# Structural and Phylogenetic Relationships Among *beta*-Lactamases

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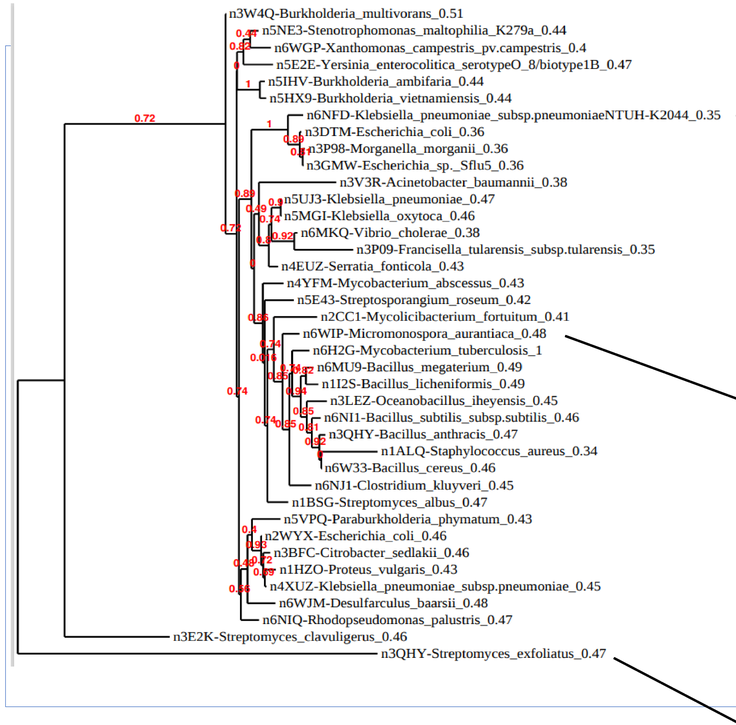
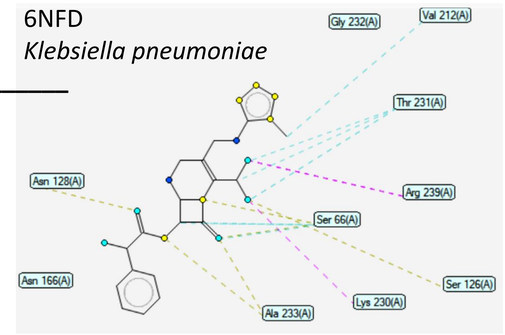
The *Mycobacterium tuberculosis beta*-lactamase (BlaC) has been extensively studied in genetic and structural studies. The enzyme, present in *M. tuberculosis* even prior to the use of *beta*-lactam antibiotics, is at least partially responsible for the resistance of tuberculosis infection to treatment by various *beta*-lactams.

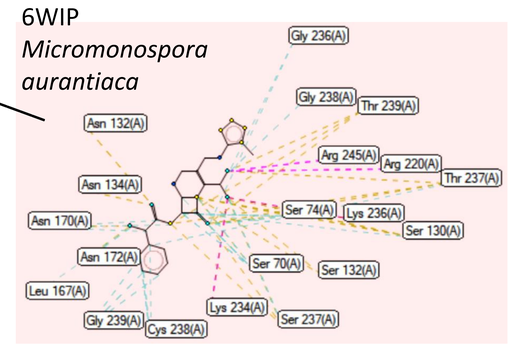
This report describes the structure of this enzyme in comparison to proteins that have closely related sequences and structures. This study relies on the previously studied phylogenetic relationships of beta-lactamases and the large number of lactamase structures that have been deposited into the PDB database.

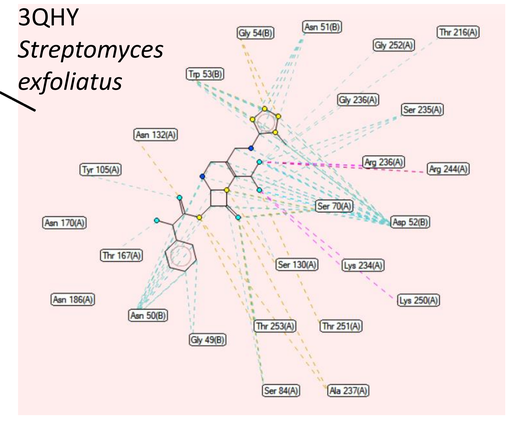
The VAST+ server on the NCBI website was used to provide lists of protein pdb structures with folding patterns that are closely related to that of BlaC. FASTA protein sequence files for the proteins identified by VAST+ were obtained from the RCSB PDB server. The FASTA protein sequence files were sorted according to the VAST-supplied percent sequence identities and, after removal of His-tag sequences, were submitted to the ngphylogeny.fr server. It was necessary to delete FASTA files of low sequence identity (below 30%) in order to generate phylogenetic trees. After protein 3D-structural alignments were prepared using Swiss Viewer, the phylogenetic trees were used to compare protein structures and the locations of active site residues.

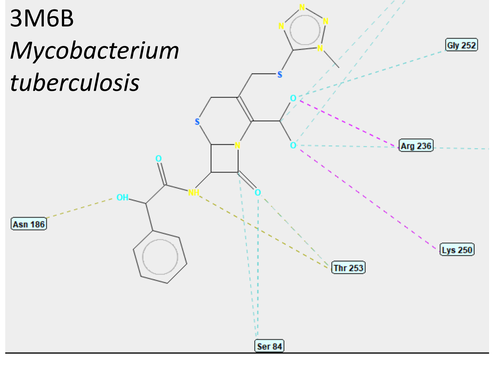
One of the goals of this work was to develop methods that facilitate undergraduate instruction in biochemistry by use of publicly available databases.

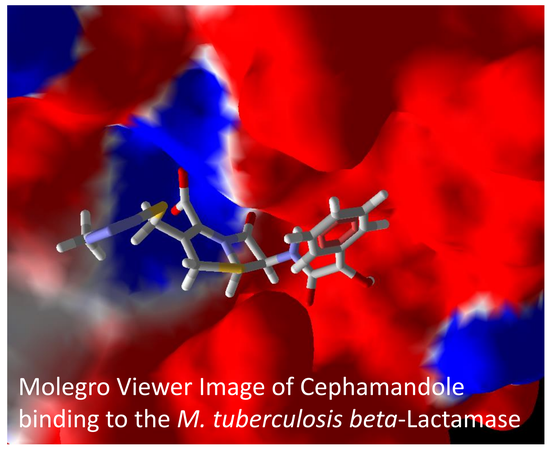


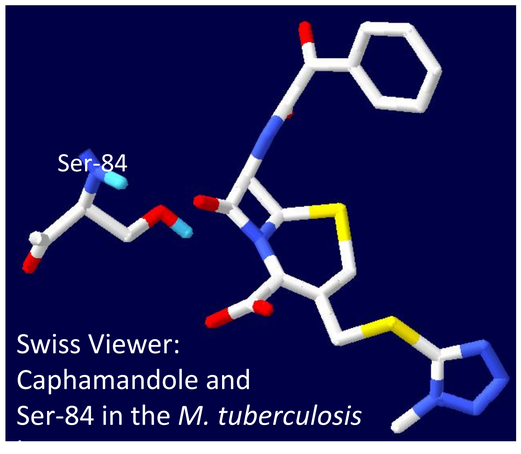




Above is a phylogeny derived from beta-lactamase FASTA protein sequences. The numbers on the right side of the genus and species name indicate the percent sequence identity to *Mycobacterium tuberculosis* beta-lactamase. The numbers on the left following the n, as in n3QHY, or 3QHY, are the PDB identifiers for those protein structures. The lines leading to the 2D interaction diagrams help illustrate the position of these proteins in the phylogram.

2-D Protein-Ligand interaction maps for beta-lactamases were generated by aligning various beta-lactamase protein structures to 3NY4.pdb, a structure of an inactive mutant containing cefamandole, a beta-lactam. Several cefamandole molecules are present in this crystal structure, the one used here is the one bound to the active site, SMX308 in the PDB file. The proteins were aligned using the iterative fit function in Swiss Viewer, and then visualized in Molegro Viewer. Molegro Viewer also provided the 2-D maps of ligand-protein interactions that can be seen on the right.

**References:**

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**Irfan View Image Manipulation:** https://www.irfanview.com/