Predicting macrolide resistance: correlation of clinical outcome and laboratory results using *PlexPCR™ M. genitalium ResistancePlus™* assay (SpeeDx)

Jalocon D[1], Couldwell DL [2,3], Jeoffreys NJ[1], Power M[2], Chen SC-A[1,3], Lewis DA[2,3]

[1]Centre for Infectious Diseases and Microbiology Laboratory Services, Pathology West – ICPMR, Westmead NSW 2145; [2] Western Sydney Sexual Health Centre, 162 Marsden Street, Parramatta, NSW 2150;[3] Marie Bashir Institute for Infectious Diseases and Biosecurity & Sydney Medical School – Westmead, University of Sydney, Sydney, NSW, Australia .

Background

Antimicrobial resistance has become a major problem in treatment of *M. genitalium* infections worldwide. Failure of first-line treatment with azithromycin is increasing due to transmitted and induced macrolide resistance. A rapid assay to simultaneously detect *M. genitalium* and macrolide resistance-associated mutations is not routinely available in clinical practice but would improve clinical care.

Methods

A retrospective clinical audit identified 108 episodes of *M. genitalium* infection from January 2013 to December 2015. Laboratory and clinic electronic databases and clinical files at Western Sydney Sexual Health Centre were accessed to identify patients who had test-of-cure (TOC) for *M. genitalium*.

Patient characteristics were recorded including antibiotic treatment prior to TOC. Available archived samples were analysed using a new multiplexed *PlexPCR™ M. genitalium ResistancePlus™* assay (SpeeDx) for the simultaneous detection of *M. genitalium* (*MgPa* gene) and associated macrolide resistance (single nucleotide polymorphisms (SNPs) in the 23S rRNA gene).

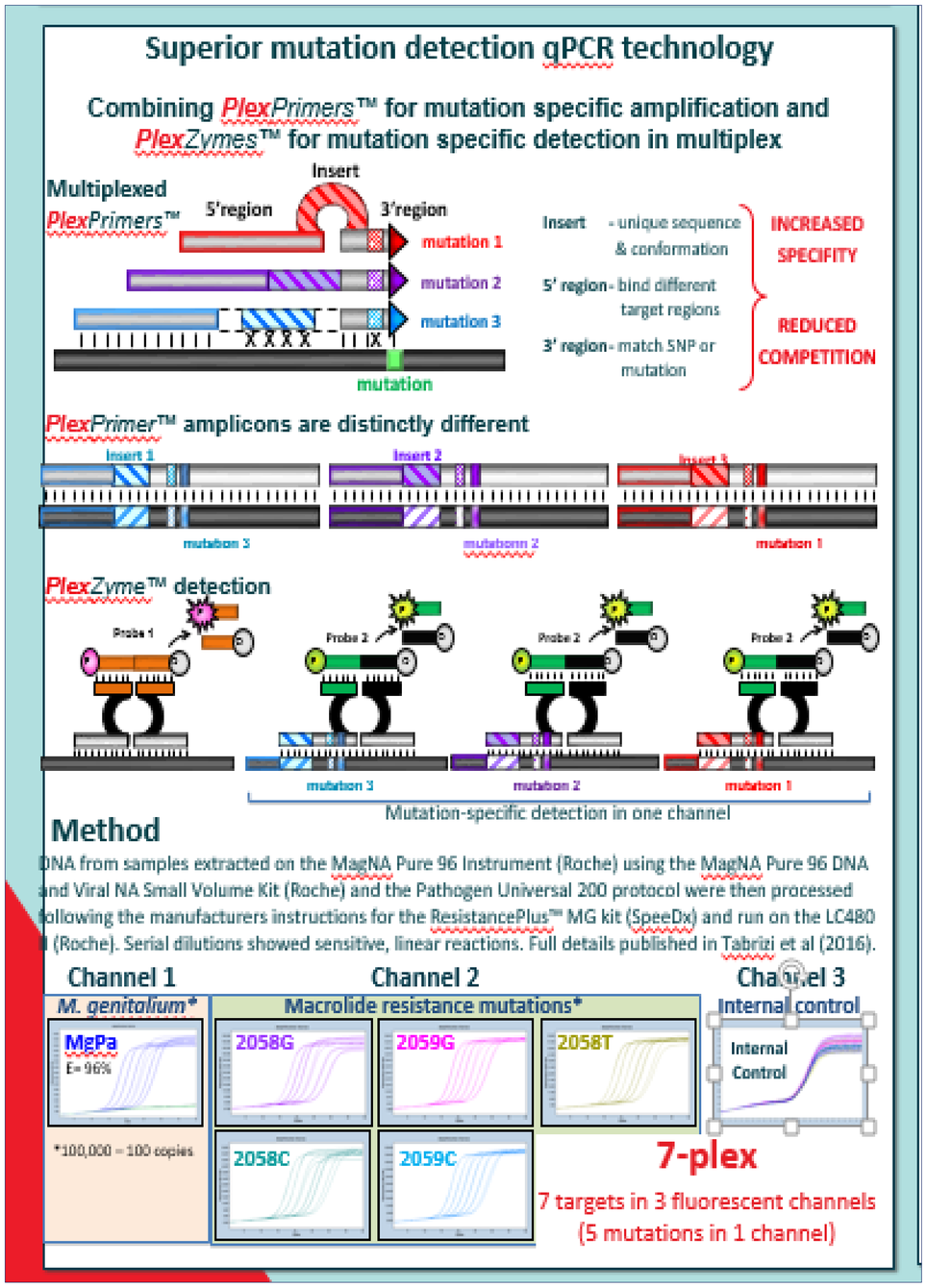
Assay results were compared with results using an in-house assay which utilises PCR and sequencing to detect SNPs at positions 2058 and 2059 in the 23S rRNA gene (*E. coli* numbering). Clinical data, antibiotic treatment and result of test-of-cure (TOC), were used to retrospectively predict the presence of macrolide resistance mutations and compared with assay results.

Results

Stored samples from 44/78 episodes of MG infection among 71 individuals where TOC was done were available. All *M. genitalium* infections were detected by the *M. genitalium ResistancePlus™* assay. The table below presents correlations with results of the in-house assay for detection of 23S rRNA gene mutations and clinical predictions. No definite clinical prediction could be made for 12 (27.3%) cases, where both azithromycin and moxifloxacin were given prior to TOC because of persistent symptoms, or time to TOC was prolonged. Clinical prediction was incorrect for one man, whose initial sample contained macrolide resistance-associated mutations, and who had a negative TOC 45 days after treatment with azithromycin 1 g.

	Number	%
Total number of samples successfully tested	44	
SpeeDx MGEN RES+*/In-house 23S SEQ PCR[#] correlation	44	100
No. of clinical predictions (Yes & No)	32	
No. of clinical predictions (possible or unknown)	12	
No. of confirmed predictions (Yes & No) by MGEN RES+ PCR*	31	96.9
No. of confirmed predictions (Yes & No) by 23S SEQ PCR[#]	31	96.9
No. of incorrect clinical predictions by MGEN RES+* & 23S SEQ PCR[#]	1	3.1

*SpeeDx MGEN RES+: *M. genitalium ResistancePlus™* assay;
[#]In-house 23S SEQ PCR: in-house assay utilising PCR and sequencing to detect23S rRNA gene mutations



Conclusion

The new multiplexed *PlexPCR™ M. genitalium ResistancePlus™* assay is a reliable method for simultaneous detection of *M. genitalium* and macrolide resistance determination.

Use of this assay would reduce time to second-line treatment, enhance antibiotic stewardship, and potentially reduce transmission of *M. genitalium*.

Disclosure of interest statement:
SpeeDx is the developer and manufacturer of the assay used in this study and supplied the test kits and technical advice for this evaluation, but was not involved in the study design or results.