

Crystal Structure of the Class D Beta-Lactamase OXA-10.

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We report the crystal structure of a class D beta-lactamase, the broad-spectrum enzyme OXA-10 from *Pseudomonas aeruginosa* at 2.0 Å resolution. There are significant differences between the overall fold observed in this structure and those of the evolutionarily related class A and class C beta-lactamases. Further, the structure suggests the unique, cation-mediated formation of a homo-dimer (Figure 1). Kinetic and hydrodynamic data shows that the dimer is a relevant species in solution and is the more active form of the enzyme. Comparison of the molecular details of the active sites of the class A and class C enzymes with the OXA-10 structure reveals that there is no counterpart to the residues proposed to act as general bases in either of these enzymes (Glu 166 and Tyr 150, respectively). Our structures of the native and chloride-inhibited form of OXA-10 suggest the class D enzymes have evolved a distinct catalytic mechanism for beta-lactam hydrolysis. Clinical variants of OXA-10 are also discussed in light of the structure.

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