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Conformational changes of nucleotide-bindings site for the antibiotics development against D-ala-D-ala ligase from Acinetobactor baumannii

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Acinetobacter baumannii, which is emerging as a multidrug-resistant nosocomial pathogen, causes a number of diseases, including pneumonia, bacteremia, meningitis, and skin infections. With ATP hydrolysis, the D-alanine-D-alanine ligase (DDL) catalyzes the synthesis of D-alanyl-D-alanine, an essential component of bacterial peptidoglycan. Structural studies showed the flexible conformational changes in the ATP-binding site, more specifically both the hydrophobic nucleotide base binding site and the hydrophilic triphosphate binding site with the movement of the central domain and serine-loop. The central domain of AbDDL (DDl from *Acinetobacter baumannii*) can have an ensemble of the open and closed conformations before the binding of substrate ATP. In other DDL structures from *Xanthomonas oryzae* pv. *oryzae and Yersinia pestis*, the serine-loop and the ω-loop showed flexible conformations, especially the serine-loop is mainly responsible for the conformational change in substrate nucleotide phosphates. Currently, computer-aided drug designing methods has been actively and efficiently used. The detailed catalytic mechanism and structural information will be helpful in applying the CADD method in drug discovery.

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