uu.se

Thymidine kinase, TK1, is a well-known enzyme of importance in nucleotide metabolism as well as an activator of antiviral and anticancer drugs as AZT. TK1 has narrower substrate specificity than the other deoxynucleoside kinases and phosphorylates only deoxythymidine and deoxyuridine. TK1-like sequences are found in a broad variety of organisms. Recently, thymidine kinase from *Ureaplasma urealyticum (Uu*-TK) was characterized.

U.urealyticum is a human pathogen colonizing the urogenital tract. Interestingly, no genes for the *de novo* synthesis of deoxyribonucleotides have been found in the *U. urealyticum* genome. Therefore, this bacterium has to rely solely on salvage for synthesis of DNA precursors making *Uu*-TK a potential target for antibacterial drugs blocking the bacterial but not the human TK1.

Here the Xray-structure of *Uu*-TK in complex with the feedback inhibitor deoxythymidine triphosphate (dTTP) is presented, [1]. The enzyme has a tetrameric structure where each subunit contains an α/β-domain and a unique lasso-type domain. The domains are connected via a structural zinc. The active site is buried between these two domains and the thymidine of dTTP is hydrogen bonded to main-chain atoms predominantly coming from the lasso loop.

[1] Welin M., Kosinska U., Mikkelsen N.E., Carnrot C., Zhu C., Wang L., Eriksson S., Munch-Petersen B., Eklund H., *Proc. Natl. Acad. Sci. USA,* 2004, **101**, 17970.

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