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A New Construct of Human Deoxycytidine Kinase Crystallizes in Multiple Complexes Allowing a More Complete View of Substrate Binding. M.H. Godsey, A. Lavie, Dept. of Biochemistry & Molecular Genetics, Univ. of Illinois at Chicago, Chicago, IL 60607, USA.

Antimetabolite anti-cancer drugs, including AraC and gemcitabine, mimic nucleotides, but must be administered as inactive, unphosphorylated prodrugs. Intracellular phosphorylation by deoxycytidine kinase (dCK) is the first and rate-limiting step in the activation of these prodrugs to their triphosphate forms. While both ATP and UTP are reported to be phosphate donors for this reaction, UTP is generally believed to be the physiologically preferred substrate. The structures of full-length human dCK in complex with ADP and three phosphate acceptor substrates have previously been reported, however this protein construct did not yield quality crystals with any other complexes. Here we report that a modified version of dCK retains near wild-type activity and has been crystallized and solved in complex with dC and UDP and with dC alone. Crystals of these complexes appear identical but grow in space groups $P2_12_12_1$ and $P2_1$ respectively, with related unit cell edges. Data were collected from both crystals to 3.0 Å resolution and the structures were solved by molecular replacement. This modified dCK crystallizes under similar conditions in other complexes, however these crystals are not yet of data-quality.