Distribution of tetracycline resistance genes in Campylobacter

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Introduction

The widespread use of antimicrobials leads to an increase in antimicrobial resistance among both pathogenic and commensal bacteria.

Tetracycline resistance in bacteria is frequently conferred by ribosome protection proteins (RPPs), which prevent tetracycline binding to the ribosome and disrupting protein synthesis.

We investigated the presence of different tetracycline resistance genes in a range of *Campylobacter* isolates from various sources (birds, animal and clinical samples) collected over a period of 15 years.

We compared the effects of changes in the amino acid sequences of wild-type Tet(O) and mosaic Tet(O) proteins from *Campylobacter* isolates, with a special focus on the electrostatic surface potential.

Methods

Genome sequences of 6,892 isolates of *Campylobacter jejuni* and *Campylobacter coli* collected and cultured from various sources were analysed.

Specific genes encoding RPPs were identified in these genomes using bioinformatic analysis: tet(O), tet(O/32/O), tet(O/M/O), tet(O/W/32/O), tet(W) and tet(O/W/O).

Structures of forty protein sequences were compared *in silico.*

Campylobacter isolates containing these sequences were tested by culturing for levels of resistance to tetracycline.

Results

2228 isolates (32%) of *Campylobacter* genomes contained a single copy of various RPP genes with most (two thirds) containing *tet*(O). The most prevalent mosaic gene was *tet*(O/32/O) (Figure 1).

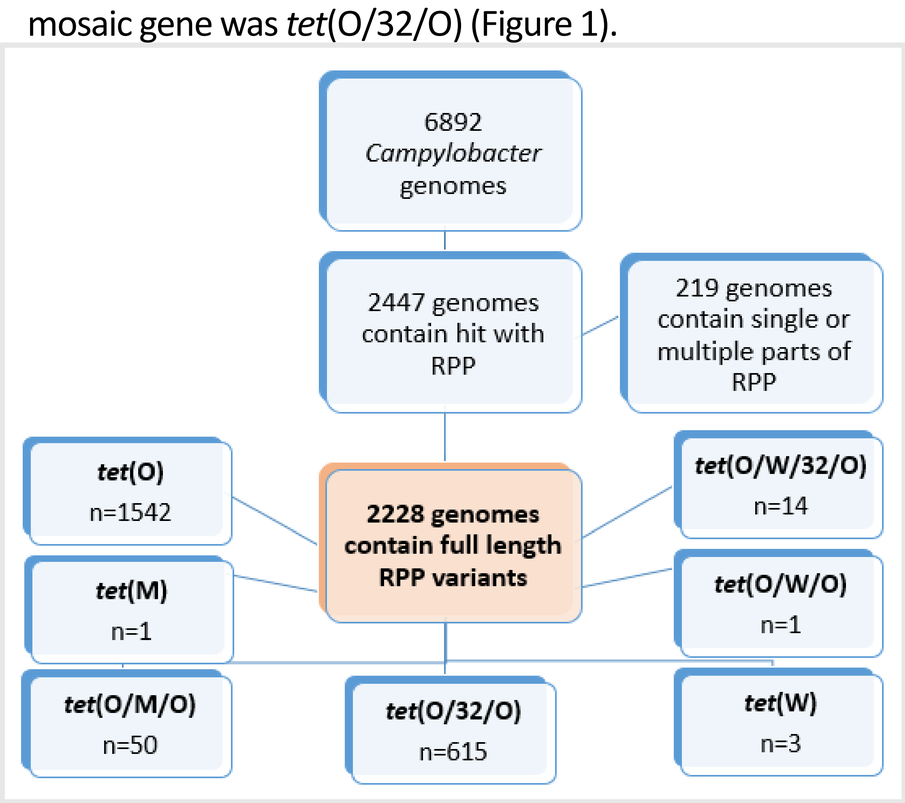


Figure 1 –Distribution of genes encoding RPP in the set of *Campylobacter* genomes:

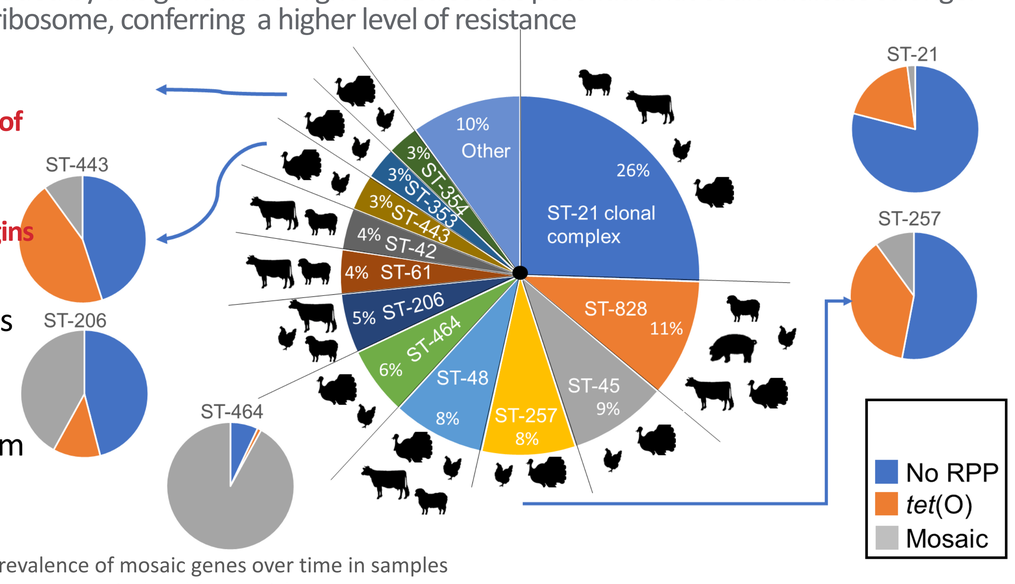
Whole genome sequences were analysed to determine the distribution of specific RPP genes.

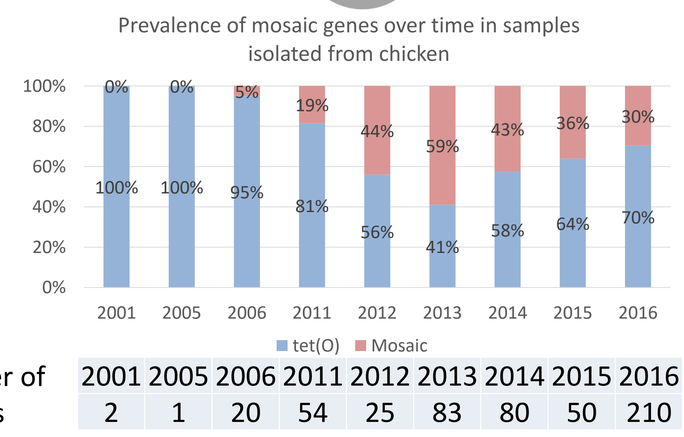
Results (cont.)

- Different serotypes of *Campylobacter* species contained different forms of mosaic genes.
- The prevalence of mosaic genes with a *tet*(O) backbone increased over the 15 year sampling period.
- The *tet*(O/M/O mosaic gene conferred the highest levels of tetracycline resistance.
- The protein encoded by this gene had a higher electrostatic potential that could indicate stronger binding to the ribosome, conferring a higher level of resistance

Figure 1 – Incidence of different sequence types and resistance genes in different origins

The prevalence of specific genes varies in different *Campylobacter* sequence types from different hosts





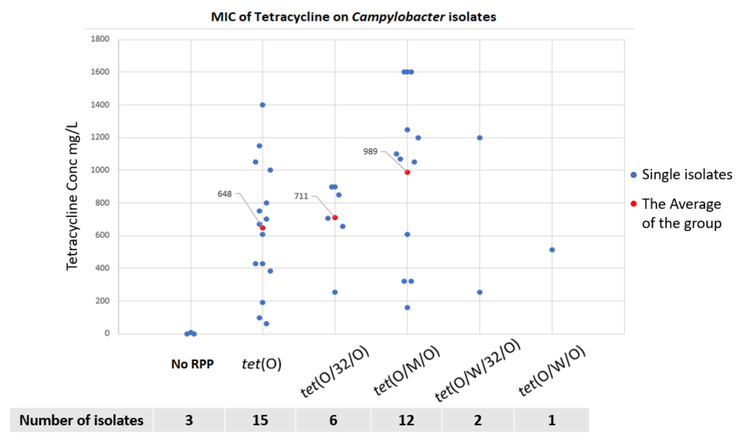
Number of isolates	2001	2005	2006	2011	2012	2013	2014	2015	2016
	2	1	20	54	25	83	80	50	210

Figure 2 – Relative incidence of *tet*(O) and mosaic genes during sampling period

The percentage of isolates containing either *tet*(O) or a mosaic form of tetracycline resistance genes increases over time

Figure 3 - the MIC of Tetracycline for Campylobacter isolates containing distinct tet(O) variants

The *tet*(O/M/O) gene confers a higher level of resistance



Number of isolates	3	15	6	12	2	1

Conclusions

- **Around 1/3 of Campylobacter isolates contain highly conserved ribosome protection type tetracycline resistance genes**
- **Two thirds of these genes are tet(O), and the remaining 1/3 are mosaic genes**
- **The prevalence of mosaic genes has increased in the last 15 years**
- **The Tet(O/M/O) protein has a distinct electrostatic potential and this protein confers a higher level of tetracycline resistance**

Acknowledgement

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