

## Cudahy High School SMART Team

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### Whaddya Mean Ending Antibiotic Resistance: *S. wadayamensis* May Hold Answers

PDB: Modified 5DJ3

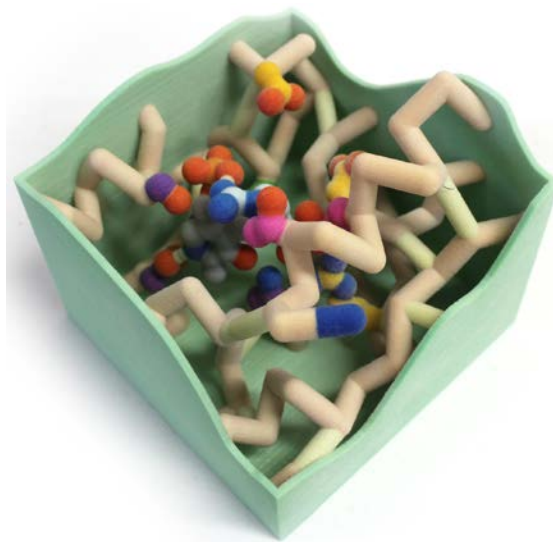
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**Format:** Alpha carbon backbone

**RP:** Zcorp with plaster

#### Description:

Antibiotic-resistant bacteria are common and hard to treat. There is potential to create synthetic antibiotics based on natural products like enduracidin and mannopeptimycin to fight drug resistant bacteria like MRSA. MppP, an enzyme from *Streptomyces wadayamensis*, is required for the biosynthesis of L-enduracididine (L-end), a non-protein forming amino acid building block found in these and other antibiotics. MppP, the first step in the L-end synthesis pathway, functions to add an oxygen atom to the L-arginine substrate, and replace the  $\alpha$ -amino group with a ketone to create 4-hydroxy-2-ketoarginine (4HKA). Hydroxylation is accomplished using a pyridoxal-5'-phosphate (PLP) cofactor, covalently bound by Lys221 to the enzyme, also held by Ser91, Asn160, Asp188, and Ser190 in the active site, which is modeled by the Cudahy SMART (Students Modeling A Research Topic) Team using 3D printing technology. During activity, PLP binds an L-arg substrate, held by Arg352, Asp27, and Asp227 as well as Thr12 and Glu15, performing a hydroxylation through which 4-hydroxy-2-ketoarginine is synthesized. The 4HKA product of the MppP-PLP dependent hydroxylation is used in subsequent reactions in the pathway leading to the creation of the amino acid L-end. Thus, MppP is a critical part of a 3-enzyme team that is responsible for making L-end. The L-end will be incorporated into the different antibiotics by other enzymes. The conversion of L-arg to L-end will help researchers in the creation of new synthetic antibiotics to fight superbugs like MRSA.



### Specific Model Information:

- Lys221 – lime green, involved in the catalytic process
- Ser 91 Asn160 Asp188 Ser190– purple, holding the PLP cofactor
- Ser190 Arg352 Asp27 – gold, hold the arginine substrate
- PLP – silver, performs hydroxylation
- Arg – light cyan, substrate
- 4HKA – light sky blue, product of hydroxylation of L-arg
- Thr12 Glu15 – fuchsia, contact and cover active site
- All Oxygen atoms – red
- All Nitrogen atoms – blue
- N-terminus – blue
- Struts – lemon chiffon, structural support for the model
- Backbone -bisque

<http://cbm.msoe.edu/smartTeams/index.php>

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