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Implementation of a pbla typing scheme reveals three main plasmid variants which are associated with TEM alleles and gonococcal lineages

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Background

Without a vaccine, the management of gonorrhoea depends on effective antibiotic treatment. However, Neisseria gonorrhoeae (the gonococcus) has acquired resistance to most available antibiotics, leaving cephalosporins as the last resort treatment. The gonococcal beta-lactamase plasmid pbla encodes the TEM beta-lactamase, which requires only one to two amino acid changes to become an extended-spectrum beta-lactamase, conferring resistance against cephalosporins. pbla is mobilisable by the gonococcal conjugative plasmid pConj, which leads to the spread of beta-lactamase-mediated resistance.

Aim/Methods

Several variants of pbla have been reported, which can differ in the TEM allele they carry and their ability to be spread by pConj. However, repeat sequences on the plasmid hinder the assembly of pbla from short-read sequencing data, leading to a lack of knowledge of the distribution of plasmid variants in the gonococcal population. Therefore, we analysed pbla sequences to devise a typing scheme, Ng_pblaST, based on variant-specific gene presence/absence. Ng_pblaST was implemented on PubMLST and used to assess the spread of pbla variants across 17,827 isolates. To gain insights into the molecular determinants of the spread of pbla variants, we investigated the impact of the variant-specific deletions on plasmid transfer and the interplay

between pbla and pConj variants.

Results
Analysis of whole genome sequence data of 17,827 isolates revealed three major pbla variants associated with distinct TEM alleles and gonococcal lineages, most prevalent in low- and middle-income countries. pbla variants are associated with pConj types and show characteristic deletions affecting plasmid biology.

Conclusions
We present a pbla typing scheme which allows the detection of pbla variants from short-read sequence data and have investigated the transfer of pbla variants by pConj types. Linking the variation and distribution of pbla variants to their transfer ability is important to monitor and predict the spread of beta-lactamase-resistance resistance in N. gonorrhoeae.

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