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メタデータ	言語: English 出版者: 公開日: 2019-12-20 キーワード (Ja): キーワード (En): 作成者: ワナラット, ワナシリ メールアドレス: 所属:
URL	https://doi.org/10.24514/00002951

The study on a bacterial adaptation by gene amplification

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The reiteration of a chromosomal DNA segment, called gene amplification, occurs spontaneously during replication in all organisms. Gene amplification plays an important role in bacterial adaptation to antibiotics. The aim of this work is to understand the gene amplification-mediated adaptive mechanism under antibiotic stress condition in *Escherichia coli* and *Bacillus subtilis*, which are well-characterized bacteria as the model organisms.

Approximately 4% of ampicillin resistant *E. coli* was found to have duplicated copy of the genomic region including a multidrug resistance gene *acrA*. These *acrA*-amplified strains exhibited resistance to many antimicrobial agents including chloramphenicol, tetracycline, erythromycin, kanamycin, novobiocin, cefotaxime and rifampicin.

B. subtilis also can acquire a higher tolerance to tetracycline by increasing the gene dosage of its resistance gene *tetB*. Here we showed that approximately one-third of total tetracycline-resistant cells had multiple copies of *tetB* gene ranging 2 to 230. Four direct repeats flanking *tetB* gene apparently contributed to the *tetB* amplification. Furthermore, the disruption of *recA* gene resulted in a 30-fold decrease in the frequency of *tetB* amplification. Our results indicate that the direct repeats and RecA have an important role for Tc-tolerance development in *B. subtilis*.