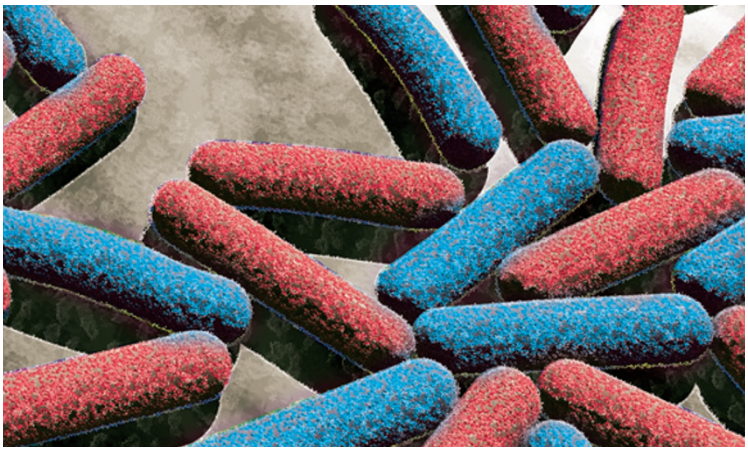
Nature Reviews Genetics | AOP, published online 3 January 2014; doi:10.1038/nrg3658

MICROBIAL GENETICS

Fitness from drug resistance



P. Morgan/NRG

The widespread use of antibiotics has driven the emergence of drug-resistance mutations in bacteria. These mutations are commonly assumed to have a fitness cost in the absence of antibiotics. However, accumulating evidence, including a new study of *Salmonella enterica* subsp. *enterica* serovar Typhi (which is the causative agent of typhoid), shows that drug-resistance mutations can confer antibiotic-independent fitness advantages.

Baker *et al.* generated 11 strains of *S.* Typhi, each with 1–3 mutations in the targets of fluoroquinolone antibiotics (that is, the DNA gyrase GyrA and/or the DNA topoisomerase ParC) on an otherwise isogenic background. These mutations are found in clinical and laboratory isolates of fluoroquinolone-resistant *S.* Typhi, and the authors confirmed that their strains indeed showed marked drug resistance. To test the fitness effects in the absence of antibiotic treatment, the authors co-cultured each strain along with the drug-sensitive control strain *in vitro* for ~150 generations. They measured the resultant proportions of strains by using high-throughput sequencing to quantify mutant and wild-type allele frequencies. Crucially, six of the drug-resistant strains still had a fitness advantage over the control strain in the absence of antibiotic treatment.

If these results are applicable to physiological settings *in vivo*, then they would imply that intentionally avoiding antibiotic use may not result in drug-resistant strains being outcompeted by drug-sensitive strains. However, given that the fitness benefits conferred by the drug-resistance mutations are greatly enhanced in the presence of antibiotics, prudent use of antibiotics will remain a valuable strategy.

Darren J. Burgess

ORIGINAL RESEARCH PAPER Baker, S. *et al.* Fitness benefits in fluoroquinolone-resistant *Salmonella* Typhi in the absence of antimicrobial pressure. *Elife* **2**, e01229 (2013)