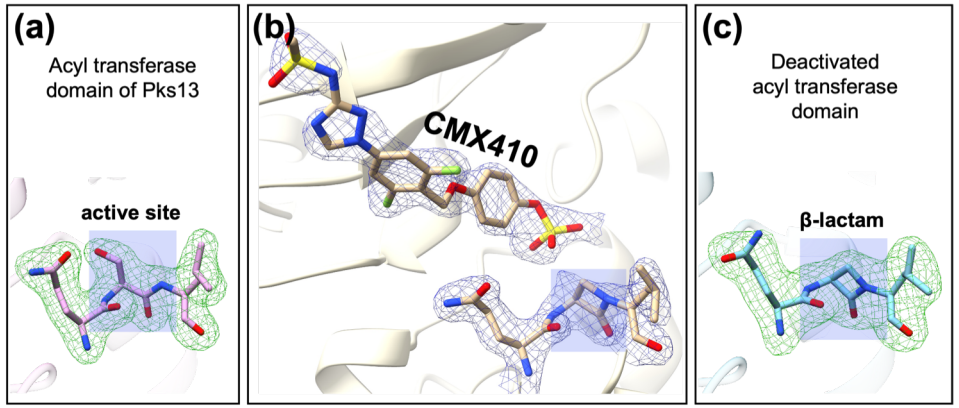
X-Rays Shed Light on Possible New Treatments for TB



Protein crystallography revealed the reaction steps between compound CMX410 and the active site of the acyl transferase domain in Pks13. (a) A catalytic amino acid in the active site (blue shaded region) on Pks13, a cell wall enzyme in *Mycobacterium tuberculosis*. (b) CMX410 converts an amino acid in the active site into β-lactam. (c) The transformed bacterial enzyme Pks13 is now permanently disabled.

Scientific Achievement

X-ray diffraction data revealed the crystal structure of CMX410, a new compound that targets a key enzyme (Pks13) in the cell membrane of the bacterium responsible for tuberculosis (TB).

Significance and Impact

CMX410 is a promising new candidate to treat TB, including multidrug-resistant strains.

Research Details

- Protein crystallography data from the Advanced Light Source, Advanced Photon Source, and National Synchrotron Light Source-II revealed the interaction between CMX410 and Pks13 that permanently disables the bacterial enzyme.
- To capture the reaction steps, the team sampled many conditions to 'trap' the intermediates as the inhibitor engaged with the enzyme.

I.V. Krieger, P. Sukheja, B. Yang, et al., *Nature* **645**, 755–763 (2025), doi: 10.1038/s41586-025-09286-3.

Work was performed at ALS/APS/NSLS-II.