

**STRUCTURAL DIFFERENCES BETWEEN  
*E. COLI* AND *A. THALIANA* MTA NUCLEOSIDASE  
SHED LIGHT ON THE DIVERGENCE IN SUBSTRATE SPECIFICITY**

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*E. coli* 5'-methylthioadenosine (MTA) / S-adenosylhomocysteine (SAH) nucleosidase (MTAN) is a dual-substrate specific enzyme that plays a key role in methionine recycling, polyamine biosynthesis, transmethylations reactions and quorum sensing. The enzyme has been identified as a target for antibiotic development because it is essential for viability in multiple pathogenic bacterial species, but is absent in mammals. MTAN is also present in plants, but the plant enzyme lacks specificity towards SAH and metabolizes only MTA. To gain insight into this loss of substrate specificity, we have determined the structures of wild-type *A. thaliana* MTAN in its apo-form and complexed with the inhibitors, formycin A and methylthiotubercidin to 2.0Å, 1.9Å and 1.8Å, respectively. The tertiary structure of *A. thaliana* MTAN is highly similar to the bacterial enzyme; however a detailed comparison of the active sites reveals significantly fewer conformational changes in the plant enzyme upon ligand binding, as well as steric hindrances in the 5'-alkylthio-binding site that would prevent SAH binding.