

W0163

Structures of 5-methylthioribose Kinase Phased by ADP-2Ho: Catalytic Mechanism and Drug Design. S-Y. Ku^{a,b}, P. Yip,^b K.A. Cornell,^c M.K. Riscoe,^d P.L. Howell^{a,b} ^aUniv. of Toronto and ^bHospital for Sick Children, Toronto, ON, Canada. ^cBoise State Univ., ID, USA. ^dPortland State Univ., OR, USA.

Methionine plays critical roles in many cellular functions but is energetically costly to synthesize; thus pathways to salvage methionine have evolved in all organisms. 5-methylthioribose (MTR) kinase is a key enzyme in this pathway in microorganisms and certain plants, and the absence of a mammalian homolog makes the enzyme a good target for the design of selective antibiotics and herbicides. Recombinant *B. subtilis* MTR kinase has been crystallized with the detergent CHAPS, and structures of the apo enzyme, ADP, AMPPCP and AMPPCP-MTR complexes determined to 2.1Å, 2.2Å, 2.0Å, and 2.3Å resolution, respectively. MTR kinase has an eukaryotic protein kinase fold, and is structurally similar to 3',5"-aminoglycoside phosphotransferase and choline kinase. No global conformation movement is observed upon substrates binding and a dissociate mechanism for phosphate transfer is proposed. The structure was phased using the anomalous signal of holmium. Two holmium ions replace the magnesium ions in the ADP-2Ho protein complex, suggesting that holmium could serve as a convenient and powerful phasing tool to aid the structure determination of other nucleotide binding proteins.