Poster Presentation

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A special halide-stabilizing pair and enantioselectivity mechanism of DatA

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A novel haloalkane dehalogenase DatA from Agrobacterium tumefaciens C58 belongs to the HLD-II subfamily and hydrolyzes brominated and iodinated compounds, leading to the generation of the corresponding alcohol, a halide ion, and a proton. DatA possesses a unique Asn-Tyr residue pair instead of the Asn-Trp residue pair conserved among the subfamily members, thus the structural basis for its reaction mechanism merits elucidation. In addition, DatA is potentially useful for pharmaceutical and environmental applications, though several crystal structures of HLD-II dehalogenases have been reported so far, the determination of the DatA structure will provide an important contribution to those fields. This work provided insight into the reaction mechanism of DatA via a combination of X-ray crystallographic and computational analysis. The crystal structures of DatA and the Y109W mutant were determined at 1.70 Å [1] and 1.95 Å, respectively. The location of the active site was confirmed by using its novel competitive inhibitor, CHES. The structural information from these two crystal structures and the docking simulation with 1,3-dibromopropane revealed that the replacement of the Asn-Tyr pair with the Asn-Trp pair increases the binding affinity for 1,3-dibromopropane, due to the extra hydrogen bond between Trp109 and halogenated compounds; and that the key residue to bind halogenated substrate is only Asn43 in the wild-type DatA, while those in the Y109W mutant are the Asn-Trp pair. Furthermore, docking simulation using the crystal structures of DatA and some chiral compounds indicated that enantioselectivity of DatA toward brominated alkanes is determined by the large and small spaces around the halogen binding site.

[1] *T. Mase, H. Yabuki, M. Okai et al. Acta Cryst., 2012, F68, 652-654.*

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