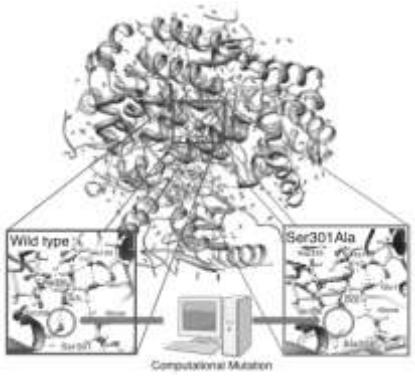
# [P2] Computational Mutation Study on Dehydration Reactions by Diol Dehydratase

Kazuki Doitomi[1], Hiromasa Tanaka[2], Takashi Kamachi[1], Tetsuo Toraya[3], Kazunari Yoshizawa[1, 2]

[1] *Institute for Materials Chemistry and Engneering, Kyushu University 744 Motooka, Nishi-ku, Fukuoka 819-0395, JAPAN.*
[2] *Elements Strategy Initiative for Catalysts and Batteries (ESICB), Kyoto University, Nishikyo-ku, Kyoto 615-8520, Japan*
[3] *Department of Bioscience and Biotechnology, Okayama University, Okayama 700-8530, Japan*

A computational mutation analysis based on quantum mechanical/molecular mechanical (QM/MM) calculations is performed for the elucidation of catalytic functions of amino acid residues at the active site of diol dehydratase in the dehydration of glycerol to afford 3-hydroxypropionaldehyde. While the wild-type diol dehydratase is subject to suicide inactivation in the dehydration process, mutants Gln336Ala and Ser301Ala are more resistant to the inactivation by glycerol [1]. In this study, the impact of the mutation is discussed of the basis of energy profiles of two reaction pathways for the dehydration of glycerol and the inactivation of the enzyme. Both the mutants efficiently distinguish between two possible binding conformations of glycerol, the GS and GR conformations, where the former is known to mainly contribute to the inactivation of the enzyme. The improved resistance to inactivation observed for the mutants can be explained by a hydrogen bonding interaction between an OH group of glycerol and Ser301 as well as steric repulsion between glycerol and Val300. The computational mutation analysis has first unveiled the vital role of Val300 in the discrimination of the GS and GR conformations, which was not clearly viewed in the wild-type enzyme. The present findings will encourage the application of computational mutation approach toward rational design of enzymes optimized for desired organic synthesis.




Bibliography :

[1] Yamanishi et al., FEBS J. 279 (2012) 793-804
[2] Doitomi, K., Kamachi, T., Toraya, T., Yoshizawa, K. Biochemistry 52 (2012) 9202-9210
[3] Doitomi, K., Tanaka, H., Kamachi, T., Toraya, T., Yoshizawa, K. Bull. Chem. Soc. Jpn. submitted