Hiroshi Ogawara: Self-resistance in *Streptomyces*, with Special Reference to β-Lactam Antibiotics. REVIEW ARTICLE

Abstract: Antibiotic resistance is one of the most serious public health problems. Among bacterial resistance, β-lactam antibiotic resistance is the most prevailing and threatening area. Antibiotic resistance is thought to originate in antibiotic-producing bacteria such as *Streptomyces*. In this review, β-lactamases and penicillin-binding proteins (PBPs) in *Streptomyces* are explored mainly by phylogenetic analyses from the viewpoint of self-resistance. Although PBPs are more important than β-lactamases in self-resistance, phylogenetically diverse β-lactamases exist in *Streptomyces*. While class A β-lactamases are mostly detected in their enzyme activity, over two to five times more classes B and C β-lactamase genes are identified at the whole genomic level. These genes can subsequently be transferred to pathogenic bacteria. As for PBPs, two pairs of low affinity PBPs protect *Streptomyces* from the attack of self-producing and other environmental β-lactam antibiotics. PBPs with PASTA domains are detectable only in class A PBPs in *Actinobacteria* with the exception of *Streptomyces*. None of the *Streptomyces* has PBPs with PASTA domains. However, one of class B PBPs without PASTA domain and a serine/threonine protein kinase with four PASTA domains are located in adjacent positions in most *Streptomyces*. These class B type PBPs are involved in the spore wall synthesizing complex and probably in self-resistance. Lastly, this paper emphasizes that the resistance mechanisms in *Streptomyces* are very hard to deal with, despite great efforts in finding new antibiotics.

Keywords: β-lactam antibiotics; β-lactamase; penicillin-binding protein; self-resistance; antibiotic resistance; *Streptomyces*; *Actinobacteria*

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