GENOME WATCH

Bacterial survival: evolve and adapt or perish

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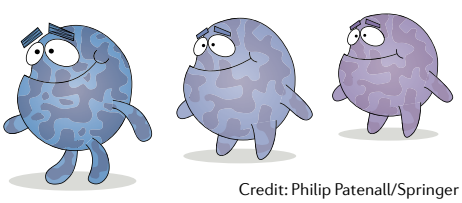
This month's Genome Watch article discusses the role of within-host adaptive evolution in bacterial pathogens for colonization and invasion of their human hosts.

The human immune system is complex and adaptively responds to new encounters with bacterial pathogens. In turn, bacterial pathogens possess innovative adaptive strategies to evade and counteract host defences. An example of such strategies is rapid genome evolution, which enables bacteria to rapidly alter their antigenic epitopes over short timescales to evade immune recognition and therefore avoid expulsion. This bacteria–host evolutionary arms race exemplifies the Red Queen hypothesis, as survival and persistence of both depends on their innate ability to constantly overcome each other's attacks. Such evolution and adaptation can be tracked in real time using whole-genome sequencing (WGS) of sequential samples.

Bartell et al.[1] used WGS and screened infection-related phenotypes in 443 longitudinal samples of *Pseudomonas aeruginosa* from 39 young patients with chronic cystic fibrosis over 10 years. Using a combination of genomic analysis and statistical modelling, they showed early rapid within-host adaptation during the first 2 years of infection and identified variants associated with naive and adapted states[1]. Furthermore, they identified within-host adaptations, their distinct trajectories and novel associations between pathoadaptive mutations and phenotypes. This study highlighted that within-host adaptation is important, complex and affects multiple infection-relevant phenotypes.

Other studies have reported similar findings over shorter timescales. For example, Pandey et al.[2] studied 149 healthy volunteers who were intranasally inoculated with *Neisseria lactamica*, a harmless commensal, and collected samples from each person at 2, 4, 8, 16 and 26 weeks. Through comparative genomic analysis of the sequenced isolates, they identified multiple convergent mutations in phase-variable loci that encode, for example, outer membrane proteins (OMPs) important for host–microorganism interactions and nutrient uptake[2]. Such parallel evolution implied within-host adaptations that may promote efficient colonization. Similar to observations by Bartell et al.[1], Pandey et al.[2] also found rapid evolution early in the infection process, whereby nucleotide substitution rates were 15 times higher during short-term infection (1 month) than long-term infection (6 months). This raised the possibility that host–pathogen encounters promote rapid evolution early during infection as the pathogen attempts to quickly adapt and stably co-exist with its host.

This assertion is supported by previous work by Linz et al.[3], which revealed a mutational burst during the acute phase of infection (<2 months) with *Helicobacter pylori*. During acute infection, substitution rates were ~40–50 times higher than the median substitution rate observed during long-term chronic infection and higher than known mutation rates of any bacteria. Crucially, the substitutions were concentrated in OMPs, which suggested that the mutational bursts were reflective of within-host adaptation to evade immune recognition and the inflammatory responses of the host, which are induced by *H. pylori* during acute infection. Work by Ailloud et al.[4] also showed rapid within-host evolution in *H. pylori* and that within-host adaptation was niche-specific due to the presence of distinct mutational signatures in strains sampled from different stomach chambers (antrum, corpus and fundus), although intragastric migration occurred aided by mutations in genes encoding OMPs associated with chemotaxis. In addition to host immunity and niche-specific metabolite concentration, Ailloud et al.[4] and Haunreiter et al.[5] showed that antibiotics have a profound effect on bacterial population structure within hosts.



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Together, these studies highlight that rapid within-host evolution rate and adaptation triggered by early encounters between the bacteria and the host optimizes bacterial fitness within hosts and is crucial for successful short-term and long-term colonization and infection dynamics. Deciphering within-host bacterial adaptations using WGS can uncover genomic changes that either promote or impede intra-host bacterial survival and possibly reveal patient-level insights that might inform personalized treatments, especially for chronically infected patients.

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Competing interests
The author declares no competing interests.