Structures Of Mfng, An O-Methyltransferase Involved In The Biosynthesis Of Marformycins, From Multiple Crystal Forms

Mitchell D. Miller[1], Kuan-Lin Wu[2], Weijun Xu[3], Han Xiao[4], George N. Phillips, Jr.[5]

[1]Rice University [2]Rice University, [3]Rice University, [4]Rice University, [5]Rice University

mitchm@rice.edu

Marformycins are anti-infective natural products isolated from a deep sea sediment-derived Streptomyces drozdowiczii strain. These cyclodepsipetides contain O-methyl-D-Tyr. Liu et al., (Org. Lett. 2015, 17, 1509–1512) identified a SAM-dependent O-methyltransferase, MfnG, in the marformycins biosynthetic gene cluster and found it capable of methylating the phenoic oxygen of both D-Tyr and L-Tyr in vitro.

To better understand this enzyme's structural recognition and function, we have determined the MfnG structure using X-ray crystallography. Despite adding S-adenosyl-L-methionine (SAM/AdoMet) to the protein during crystallization, we found the spent product, S-Adenosyl-L-homocysteine (SAH/AdoHcy), bound. Since the SAH is unreactive, we were able to soak in L-Tyrosine to obtain a structure with the methyl doner product (SAH) and a methyl acceptor substrate (L-Tyr).

We found MfnG could crystalize from a number of different screening conditions and that these crystals had different unit cell parameters. To date, we have phased 5 forms (2 forms in P212121forms in P21 and a P1 form), which contain one to four dimers (2-8 protomers) per asymmetric unit. Here we compare the packing arrangement in these different crystal packing forms.

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