

Washington University in St. Louis

Washington University Open Scholarship

Volume 12

Washington University
Undergraduate Research Digest

Spring 2017

Designing β -Lactamase Inhibitors to Restore the Efficacy of Existing Antibiotics

Katelyn Moeder

Washington University in St. Louis

Follow this and additional works at: https://openscholarship.wustl.edu/wuurd_vol12

Recommended Citation

Moeder, Katelyn, "Designing β -Lactamase Inhibitors to Restore the Efficacy of Existing Antibiotics" (2017).
Volume 12. 140.

https://openscholarship.wustl.edu/wuurd_vol12/140

This Abstracts J-R is brought to you for free and open access by the Washington University Undergraduate Research Digest at Washington University Open Scholarship. It has been accepted for inclusion in Volume 12 by an authorized administrator of Washington University Open Scholarship. For more information, please contact digital@wumail.wustl.edu.

DESIGNING β -LACTAMASE INHIBITORS TO RESTORE THE EFFICACY OF EXISTING ANTIBIOTICS

Katelyn Moeder

Mentor: Greg Bowman

We use a combination of computer simulations and biochemical experiments to discover druggable pockets in proteins that are not present in their crystallographic structures, which we call cryptic sites. TEM-1 β -lactamase is an enzyme that degrades common β -lactam drugs, rendering bacteria resistant to common antibiotics such as penicillin. By developing β -lactamase inhibitors that bind cryptic sites, we will restore the efficacy of many existing antibiotics. A high-throughput screen was developed and used to discover an inhibitor and two activators, and we are currently trying to verify that these compounds bind in their predicted cryptic pockets by mutating key binding residues identified by computational docking experiments. Through the mutation of these residues, we have been able to alter the effects of one of the compounds on the enzyme, giving strong evidence that the compound binds in the predicted site. We are currently collecting more data on the binding of the other two compounds, and there is evidence both of these compounds bind in their predicted cryptic sites. We are also working on obtaining structural data in the form of NMR and crystallography to compare against our docking and experimental results.