

Structures, functions, regulations and physiological roles of xenobiotic exporters

Akihito YAMAGUCHI

(Osaka University, Institute of Scientific and Industrial Research, Professor)

【Outline of survey】

On the basis of our achievement of world-first determination of crystal structure of a bacterial major xenobiotic exporter AcrB, we focused to reveal the structural universality and diversity, their expression control mechanism, and their intrinsic physiological roles. Xenobiotic exporters are widely distributed in living organisms. In this project, we mainly focused into xenobiotic exporters in *Salmonella*. We try to crystallize all nine xenobiotic exporters in *Salmonella* and reveal their structures in common and difference. We revealed the mechanism of indole-sensing and induction of xenobiotic exporter genes in *Salmonella* as a inter-species signal sensing between *E. coli* and *Salmonella*. We also revealed the mechanism how xenobiotic exporters essentially contribute to the pathogenicity of *Salmonella*. Through these studies, we established the xenobiotic exporters as a novel target of antibacterial drugs.

【Expected results】

Xenobiotic exporter-based hospital-acquired multidrug resistant pathogens have become a serious problem in modern chemotherapy. We previously performed comprehensive expression cloning of potential xenobiotic exporter genes in *E. coli*, and revealed that it has 20 xenobiotic exporter genes being potential drug resistance factors. Some of them are essential for bacterial pathogenicity. In this project, we focused into *Salmonella* and study on the mechanisms of xenobiotic exporter gene expression and the relationship with bacterial pathogenicity. As a result, we expect that completely novel antibacterial drugs which do not kill bacteria but stop pathogenicity. Such antibacterial drugs may be a final solution of the problem of drug resistance.

【References by the principal investigator】

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【Term of project】 FY2007 – 2011

【Budget allocation】 18,000,000 yen

(2007 direct cost)

【Homepage address】

<http://www.sanken.osaka-u.ac.jp/labs/cmb/>