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The High Resolution Structure and Function of Cytochrome P450(CYP158A2) From *S. coelicolor* A3(2). Bin Zhao and Michael R. Waterman, Dept. of Biochemistry, Vanderbilt Univ. School of Medicine, Nashville, TN 37232-0146, USA.

The genus Streptomyces produces over two-thirds of naturally occurring antibiotics and a wide array of other secondary metabolites. *S. coelicolor* A3(2) has been as a model system for the study of Streptomyces and for genetic control of antibiotic production. CYP158A2 is a member of a 3-gene operon in *S. coelicolor* which includes a polyketide synthase III gene and an open reading frame of undefined function. We have determined that the function of CYP158A2 involved in biosynthetic conversion of malonylCoA to flaviolin and flaviolin dimmers which are known to have antibiotic activity and to be pigments which may protect the organism from ultraviolet light. In order to reveal the relationship of structure/function and to establish a basis for site-directed mutagenesis for production of novel antibiotics, two different conformational structures of CYP158A2 were determined at 1.5-1.75Å. It is clear that CYP158A2 undergoes a significant conformational change in the BC loop and F/G region upon azole inhibitor binding. Our structural analysis of the enzyme folding and secondary structural rearrangements suggests that CYP158A2 might oscillate between open/closed conformations triggered by substrate/inhibitor binding and product release.