

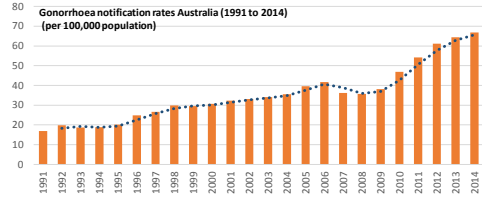
An Australia-wide molecular study of *Neisseria gonorrhoeae* identifies frequent occurrence of a key cephalosporin resistance mechanism

Trembizki E, Regan DG, Donovan B, Chen MY, Guy RJ, Lahra MM, Whitley D, on behalf of GRAND study investigators. QPID laboratory, QCMRI, The University of Queensland, Australia



Background

- WHO estimates: approx. 100 million cases of gonorrhoea globally. → disease burden is highest in low income settings.
- Rates are increasing (15,675 notifications in Aust. in 2014)

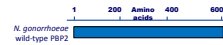


Background

- Rise in ceftriaxone MICs → decreased susceptibility (DS)
- Increasing reports of ESC treatment failures, primarily cefixime but also ceftriaxone in cases of pharyngeal infections. → Mostly due to the dissemination of resistant clones
- Predominantly mosaic Penicillin Binding Protein 2 (PBP2) 7363 and 1901 MLST types.

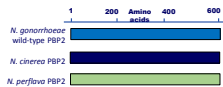
Mosaic PBP2; HOW?

- Altered PBP2 protein → Mosaic PBP2; arising from recombination events.



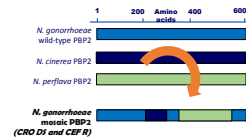
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- **Phase 1:** To better understand the spread of NG and resistance.
- Genotyping isolates from throughout Australia.



- Phase 2:** Molecular AMR testing of NG NAAT-positive clinical samples
- Focus on the NT.



*David Whitley, Tuesday 2pm;
Molecular aspects of antimicrobial resistant Neisseria gonorrhoeae*



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SNP-MLST + AMR mutations + AMR Profile = **Strain**



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Sequenom Massarray platform



- Uses MALDI-TOF MS.
- Multiplexing 12 or 14 SNPs per single reaction
- 384 well plate, 10 hours
- Cost per isolate = approx. \$15.0 per isolate

SNP-MLST + AMR mutations + AMR Profile = **Strain**



Total isolates = **2218** (90.5% isolates in first half of 2012)

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271

SNP-MLST + AMR mutations + AMR Profile = Strain



2218 isolates / 271 strains

- Dominated by certain strains
- Top 40: 80% of isolates
- Top 10: 50% of isolates
- Top 3: 25% of isolates

271

SNP-MLST + AMR mutations + AMR Profile = Strain



Strain	Total isolates	Gender		?
		male	female	
NG1	232	144	89	
NG2	167	162	4	2
NG3	151	93	60	1
NG4	110	109	5	1
NG5	91	97		1
NG6	65	70	2	
NG7	65	66	2	1
NG8	61	65		
NG9	57	55	1	1
NG10	53	56		

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Heterosexual
MSM

SNP-MLST + AMR mutations + AMR Profile = Strain



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		male	female		Pen.	Tet.	Spect	Ceft.	Cip.	Azith.
NG1	232	144	89		LS	neg	S	S	S	S
NG2	167	162	4	2	LS	neg	S	S	S	S
NG3	151	93	60	1	LS	neg	S	S	S	S
NG4	110	109	5	1	CMRP	neg	S	S	S	S
NG5	91	97		1	PPNG	neg	S	S	S	S
NG6	65	70	2		LS	neg	S	S	QRNG	S
NG7	65	66	2	1	CMRP	neg	S	S	QRNG	S
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1901	32	Mosaic PBP2			LS	neg	S	S	S	S	
NG3	151	93	60	1	LS	neg	S	S	S	S	
NG4	110	109	5	1	CMRP	neg	S	S	S	S	
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SNP-MLST + AMR mutations

1901 + Mosaic PBP2 = 188/2218 (8.1%)

Mosaic-1901; geographic distribution?

Mosaic-1901; geographic distribution?

→ Dominates metropolitan regions
→ Mainly found in VIC and NSW

# Isolate	Aus. States and territories						Total
	NSW	VIC	QLD	WA	SA	NT	
# mPBP2-1901	84	82	17	4	1	0	188
%	11%	13%	5.2%	1.5%	0.7%	0%	8.1%

Metropolitan

Mosaic-1901; gender distribution?

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→ Dominates MSM population
→ However, isolated from female patients as well

Male	Female	Unknown
178	8	2

Heterosexual networks as well

Mosaic-1901; resistance profile?



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	Ceftriaxone MICs (mg/L)				
	0.008	0.016	0.03	0.06	0.125
mPBP2-1901 %	3.2%	15.4%	44.7%	34.6%	1.6%

Mosaic-1901; resistance profile?



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Also typically: resistance to **Penicillin** (67.5%) and **ciprofloxacin** (98.4%).

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Most isolates MICs 0.12-0.25mg/L. **However:**
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Concern:

→ These strains just require two mutations to be resistant to both ceftriaxone and azithromycin
→ A501P (PBP2) + C2611T (23S) = ceftriaxone and azithromycin resistant.

Mosaic-1901; summary



- mPBP2-1901 is a highly successful strain in our population.
 - first described in Aust. ~ 10 years ago;
 - now comprises 8.1% of the isolate population in Australia
- Most states and territories.
- Bacterial culture doesn't 'flag' a large proportion of these strains

✓ **STRENGTHENING AMR SURVEILLANCE CAPABILITIES IS CRUCIAL**



Acknowledgements

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