



“environmental changes ... might explain the recent increases in the frequencies of some bacterial diseases”

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PATHOGEN GENETICS

Temporary survival of the fittest?

The core genome of *Salmonella enterica* serovar Paratyphi A — a common cause of enteric fever in humans — has not changed substantially over the past ~450 years, new research shows. Progressive, Darwinian selection has occurred only transiently over time in this species, meaning that many of these genetic changes are subsequently lost.

Bacterial pathogens are often thought to undergo progressive evolution, which increases fitness through the gain of novel genetic mutations. Searching for evidence of Darwinian selection that might have driven the evolution of pathogenicity in *Salmonella enterica* serovar Paratyphi A, the team sequenced 149 genomes, including 42 old strains that were isolated between 1917 and 1980. A total of 4,584 single nucleotide polymorphisms were identified, which allowed the team to reconstruct genealogies, and infer the evolutionary history and spread of the pathogen worldwide.

The most recent common ancestor of Paratyphi A was estimated to have existed in 1549, setting a limit for the time this pathogen has been infecting humans. The population size of Paratyphi A has increased with global migrations, although the population size did decrease substantially in the 1950s, which could possibly reflect the introduction of antibiotics. Interestingly, although the researchers found that some mutations that confer resistance to antibiotics were repeatedly acquired and lost in the core genealogy, none of these mutations seemed to be lineage-specific, which indicates that these mutations have not been under progressive Darwinian selection.

To further investigate regions in the core genome, the team developed a Hidden Markov Model, DHMM, which is a statistical probability model capable of identifying non-coding regions as well as coding regions that might be under positive selection.

Notably, the variants identified with this method were mostly associated with metabolic functions. Similar to the antibiotic resistance-conferring mutations, the identified mutational events occurred fairly recently, which indicates that these variants are also transient, and are continuously lost to purifying selection.

Taken together, these data imply that the core Paratyphi A genome, and the ability to infect humans, has remained fairly unchanged over the past ~450 years. Notably, the researchers propose that environmental changes, rather than progressive evolution, might explain the recent increases in the frequencies of some bacterial diseases. “An inability to identify lasting Darwinian selection over decades to centuries is probably true of many bacteria and other pathogens,” says senior author Mark Achtman.

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ORIGINAL RESEARCH PAPER Zhou, Z. *et al.* Transient Darwinian selection in *Salmonella enterica* serovar Paratyphi A during 450 years of global spread of enteric fever. *Proc. Natl Acad. Sci. USA* <http://dx.doi.org/10.1073/pnas.1411012111> (2014)