

## GENOME WATCH

# Your gut microbiota are what you eat

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This month's Genome Watch highlights recent studies that have characterized the reservoir of antibiotic resistance genes in the human gut microbiota.

It is well known that antibiotic exposure is a major contributor to the emergence of resistance, which has led to the concept of the 'resistome' — a term that describes the collection of antibiotic resistance genes in specific niches, such as the gut and the environment. However, the effects of antibiotic consumption on the prevalence and diversity of resistance genes in these communities is poorly studied. Two metagenomic studies<sup>1,2</sup> have recently reported an unexpectedly high abundance and diversity of resistance genes in the gut microbiota and show that this seems to be tightly linked to the consumption of antibiotics.

Hu *et al.*<sup>1</sup> analysed the faecal microbiome of 162 individuals from Denmark, Spain and China, and compared these data to environmental and agricultural metagenomic data sets.

Antibiotic resistance genes accounted for 0.008–0.171% of the total number of environmental genes, whereas the levels of resistance genes were significantly higher in the gut microbiome, reaching an average

of 0.266% of the total number of gut genes. Individuals from China showed the highest diversity of resistance genes, whereas individuals from Denmark showed the lowest levels of diversity and abundance. Forslund *et al.*<sup>2</sup> also found a higher abundance of resistance determinants in the microbiota of individuals from Spain, Italy and France compared with individuals from Denmark, the United States and Japan.

Common antibiotic resistance genes, including genes that confer resistance to tetracycline, vancomycin, cephalosporins, bacitracin and the macrolide–lincosamide–streptogramin group, were detected in all populations<sup>1,2</sup>. However, the prevalence of these genes varied among countries and with the time of sampling. Interestingly, these variations were strongly dependent on the use of antibiotics, and it was therefore suggested that the enrichment of resistance genes in Chinese individuals reflects the overuse of antibiotics in this country.

In another study, Mather *et al.*<sup>3</sup> sequenced the genomes of 373 *Salmonella enterica* subsp. *enterica* serovar Typhimurium (*S. Typhimurium*) DT104 isolates from humans and animals, and used phylogenetic approaches to trace the origins of both populations and to quantify the diversity of resistance genes. Surprisingly, they found that the diversity of antibiotic resistance genes in human isolates was greater than that in animal isolates, which challenges the traditional view that antibiotic use in veterinary medicine is a major contributor to the resistance burden in humans. In addition, these data revealed that most *S. Typhimurium* strains and their resistance genes show limited transmission and are separately maintained within each population.

Forslund *et al.*<sup>2</sup> found that antibiotic resistance genes can persist in the human gut microbiota for

at least a year, despite the vast majority of such mutations having a fitness cost. So, how do these genes persist in the absence of selective pressure from antibiotics? To investigate this, Snitkin *et al.*<sup>4</sup> sequenced longitudinal isolates of *Acinetobacter baumannii* from four patients while they were receiving colistin treatment and after the drug had been withdrawn. Mutations at the *pmr* locus (which encodes a two-component signal transduction system) conferred colistin resistance and, after drug removal, the ancestral colistin-susceptible isolates re-emerged. However, in one patient the resistance mutations persisted after drug withdrawal owing to secondary mutations in the regulatory region of the *pmr* locus, which compensated for the fitness cost. This study highlights that resistance mutations can be maintained in the absence of drug selective pressure, as a result of compensatory mutations that ameliorate the fitness cost.

The misuse and overuse of antibiotics is an increasing threat to society. Together, these studies highlight that the consumption of antibiotics can select for the emergence of persistent reservoirs of antibiotic resistance genes in the gut microbiota, which emphasizes the need to watch out for what you eat!

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### Competing interests statement

The author declares no competing interests.