ECM 2025 Conference
The 3rd International Electronic Conference on Microbiology
01–03 April 2025 | Online
MDPI

RecA Inhibitor Mitigates Bacterial Antibiotic Resistance

Jin Ma, Keke Shang, Liwen Xu, Qing-Yu He, Gong Zhang
Key Laboratory of Functional Protein Research of Guangdong Higher Education Institutes, Institute of Life and Health Engineering, Jinan University, Guangzhou 510632, China. ✉zhanggong-uni@qq.com

1. Abstract

Bacterial antibiotic resistance (AR) has become a critical global health threat. AR is mainly driven by adaptive resistance mutations and horizontal gene transfer of resistance genes, both of which are enhanced by the genome recombination. We have previously discovered that genome recombination-mediated tRNA up-regulation is important for AR especially at early stages. RecA is the most important genome recombination factor. Therefore, RecA inhibitors should be effective to reduce AR. In this study, we found that BRITE338733 (BR), a RecA inhibitor, can prevent ciprofloxacin (CIP) resistance in subculturing *Escherichia coli* strains BW25113 in the early stages (up to the 7th generation). In the presence of BR, the tRNA was decreased, so that the bacteria cannot evolve resistance via the tRNA up-regulation-mediated AR mechanism. RecA expression level was also not increased when treated with BR. Transcriptome sequencing revealed that BR could inhibit oxidative phosphorylation, the electron transport chain process, and translation, thereby reducing the bacteria energy state and protein synthesis. Also, the effective concentrations of BR do not harm the human cell viability, indicating its clinical safety. These findings demonstrate that BR effectively delays the emergence of spontaneous antibiotic resistance by targeting RecA-mediated pathways. Our findings shed light of a new strategy to counteract the clinical AR: applying BR with the antibiotics together at the beginning.

Keywords: Bacterial resistance, *Escherichia coli*, translation, RecA inhibitor, RecA, tRNA

2. Results

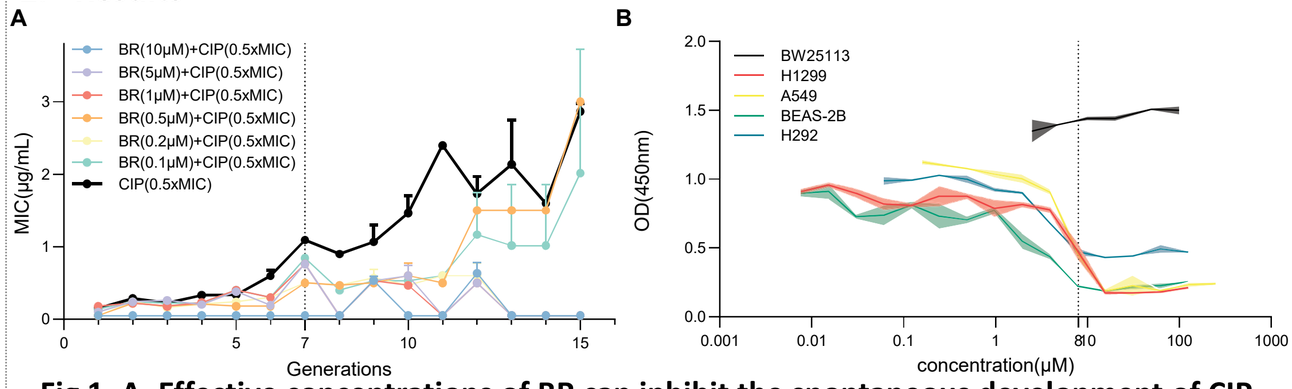

Fig 1. A. Effective concentrations of BR can inhibit the spontaneous development of CIP resistance to BW25113 in the early stage. B. BR is relatively safe for bacterial and cell proliferation

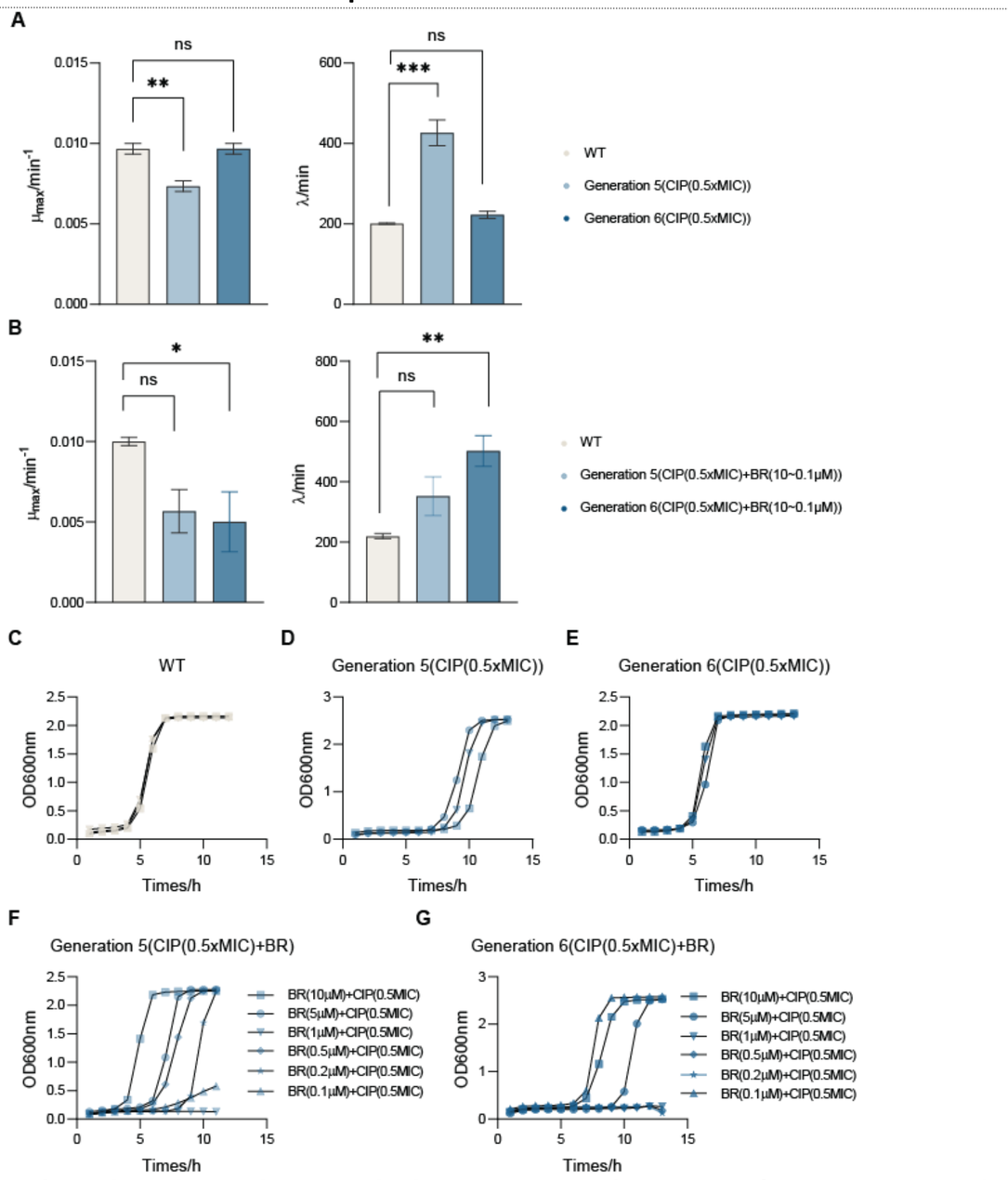

Fig 2. BR significantly reduces the growth characteristics of BW25113 (maximum growth ratio, lag time) in the early stage.

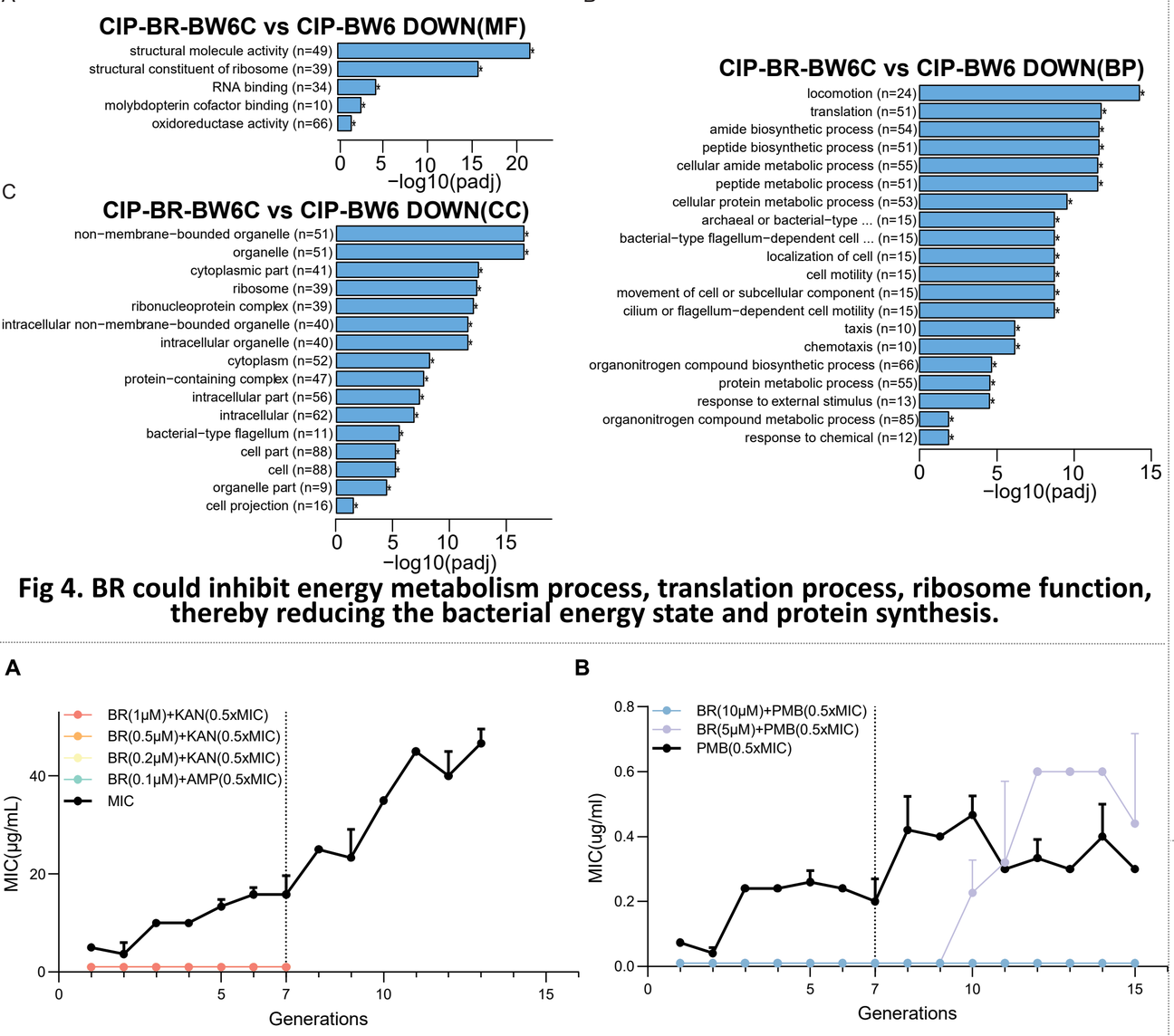

Fig 4. BR could inhibit energy metabolism process, translation process, ribosome function, thereby reducing the bacterial energy state and protein synthesis.

Fig 5. During KAN (Kanamycin) and PMB (Polymyxin B) acclimatization, effective concentrations of BR can also inhibit the production of spontaneous drug resistance in the early stage.

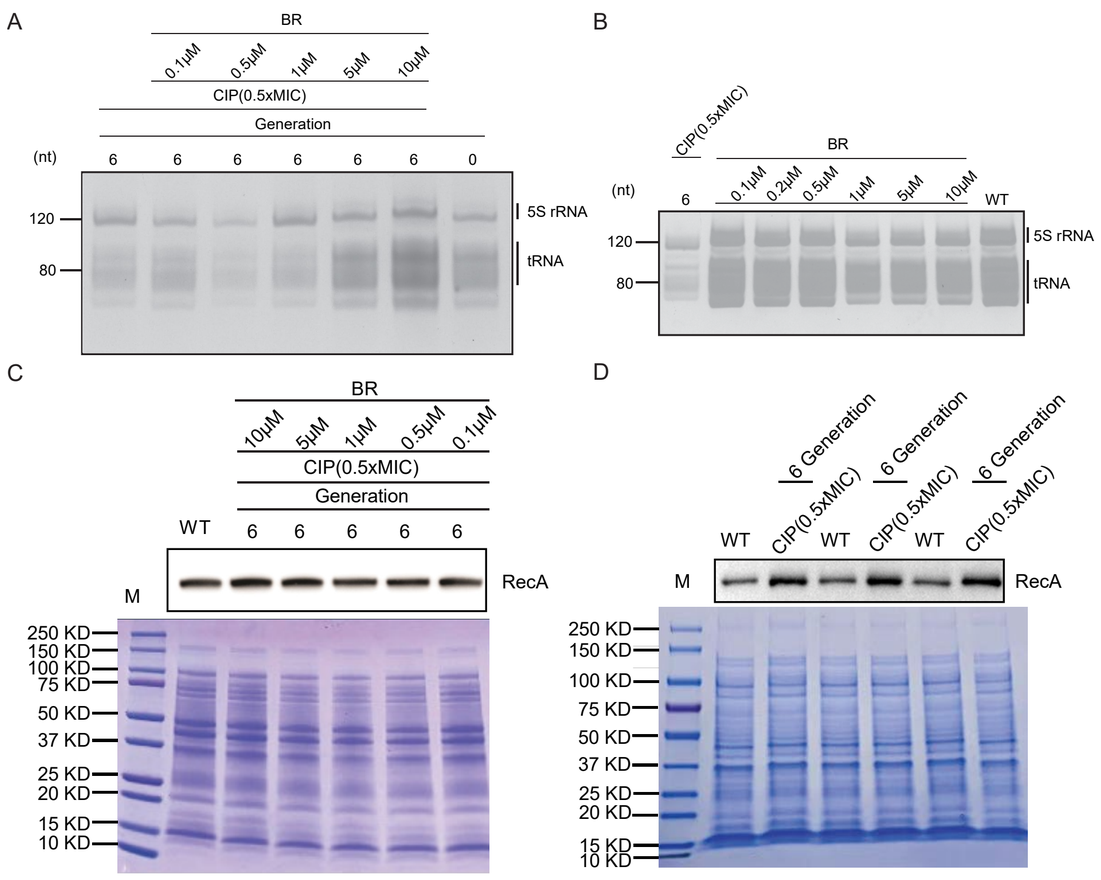

Fig 3. A,B. Effective concentrations of BR reduce tRNA levels within bacteria. C,D. RecA expression level was also not increased when treated with BR.

3. Conclusion

- BRITE338733 (BR), a RecA inhibitor, can prevent ciprofloxacin (CIP) resistance in subculturing Escherichia coli strains BW25113 in the early stages (up to the 7th generation).
- The effective concentrations of BR do not harm the human cell viability.
- The effective concentrations of BR reduce tRNA levels within bacteria, meanwhile not to increase RecA expression level.
- BR could inhibit energy metabolism processes, translation process, ribosome function, thereby reducing the bacterial energy state and protein synthesis.
- During KAN and PMB acclimatization, effective concentrations of BR can also inhibit the production of spontaneous drug resistance.

4. Acknowledgments

- The authors declare no conflicts of interest.
- This work was supported by the Ministry of Science and Technology of China, National Key Research and Development Program (2023YFA0915800).