Development of methods to rapidly track pathogen and antibiotic resistance profiles from skin sores in Northern Australia

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menzies school of health research

HOT NORTH Program

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

Welcome!

I’d like to acknowledge the Yawuru people and wish to pay my respects to their Elders past, present and future.

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Skin Health Epidemiology

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

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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

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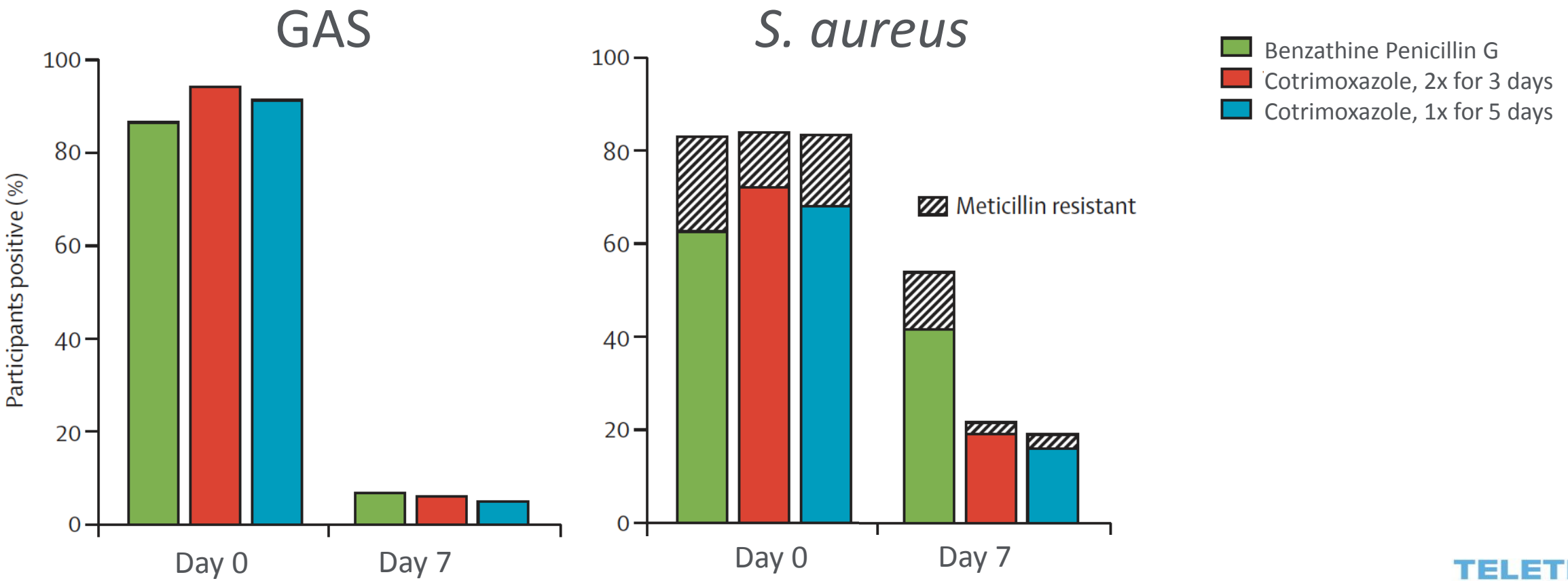
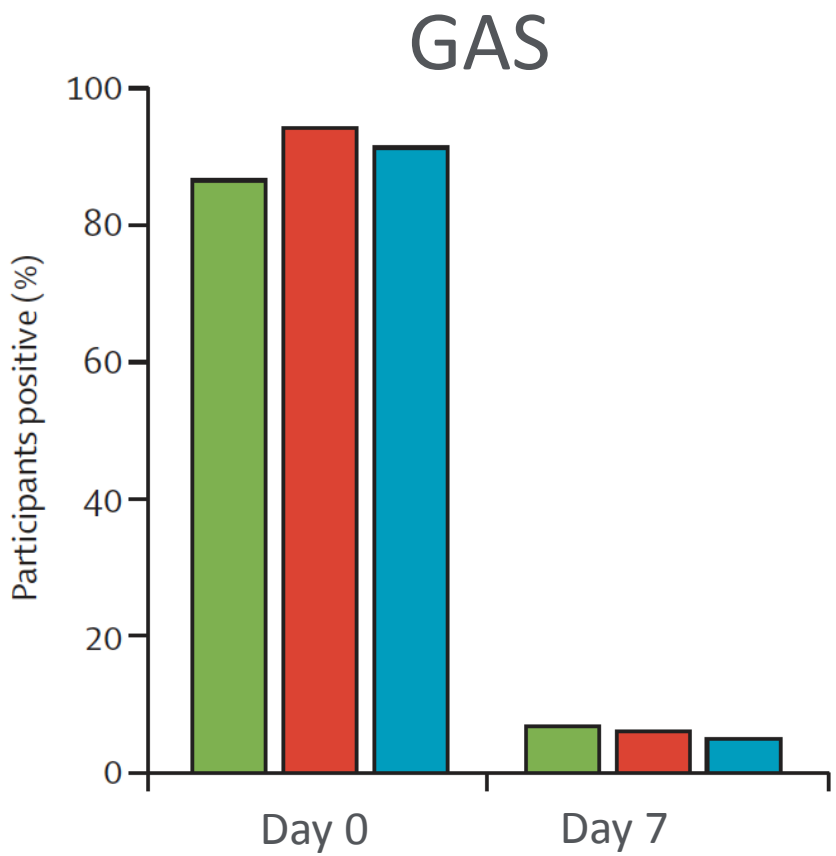
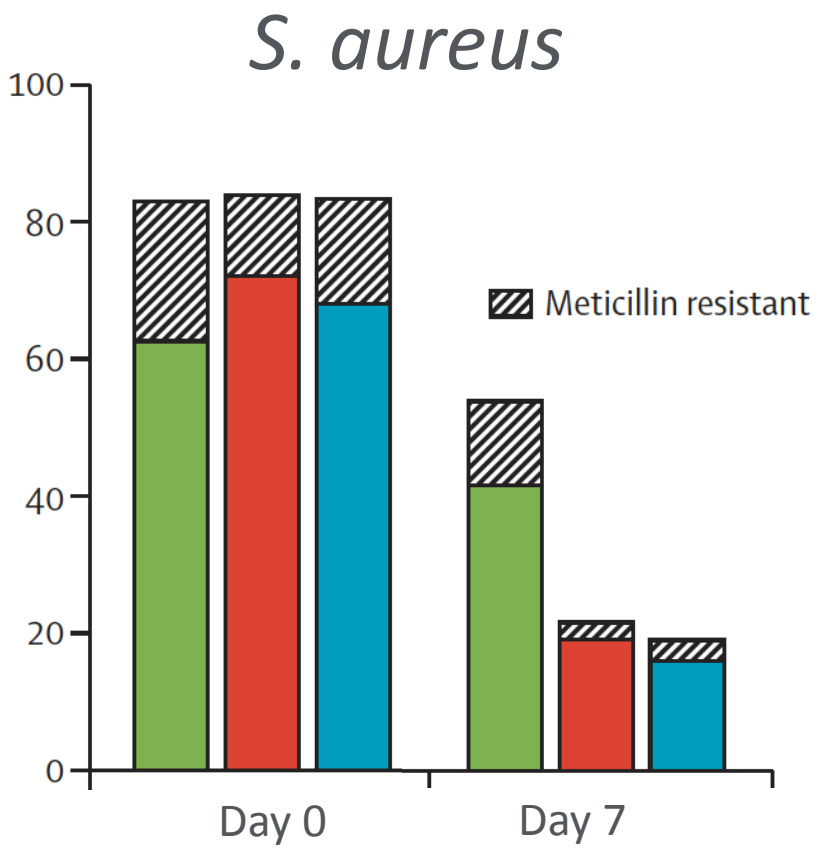
Skin Sore trial

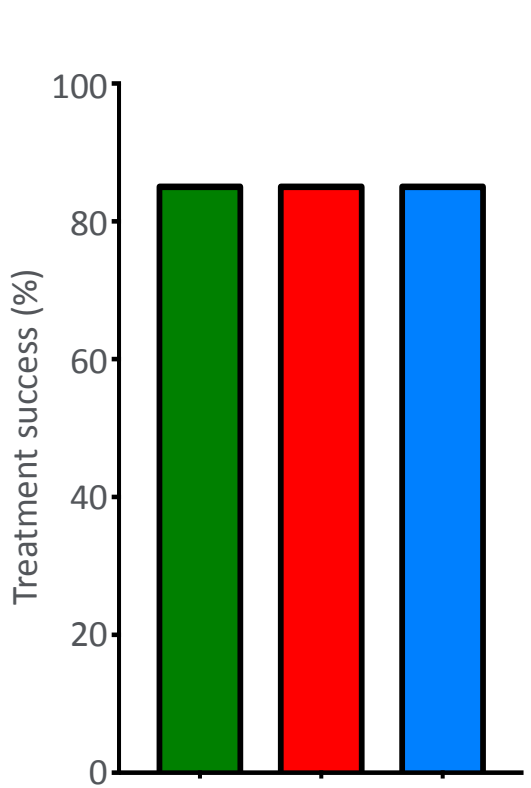


Bowen *et al.* 2014. Lancet

Skin Sore trial







GAS clearance predicts treatment success (**OR 5.2)**

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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

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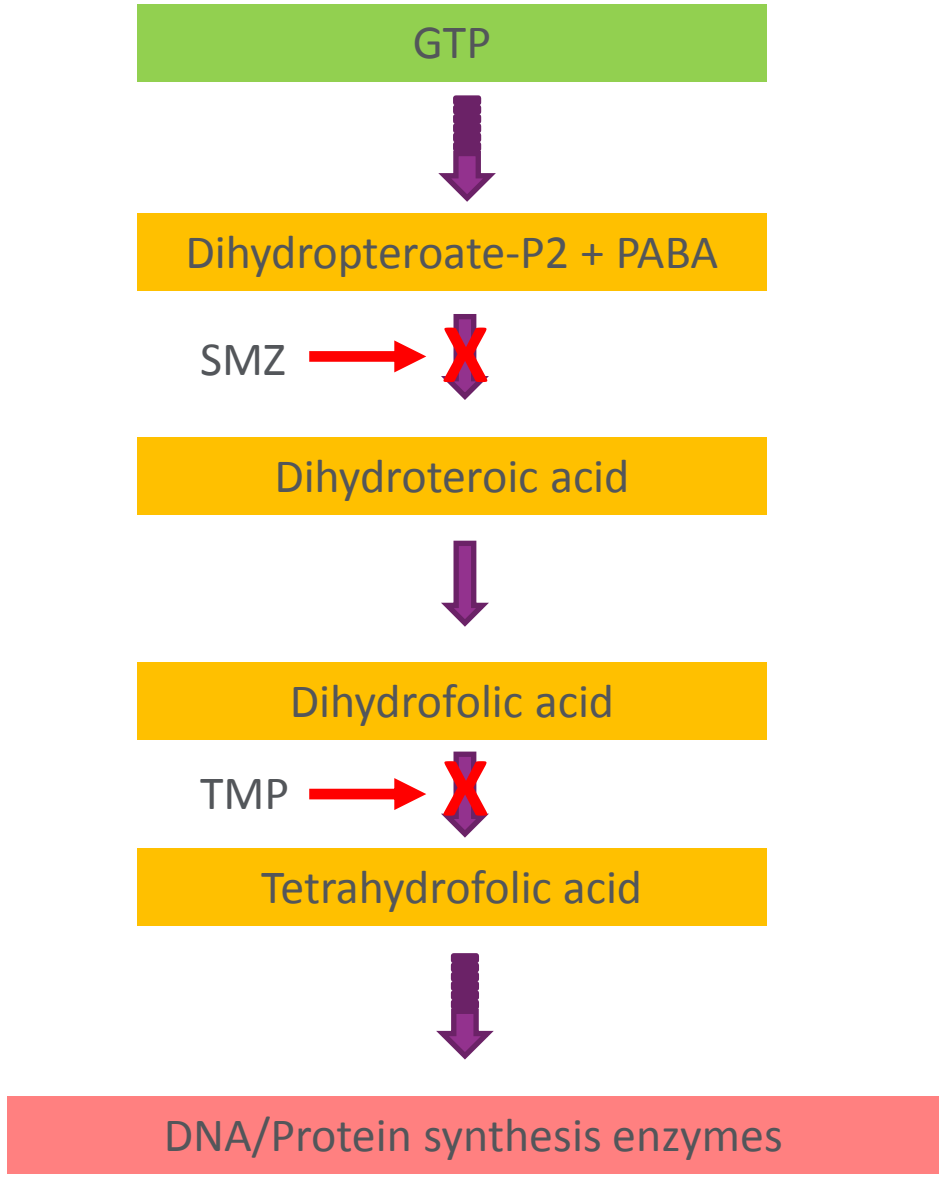
Cotrimoxazole (SXT)

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



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?)

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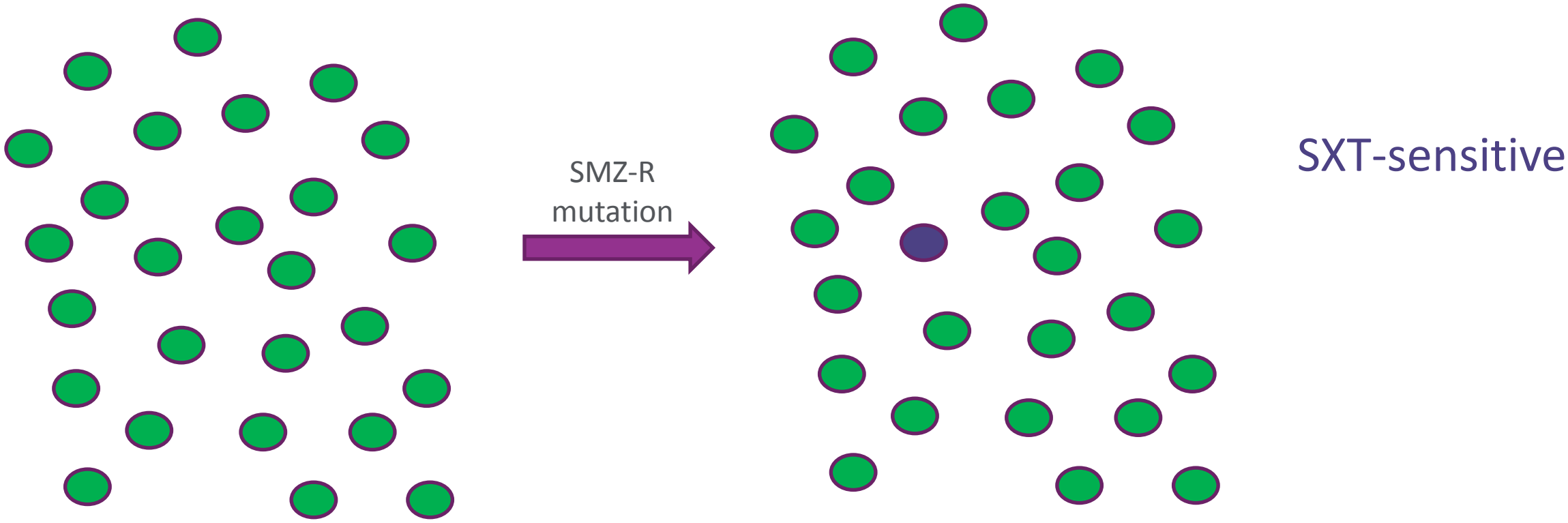
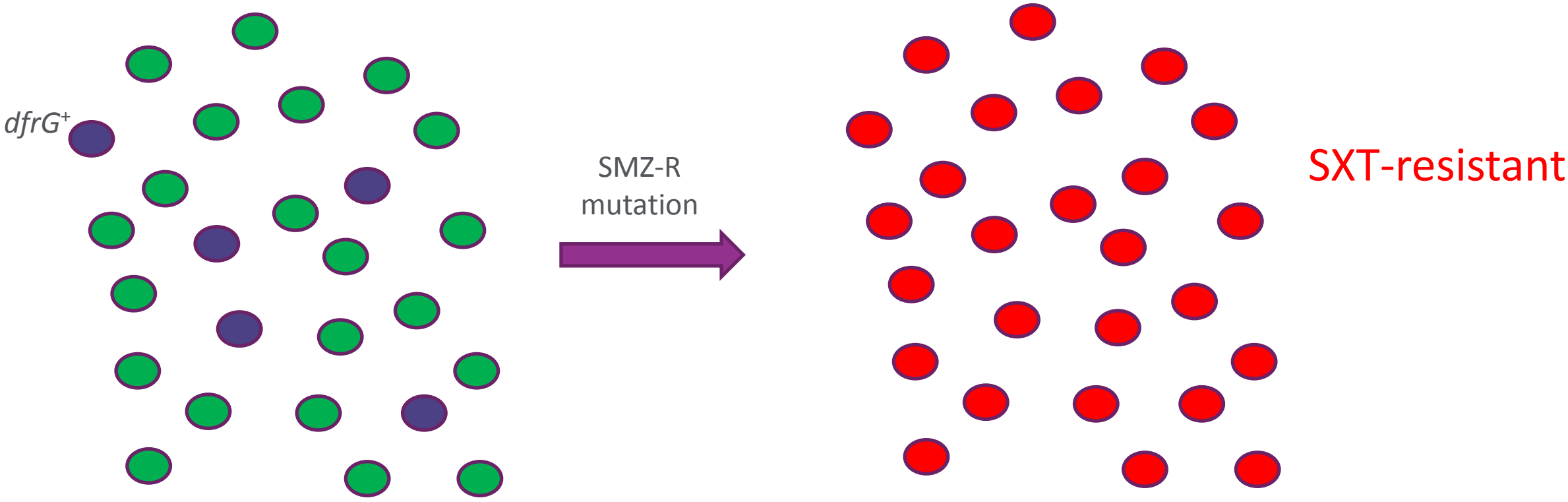
Scenario 1 *dfrG*$^{-}$



Scenario 2 *dfrG*$^{+}$



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

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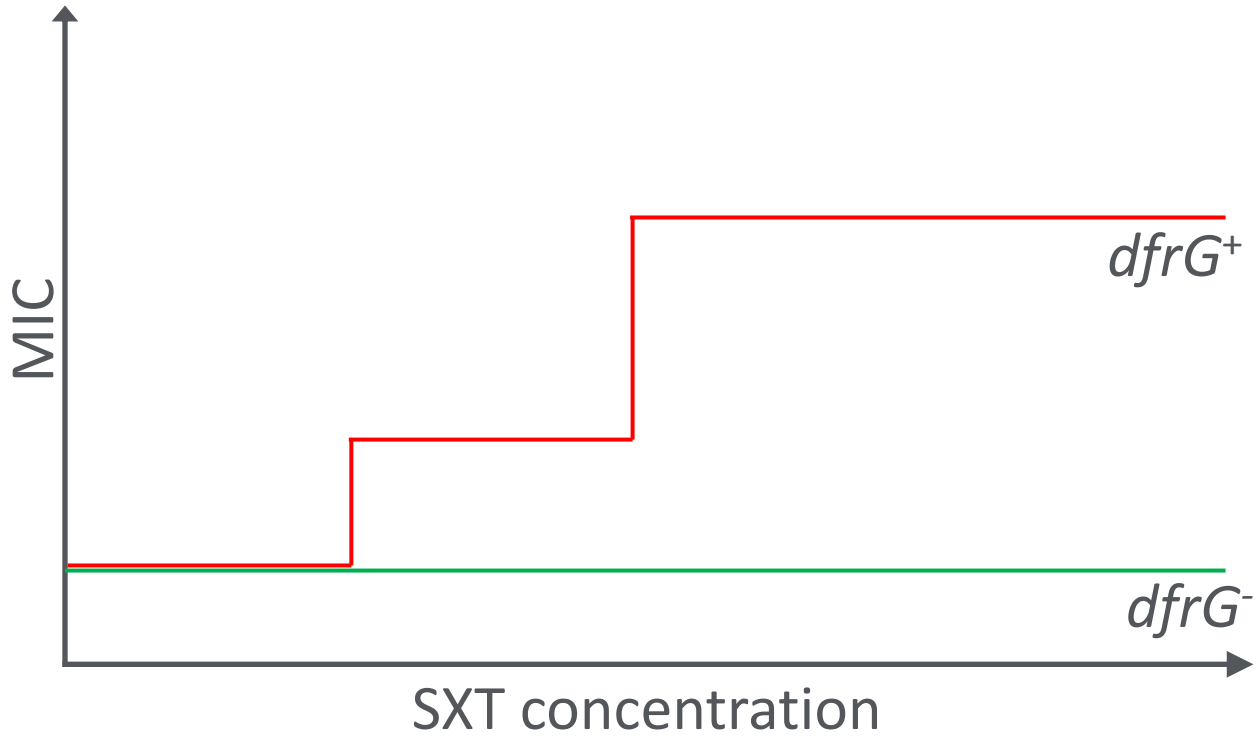
What is the potential to switch?



- *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

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Metagenomics

Skin sore Swab

DNA extraction

Sequencing

Reads

100-150 bp

Assembly

Contigs

1000+ bp

Search against database

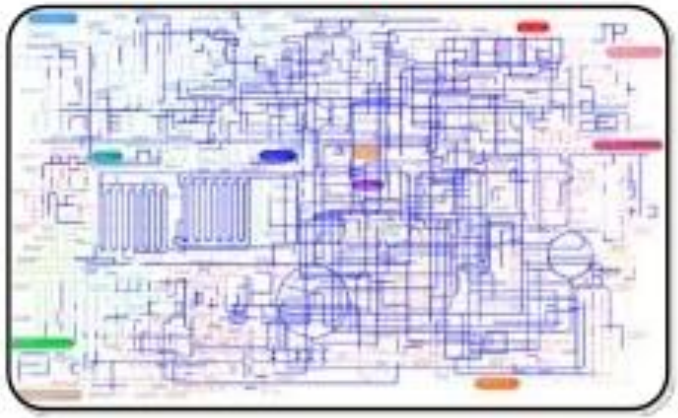
Phylogenetic classification

Who is there?

Bacterium A
Bacterium B
...
Bacterium X

Functional classification

What can they do?



Gene A
Gene B
...
Gene X

Phil Giffard, Menzies

CSV XLS Printable

ARMA Report

Showing the result of the Anti-microbial resistance app

41 reads were analysed

41 reads were successfully aligned

159 Alignments

43 Protein Homolog Alignments

19 Protein Homolog Reads

Currently Showing:

Genes: 6 of 2057

Drugs: 125 of 288

Clusters: 6 of 697

Filters

Filter by gene name:

Filter by drug:

Min alignment count per gene:

2 100

Genes | Drugs | Sankey

Name	▲ Reads
chlortetracycline	5
doxycycline	5

Gene Name	▲ Reads	Avg. accuracy	Species
arlS	4	0.92	Staphylococcus aureus subsp. a...
mgrA	1	0.95	Staphylococcus aureus subsp. a...

Where to next?

- Rapid molecular diagnostics
  - Nanopore sequencing/AMR profiling

Swab

Microbiome – bacteria present

Resistome – AMR genes present

- AMR surveillance
- Environmental sampling

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Thank you!

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  - Menzies School of Health research
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