

## W0310

**Structure of Thymidylate Synthase Complementing Protein (TSCP, ThyX) from *Mycobacterium tuberculosis*.** P. Sampathkumar<sup>1,3</sup>, S. Turley<sup>1,3</sup>, C.H. Sibley<sup>2</sup>, H.G. Rhie<sup>4</sup>, J.E. Ulmer<sup>2</sup>, W.G.J. Hol<sup>1,3</sup>, Dept. of <sup>1</sup>Biochemistry and <sup>2</sup>Genome Sciences, <sup>3</sup>Howard Hughes Medical Inst., Univ. of Washington, Seattle, WA 98195. <sup>4</sup>Dept. of Biology, Kyung Hee Univ., Seoul, Korea.

Thymidylate synthase complementing protein (ThyX) is a recently discovered thymidylate synthase (TS). Several human pathogens depend on ThyX for their thymidylate requirements. Absence of ThyX in humans makes it a potential antibacterial drug target. ThyX and TS share no sequence or structural similarity although both enzymes mediate the conversion of 2'-deoxyuridine-5'-monophosphate (dUMP) to 2'-deoxythymidine-5'-monophosphate (dTMP) in the presence of methylenetetrahydrofolate. ThyX catalysis requires reduced FAD. Only in the case of mycobacteria, including *Mycobacterium tuberculosis* and *M. leprae*, both ThyX and TS are observed. It still needs to be established if ThyX is essential for *M. tuberculosis*, and in which stage of parasite growth.

Structure of a double SeMet mutant of MtbThyX was determined in the presence of bound FAD and substrate analog bromo-dUMP at 2.0Å resolution using a combination of anomalous dispersion and molecular replacement techniques. Overall structure is similar to that of the *T.maritima* ThyX. Details of the structure in the context of design of inhibitors will be presented.