

A multidrug resistant pneumococcal CC230 sub-lineage harbouring a mosaic *tet*(S/M) gene encoding tetracycline resistance in South Africa

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Background

A mosaic *tet*(S/M) gene encoding tetracycline resistance has been found in *Streptococcus* spp., but rarely reported in pneumococci. We assessed a global collection of pneumococcal genomes to identify *tet*(S/M) and characterise their geographical distribution and genetic background.

Methods

- Bacterial collection:** We detected the mosaic *tet*(S/M) encoding tetracycline resistance in a global collection of 12,254 pneumococcal isolates, which represented 30 countries in Africa (59.3%), Asia (17.2%), North America (12.0%), South America (8.3%), and Europe (3.2%). The collection consisted of disease (n=7,391) and carriage (n=4,863) isolates.
- Processing of data:** Recombination-removed phylogeny was built using GUBBINS and RAxML, antibiotic resistance determinants were detected using ARIBA. Phandango and EasyFig were used to visualise trees and ICE comparison, respectively.

Results

1. The majority of *tet*(S/M)-positive isolates were collected from invasive disease among children aged ≤ 5 years old in South Africa

The *tet*(S/M) gene was identified in 130 isolates from South Africa (n=123), Malawi (n=4), and one each from Brazil, Mozambique, and the USA. The majority were isolated from sterile body sites: blood (n=73), cerebral fluid (n=29), and pleural fluid (n=4); and from nasopharynx (n=24). In South Africa, 78.9% (97/123) of *tet*(S/M)-positive isolates was collected from invasive disease among children aged ≤ 5 years old (Figure 1).

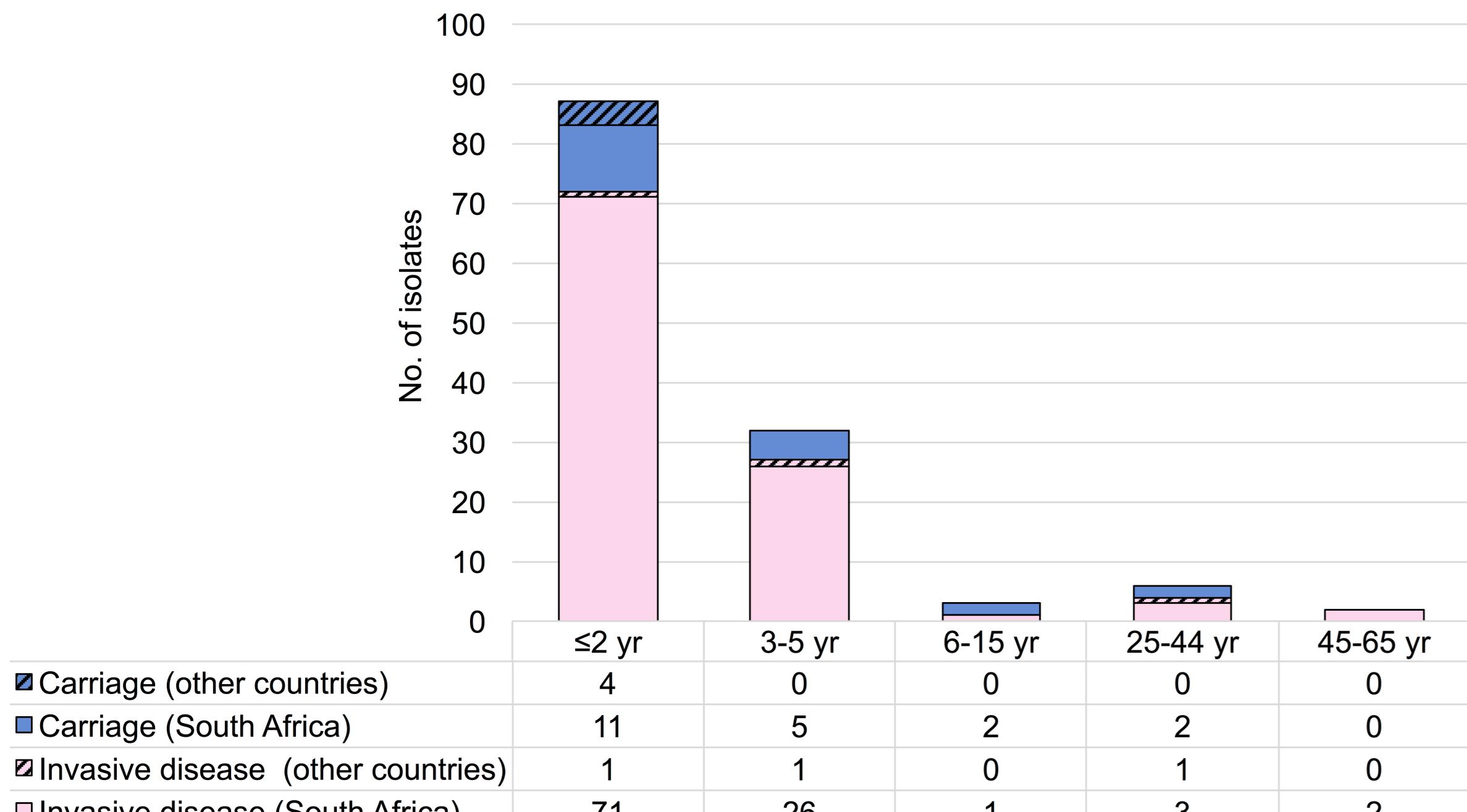


Figure 1. Number of *tet*(S/M)-positive pneumococcal isolates by clinical manifest and country

2. The mosaic structure of *tet*(S/M) in *S. pneumoniae* was unique from other *Streptococcus* spp. (Figure 2).

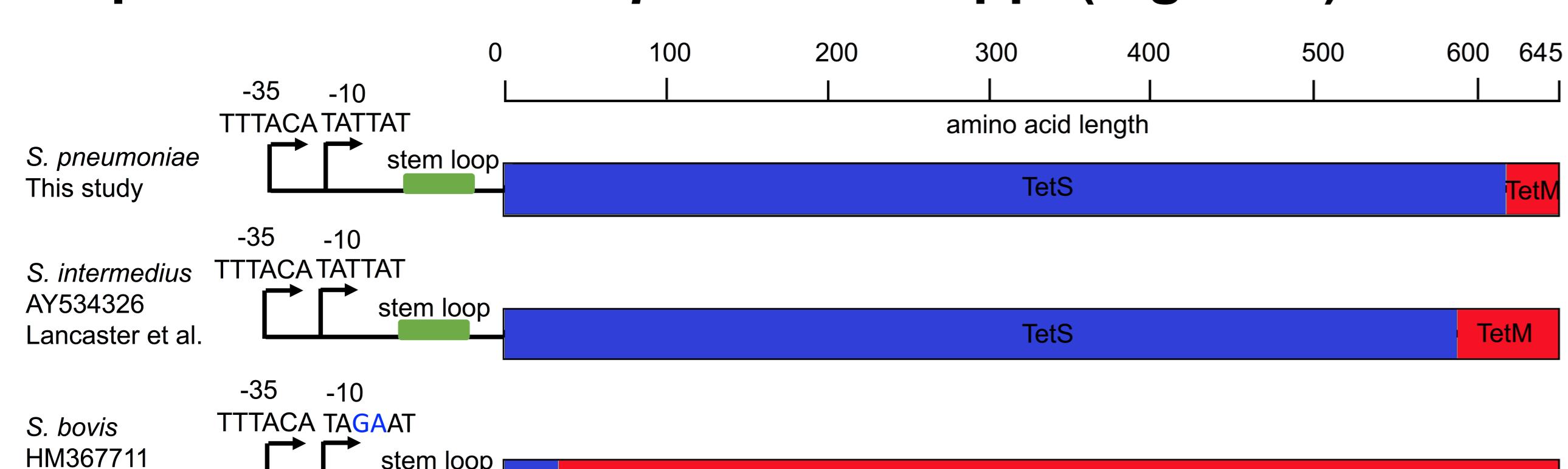


Figure 2. Mosaic structure of three *tet*(S/M) genes in this and previous studies

3. The *tet*(S/M)-positive isolates formed a multidrug-resistant sub-lineage which belong to CC230 (PMEN global clone Denmark¹⁴⁻³², PMEN32)

- All *tet*(S/M)-positive isolates belonged to CC230, except for one from Brazil that belonged to CC320.
- The CC230 *tet*(S/M)-positive isolates formed a sub-lineage within a CC230 phylogeny (Figure 3).
- The CC230 *tet*(S/M) isolates exhibited resistance to penicillin, erythromycin, tetracycline and cotrimoxazole and were mainly associated with serotype 14 (n=127/129), to a lesser extent, serotype 23A (n=2/129)

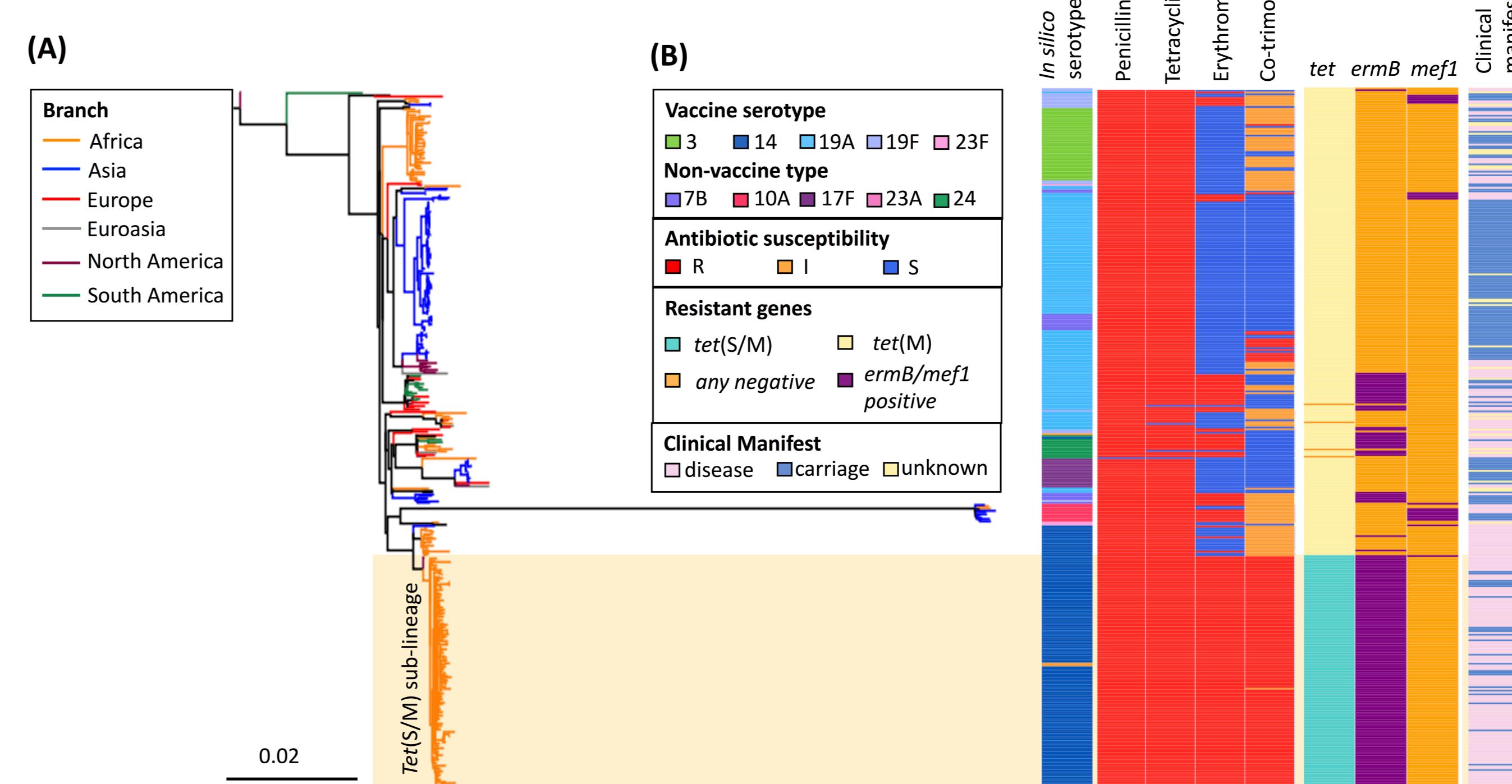


Figure 3. A SNP tree was constructed with CC230 *tet*(S/M)-positive isolates (n=129) and *tet*(S/M)-negative carriage/disease isolates (n=260) collected from twenty countries.

4. The *tet*(S/M) gene within CC230 was located in a conserved Tn916 transposon that inserted within ICESp14ST230, a Tn5253-like ICE element that co-carried ermB (Figure 4).

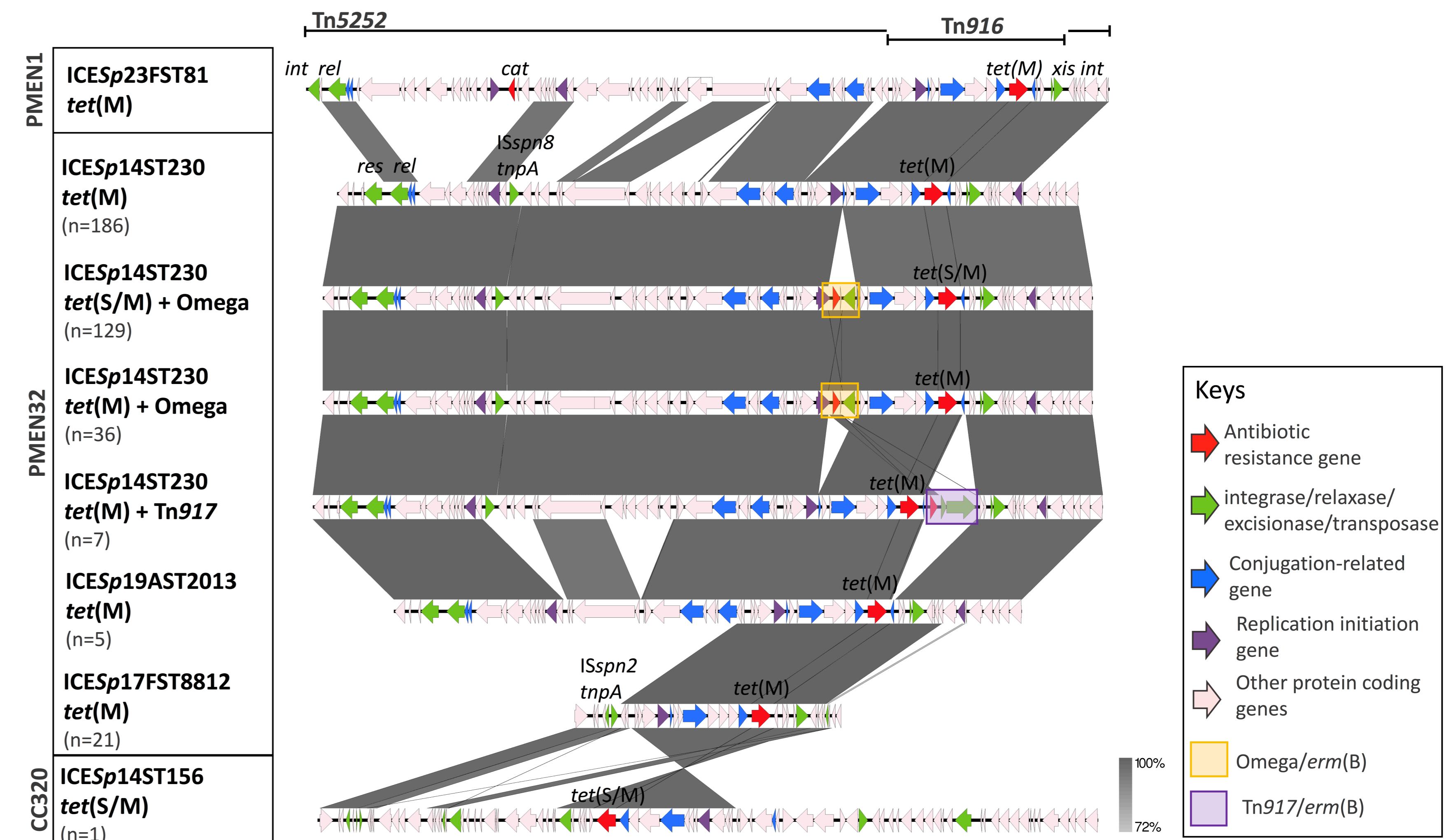


Figure 4. Comparison of ICE elements in this collection with Spain^{23F-1} (PMEN1)

Conclusions

There was a low prevalence of *tet*(S/M) within the GPS dataset, and the conserved genomic location of *tet*(S/M) and closely related genetic background suggested a clonal spread of a *tet*(S/M)-positive CC230-sublineage within South Africa.

