The phenotypic evolution of Pseudomonas aeruginosa populations changes in the presence of subinhibitory concentrations of ciprofloxacin - DTU Orbit (09/11/2017)

The phenotypic evolution of *Pseudomonas aeruginosa* populations changes in the presence of subinhibitory concentrations of ciprofloxacin

Ciprofloxacin is a widely used antibiotic, in the class of quinolones, for treatment of *Pseudomonas aeruginosa* infections. The immediate response of *P. aeruginosa* to subinhibitory concentrations of ciprofloxacin has been investigated previously. However, the long-term phenotypic adaptation, which identifies the fitted phenotypes that have been selected during evolution with subinhibitory concentrations of ciprofloxacin, has not been studied. We chose an experimental evolution approach to investigate how exposure to subinhibitory concentrations of ciprofloxacin changes the evolution of *P. aeruginosa* populations compared to unexposed populations. Three replicate populations of *P. aeruginosa* PAO1 and its hypermutable mutant Δ*mutS* were cultured aerobically for approximately 940 generations by daily passages in LB medium with and without subinhibitory concentration of ciprofloxacin and aliquots of the bacterial populations were regularly sampled and kept at -80 °C for further investigations. We investigate here phenotypic changes between the ancestor (50 colonies) and evolved populations (120 colonies/strain). Decreased protease activity and swimming motility, higher levels of quorum-sensing signal molecules and occurrence of mutator subpopulations were observed in the ciprofloxacin-exposed populations compared to the ancestor and control populations. Transcriptomic analysis showed downregulation of the type III secretion system in evolved populations compared to the ancestor population and upregulation of denitrification genes in ciprofloxacin-evolved populations. In conclusion, the presence of antibiotics at subinhibitory concentration in the environment affects bacterial evolution and further studies are needed to obtain insight into the dynamics of the phenotypes and the mechanisms involved.

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