Tackling antibiotic resistance by inducing transient and robust collateral sensitivity

Hernando-Amado, S., Laborda, P. & Martínez, J.L. *Nat Commun* 14, 1723 (2023).

Presenter: Yun-Sheng Hung **Date/Time:** 2024/04/25 15:10-16:00

Commentator: Masayuki Hashimoto Ph.D. **Location:** Room 601, Med College Building

Background:

Antibiotics resistance (AR) is a phenomenon that bacteria resist to antibiotics, however, when bacteria resist to some antibiotics, it might present collateral sensitivity (CS) to other certain antibiotics. Therefore, it is said that CS is a trade-off of AR evolution in mutants that acquired AR. *P. aeruginosa*, an opportunistic pathogen, could resist to ciprofloxacin by pumping it out through MexCD-OprJ efflux pump. When resistance of ciprofloxacin increases in mutants that over-express *mexCD-oprj*, it presents CS to aminoglycosides and β-lactams. In this study, the author tried to induce transient CS to tobramycin in *P. aeruginosa* through inducer, dequalinium chloride (DC). And tried to eradicate antibiotic-resistant mutants and clinical strains of *P. aeruginosa* through transient DC.

Objectives/Hypothesis:

To induce robust and transient CS to tobramycin in antibiotic-resistant mutants of *P. aeruginosa* and try to drive the mutants and clinical strains to extinction through transient CS.

Result:

In this study, the author treated PA14 strain and its mutants in the presence and absence of DC, then tested the minimal inhibitory concentration (MIC) of different antibiotics. The author found that DC could induce robust and transient CS specifically to aminoglycosides such as tobramycin. Then, they try to treat the mutants in different strategy of DC and tobramycin treatment and found that the combination treatment of DC and tobramycin is efficient in eradicating *P. aeruginosa* mutants. Finally, to see if the combination treatment is efficient in eradicating clinical isolates, they treat the clinical isolates from hospital in Spain with the combination treatment of DC and tobramycin. The result shows that the combination treatment of DC and tobramycin could drive the clinical isolates of *P. aeruginosa* to extinction.

Conclusion:

The author's work indicates that dequalinium chloride could induce robust and transient collateral sensitivity to tobramycin in *P. aeruginosa* mutants. Also, the combination treatment of DC and tobramycin on the antibiotic-resistant mutants and clinical strains of *P. aeruginosa* indicates that CS is capable of eradicating certain bacterial pathogens. Collateral sensitivity may be a new strategy to conquer the acquisition of antibiotics resistance in different bacteria mutants.