Dear editor

The work performed by Ito et al was much appreciated since the authors addressed a novel and important issue in antibiotic rational uses, particularly the resistance of Cefmetazole in ESBL-producing E. coli and the involved gene regulations. Cefmetazole have been used as an alternative to carbapenems in addition to the use of quinolone and antibiotic rational uses, particularly the resistance of Cefmetazole in ESBL-producing isolates. Therefore, the transcription (mRNA) levels of porin encoding genes (ompF, ompC), chromosomal β–lactamase AmpC encoding genes (acrA, yhiV, mdfA), and drug efflux pump were detected in this particular study. However, as also discussed well in their discussion section, these mechanisms were not the novel part.

Interestingly, after passage culture with the antibacterial-free medium, only 4 strains from these 11 isolates remain resistant to Cefmetazole, while the others gained susceptibility. The purpose of the authors was to unravel the mechanisms involved in the resistance acquisition against Cefmetazole in ESBL-producing E. coli clinical isolates, with the use of ESBL-non-producing isolates as the controls.

The previous study, reported more than thirty years ago, addressed the potential mechanism of action of Cefmetazole in methicillin and cephem-resistant (MR) strains of Staphylococcus aureus. However, the progression in this particular issue is relatively slower than the mechanism study of other type of antibiotic, especially in ESBL-producing E. coli. In this study, authors tried to explore the mechanism of how Cefmetazole resistance acquisition occurred in ESBL-producing E. coli isolates. Therefore, the transcription (mRNA) levels of porin encoding genes (ompF, ompC, phoE), chromosomal β–lactamase AmpC encoding genes (acrA, yhiV, mdfA), and drug efflux pump were detected in this particular study. However, as also discussed well in their discussion section, these mechanisms were not the novel part.

Moreover, the authors also combined the use of Relebactam (the β–lactamase inhibitor) in observing the effects obtained in Cefmetazole use in E. coli isolates, which resulted in alteration in Cefmetazole susceptibility. The addition of Relebactam suppressed the resistance toward Cefmetazole. However, the remaining question is, while β–lactamase was inhibited, what mechanism was underlying the suppression of Cefmetazole resistance acquisition? Is the effect caused by inhibiting β–lactamase alone enough to suppress antibiotic resistance? Should the upstream regulators be checked for details of their mechanisms, since the authors themselves mentioned that the Relebactam probably caused the porin deficiency. Novel regulation and details of the mechanisms involved probably could be unraveled if any transcription factors or specific motifs in DNA level were to be predicted and proven.

If there are any predicted TFs, which is unique in ESBL-producing E. coli, then we recommend that this issue be unraveled in future studies.
Disclosure
The authors report no conflicts of interest in this communication.

References