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**Structural Characterization of the Closed Conformation of Mouse Guanylate Kinase.** N. Sekulic, L. Shuvalova and A. Lavie, Univ. of Illinois at Chicago, Chicago, IL.

Guanylate kinase is nucleoside monophosphate kinase that catalyses the reversible phosphoryl transfer from ATP to GMP to yield ADP and GDP. In addition to phosphorylating GMP, antiviral prodrugs such as acyclovir, ganciclovir and carbovir, and anticancer prodrugs such as the thiopurines, are dependant on GMPK for their activation. Hence, structural information on mammalian GMPK could play a role in the design of improved antiviral and antineoplastic agents.

Here we present the structure of the mouse enzyme in an abortive complex with the nucleotides ADP and GMP, refined at 2.1 Å resolution with a final crystallographic R-factor of 0.20 ( $R_{\text{free}} = 0.24$ ). Guanylate kinase is a member of the nucleoside monophosphate-kinase family that share a similar fold consisting of 3 structurally distinct regions termed CORE, LID and NMP-binding. Previous studies on the yeast enzyme have shown that these parts move as rigid bodies upon substrate binding. It has been proposed that consecutive binding of substrates leads to “closure” of the active site bringing the NMP-binding and LID regions closer to each other and to CORE. Our structure supports this hypothesis. It also reveals the binding site of ATP, and implicates arginines 43, 137, and 147 (in addition to the invariant P-loop lysine) as candidates for catalyzing the chemical step of the phosphoryl transfer.