Tracking AMR in skin bacteria in the Kimberley

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HOT NORTH Program

Proudly supported by the people of Western Australia through Channel 7's Telethon

1. Skin Infections





SToP Trial - Kimberley



SToP Trial: Antibiotic resistance monitoring

- To understand impact of prescribing on resistance
 - Monitor any emergence and spread of AMR strains
- To inform current and future treatment guidelines
- Questions:
 - What is the potential for SXT resistant GAS and *S. aureus* emerging?
 - How do we monitor for emergence?





- **GTP** • SXT = trimethoprim (TMP) + sulfamethoxazole (SMZ) Dihydropteroate-P2 + PABA SMZ ----- Dihydropteroate synthase (FoIP) **Dihydroteroic acid** Dihydrofolic acid Dihydrofolate reductase (DfrB) TMP ------Tetrahydrofolic acid **DNA/Protein synthesis enzymes** INSTITU
- SXT-resistance requires resistance to both TMP and SMZ



- SXT = trimethoprim (TMP) + sulfamethoxazole (SMZ)
- SXT-resistance requires resistance to both TMP and SMZ



Antibiotic Resistance

- Reported clinically but not defined genetically
- Trimethoprim Resistance
 - dfrG in S. aureus in WA and NT, and in GAS (eg. India)



Antibiotic Resistance

Cotrimoxazole (SXT)

- Reported clinically but not defined genetically
- Trimethoprim Resistance
 - dfrG in S. aureus in WA and NT, and in GAS (eg. India)

What risk does underlying TP-R or SX-R pose on the likelihood of developing SXT resistance? (should we be monitoring TP and SX susceptibility?)



Scenario 1 TP-S, SX-S



Scenario 2 TP-R, SX-S



Project overview

- 1. What is the capacity for GAS and *S. aureus* to become SXT-R?
 - Requirement for underlying TP-R or SX-R to generate SXT-R?
 - WGS GAS isolates from Germany with reduced SXT susceptibility.
- 2. DNA sequencing pipeline for monitoring strain and AMR profiles directly from skin sore swabs. Phil Giffard - Menzies





Potential for SXT resistance?







This aim will identify SXT-R genes and mutations, and underlying TP-R and SX-R-requirement

Inform whether we should routinely screen for SX-R and TP-R as well as SXT-R





Project overview

- 1. What is the capacity for GAS and *S. aureus* to become SXT-R?
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doxycycline

5

mgrA

CSV XLS Printable

Staphylococcus aureus subsp. a...

ARMA Report

Showing the result of the Anti-microbial resistance app

41 reads were analysed 41 reads were successfully aligned 159 Alignments					▼ Filters Filter by gene name:	
43 Protein Homolog Alignments 19 Protein Homolog Reads					Filter by drug:	
Currently Showing: Genes: 6 of 2057 Drugs: 125 of 288 Clusters: 6 of 697					2 100	
Genes		Drugs			Sankey	
ame	▲ Reads	Gene Name	A Reads	Avg. accuracy	Species	
lortetracycline	5	arlS	4	0.92	Staphylococcus aureus subsp. a	

1

0.95



Thank you!

- Acknowledgments
 - Telethon Kids Institute
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 - Menzies School of Health research
 - Phil Giffard, Tegan Harris, Deb Holt
 - Doherty Institute
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- HOT NORTH Career Development Fellowship and pilot project funding!



WESFARMERS CENTRE OF VACCINES & INFECTIOUS DISEASES



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THE END





Where to next?

- Rapid molecular diagnostics
 - Nanopore sequencing/AMR profiling



- AMR surveillance
- Environmental sampling





Skin Health Epidemiology

- Impetigo Group A Streptococcus (GAS) and Staphylococcus aureus
- Scabies, Crusted Scabies





SToP Trial: See, Treat and Prevent skin infections

- **"See":** training of health care workers, teachers and carers in recognising skin infections and referring for treatment
- "Treat": streamlined treatment for impetigo (cotrimoxazole), scabies (ivermectin) and crusted scabies (chronic disease model of care)
- "Prevent": Wrap around Health Promotion and Environmental Health activities that are community led and partnering with local stakeholders





Skin Sore trial







Skin Sore trial



Discover, Prevent, Cure,

SToP Trial: Antibiotic resistance monitoring

- To understand impact of prescribing on resistance
 - Monitor any emergence and spread of AMR strains
- To inform current and future treatment guidelines



- SXT = trimethoprim (TMP) + sulfamethoxazole (SMZ)
- Resistance to SXT requires resistance to both TMP and SMZ





1. Skin Infections



Impetigo Group A *Streptococcus* (GAS) and *Staphylococcus aureus*





Antibiotic Resistance

- Cotrimoxazole (SXT) Reported clinically in GAS and *S. aureus*
 - dfrG identified in S. aureus in WA and NT
 - dfrG in GAS (eg India)
- Possibility for transfer?

What risk does *dfrG* pose on the likelihood of developing SXT resistance? (should we be monitoring TMP susceptibility?)



Project overview

- 1. Define genetic basis of SXT-R GAS and *S. aureus*
 - Sequence GAS isolates from Germany reported to have reduced SXT susceptibility (4-8 µg/ml; resistance ≥2 µg/ml).
 - Identify requirement for underlying TMP-R to generate SXT-R under SXT selection



What is the potential to switch?



- *in vitro* evolution
- Identify the frequency of cotrimoxazole mutants under selection
- Importantly identify whether dfrG⁻ evolve SXT-R?
- What mutations are associated with the emergence SXT-R?

This aim will identify SXT-R genes and mutations, and *dfrG*-requirement

Inform whether we should routinely screen for TMP-R as well as SXT-R



Project overview

- 1. Define genetic basis of SXT-R GAS and *S. aureus*
 - Identify requirement for TMP-R to generate SXT-R under SXT selection
- 2. Develop a DNA sequencing pipeline for monitoring strain and antimicrobial resistance profiles of GAS and *S. aureus* directly from skin sore swabs





Thank you!

- Acknowledgments
 - Telethon Kids Institute
 - Asha Bowen, Jonathan Carapetis
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 - Pilot project funding!



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HOT NORTH Program





Skin Sore trial





Skin Sore trial



GAS clearance predicts treatment success (OR 5.2)

SToP Trial: See, Treat and Prevent skin infections

- **"See":** training of health care workers, teachers and carers in recognising skin infections and referring for treatment
- **"Treat":** Treatment for impetigo (cotrimoxazole), scabies (ivermectin)
- "Prevent": Community-led Health Promotion and Environmental Health activities

Asha Bowen – Telethon Kids & PMHC



SToP Trial: Antibiotic resistance monitoring

- To understand impact of prescribing on resistance
 - Monitor any emergence and spread of AMR strains
- To inform current and future treatment guidelines





Antibiotic therapies

- Probably need a table of some sorts......
- GAS penicillin no resistance ever reported / adherence issues
- Others?
- GAS sxt resistance has been reported but not defined genetically
 - No resistant isolates identified in SST in NT indicating that it is not prevalent
 - in a naive pop'n, so question is how likely is SXT-R with expnading use
 - also, how will we monitor for it?





Skin Sore trial







Skin Sore trial



Discover, Prevent, Cure,

