Healthcare Innovations
How practice has changed

HERSTON HEALTH PRECINCT SYMPOSIUM 2021

TRAN-0014

6 - 10 September 2021
Education Centre
RBWH

Enhancing individualised treatment for *Mycoplasma genitalium* infection

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Purpose of the study

Mycoplasma genitalium has emerged as a global public health threat, due to its rapid accumulation of antimicrobial resistance. Detection of macrolide resistance is already well established in laboratory and clinical practice. However, widespread macrolide resistance renders individualised macrolide treatment virtually useless, leading to increased moxifloxacin use. Implementation of rapid diagnostics for the detection of moxifloxacin resistance is now urgently needed.

Methods

We examined the molecular epidemiology of moxifloxacin resistance in Queensland and established the serine-83 to isoleucine (S83I) in ParC was the most prevalent marker of resistance to fluoroquinolones. We designed a rapid molecular test capable of differentiating wild-type and S83I mutation in ParC. Validation was performed using a sample bank of 423 *M. genitalium*-positive samples obtained from Pathology Queensland. This assay was compared with additional molecular assays, deep sequencing and “gold standard” Sanger sequencing for the detection of fluoroquinolone resistance mutations.

Sanger Sequencing (from previous work*)	Additional testing performed in this study					Correlation of results across PCR/ sequencing methods
	TaqMan S83 result	S83 Allele-specific (ASP) assay result	D87 Allele-specific (ASP) assay result	Deep sequencing result	No. of samples (n = 27)	
Mixed S83I & S83 WT	Mixed (S83I & WT S83)	Mixed (S83I & WT S83)	WT D87	Mixed S83 (S83I & WT S83), WT D87	1	**All methods**
WT S83 & D87	WT S83	WT S83	n/d	WT S83 & Mixed D87 (D87Y & WT D87)	1	One method only
	WT S83	Mixed (S83I & WT S83)	WT D87	n/p	5	One method only
	WT S83	Mixed (S83I & WT S83)	WT D87	WT S83 & D87	5	One method only
	n/a	Mixed (S83I & WT S83)	WT D87	n/p	1	One method only
	Mixed S83 (S83I & WT S83)	Mixed (S83I & WT S83)	WT D87	n/p	4	**Two methods**
S83I & WT D87	S83I	S83I	WT D87	Mixed (S83I & WT S83) & WT D87	2	One method only
	S83I	S83I	WT D87	Mixed S83 (S83I, S83N & WT S83) & WT D87	1	One method only
	S83I	Mixed (S83I & WT S83)	n/d	n/p	1	One method only
	S83I	Mixed (S83I & WT S83)	WT D87	n/p	1	One method only
	Mixed (S83I & WT S83)	Mixed (S83I & WT S83)	WT D87	Mixed S83 (S83I & WT S83) & WT D87	1	**Three methods**
	Mixed S83 (S83I & WT S83)	S83I	WT D87	n/p	1	One method only
S83N & WT D87	No amplification	S83N	WT D87	Mixed S83 (S83I, S83N, WT) & WT D87	1	One method only
	No amplification	Mixed (S83N & WT S83)	WT D87	Mixed S83 (S83I, S83N & WT), WT D87	1	**Two methods**
S83R & WT D87	WT S83	n/d	n/d	Mixed S83 (S83R & WT S83) & WT D87	1	One method only

Figure 1: Summary of results of the 27 samples indicated to harbour mixtures of fluoroquinolone-susceptible and -resistant strains.

Results

The assay was able to determine the presence of S83I mutation in ParC, and was consistent with other molecular techniques used in this study. Results also showed evidence of mixtures of fluoroquinolone-susceptible and -resistant strains in up to 27/423 samples (6.4%). We observed that Sanger sequencing failed to detect fluoroquinolone resistance in up to 3.8% (16/423) of samples.

Discussion

We have a developed a rapid test for the detection of fluoroquinolone susceptibility and resistance in *M. genitalium*. In the context of rapidly rising fluoroquinolone resistance particularly in the Asia-Pacific region, we believe there is an important need for such tests to be incorporated into standard laboratory diagnostics, with the view to guide clinicians in the selection of antimicrobials to treat this challenging STI. This assay has now been adopted and implemented by Pathology Queensland.