Time-Resolved Tracking of Mutations Reveals Diverse Allele Dynamics during Escherichia coli Antimicrobial Adaptive Evolution to Single Drugs and Drug Pairs

Understanding the evolutionary processes that lead to antibiotic resistance can help to achieve better treatment strategies. Yet, little is known about the dynamics of the resistance alleles during adaptation. Here, we use population sequencing to monitor genetic changes in putative resistance loci at several time-points during adaptive evolution experiments involving five different antibiotic conditions. We monitor the mutational spectra in lineages evolved to be resistant to single antibiotics [aminoglycoside (AMK), chloramphenicol (CHL), and ciprofloxacin (CIP)], as well as antibiotic combinations (AMK + CHL and CHL + CIP). We find that lineages evolved to antibiotic combinations exhibit different resistance allele dynamics compared with those of single-drug evolved lineages, especially for a drug pair with reciprocal collateral sensitivity. During adaptation, we observed interfering, superimposing and fixation allele dynamics. To further understand the selective forces driving specific allele dynamics, a subset of mutations were introduced into the ancestral wild type enabling differentiation between clonal interference and negative epistasis.

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