Alternative mechanisms of β-lactam antibiotic degradation by bacterial β-lactamases and transpeptidases

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β-Lactams, one of the most clinically important classes of antibiotics, act by covalently inhibiting transpeptidase enzymes, thereby disrupting bacterial cell wall biosynthesis. However, the efficacy of the β-lactam antibiotics is critically threatened by bacterial resistance mechanisms, particularly the production of β-lactamases. As new generations of β-lactam antibiotics and β-lactamase inhibitors are developed and utilized in the clinic, new β-lactamases and transpeptidases are selected for that overcome them. Our lab combines chemical, biochemical, biophysical, and microbiological approaches to study β-lactamases and transpeptidases, looking at their interactions with β-lactam antibiotics, and how they may evolve in response to new antibiotics and inhibitors. We have recently uncovered alternative mechanisms by which β-lactamases and transpeptidases degrade β-lactam antibiotics, contrasting conventional views regarding the activities of these enzymes. These studies may help guide the development of new antibiotics that are themselves resistant to bacterial resistance mechanisms.