Applying GAS Genomics in Public Health

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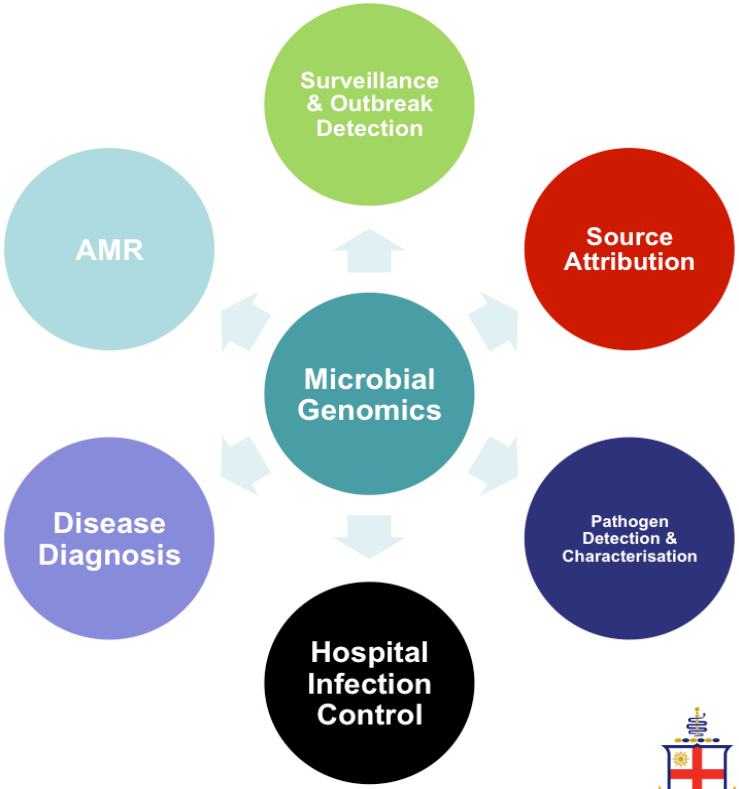
Applications of WGS in Clinical Microbiology



The University of Melbourne

11 February - 1 March 2019
23rd Public Health Summer School
University of Otago, Wellington

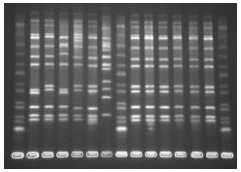
Doherty Institute
A joint venture between the University of Melbourne and Melbourne Health

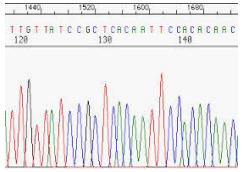
The Royal Melbourne Hospital

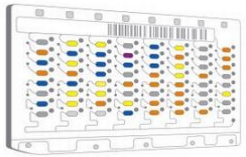
The University of Melbourne

The All in One Assay

Traditional Techniques



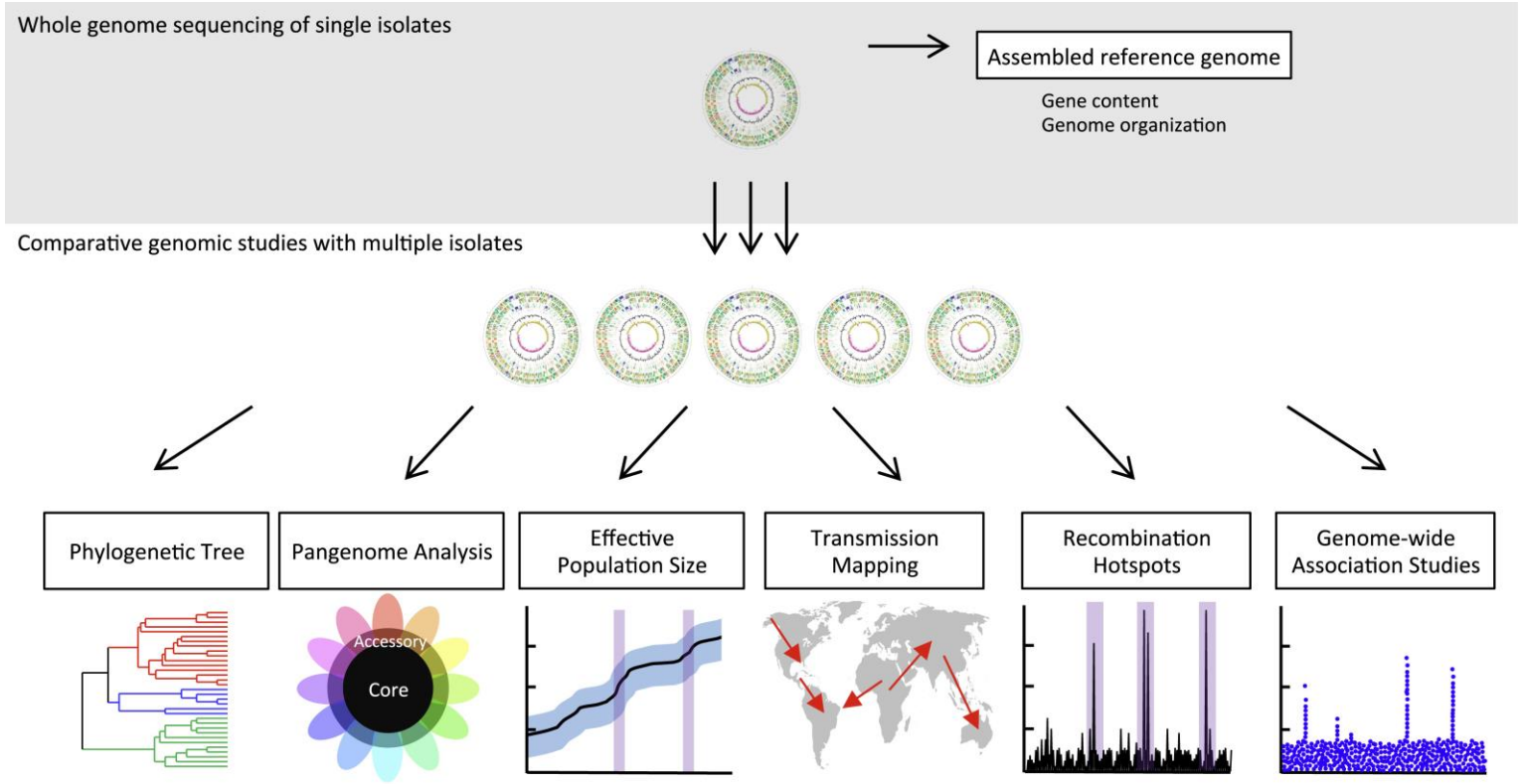




Whole Genome Sequencing (WGS)

Pathogen Genomic Epidemiology

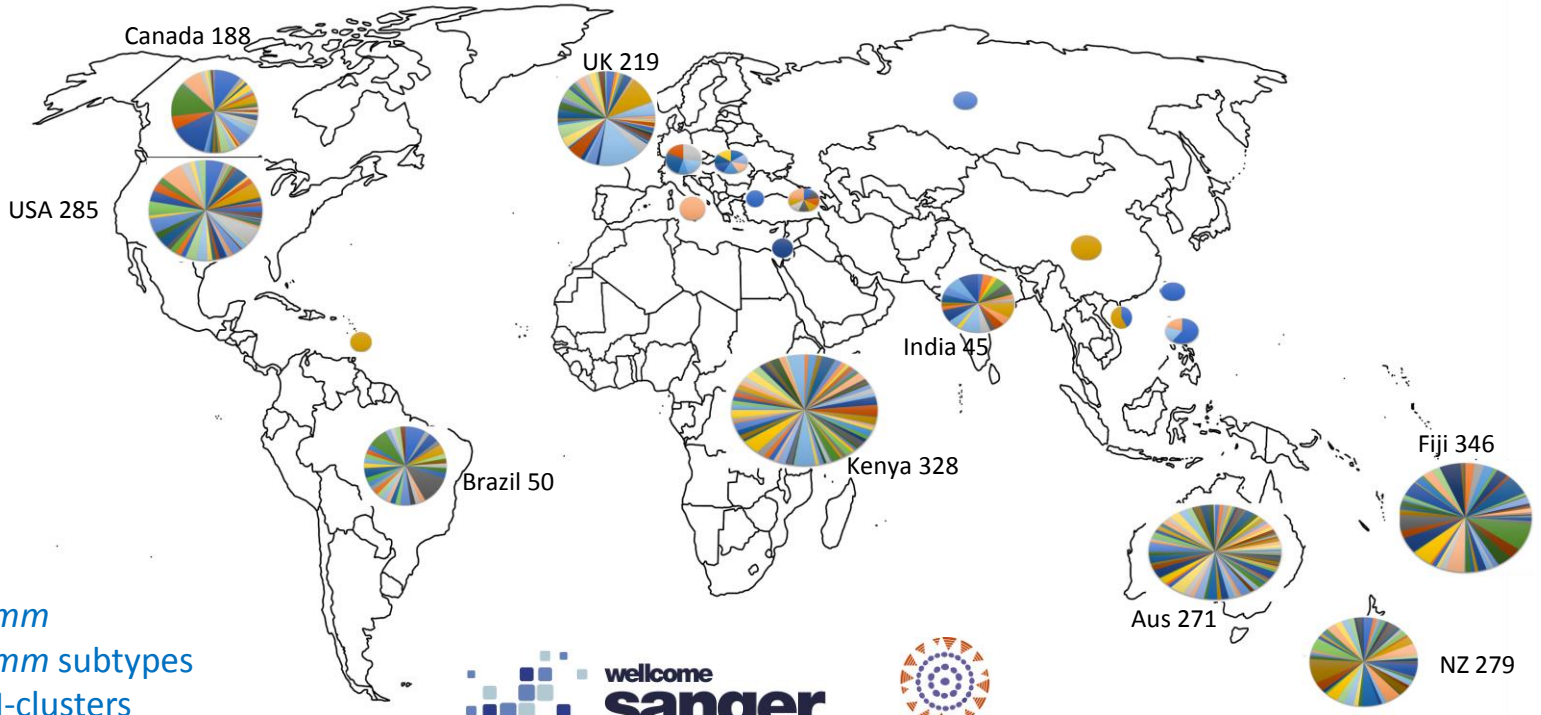
Linking genomics with epidemiology



Klemm and Dougan. 2016. Cell Host Microbe. 19(5), 599–610

‘Global’ GAS Population Genomics

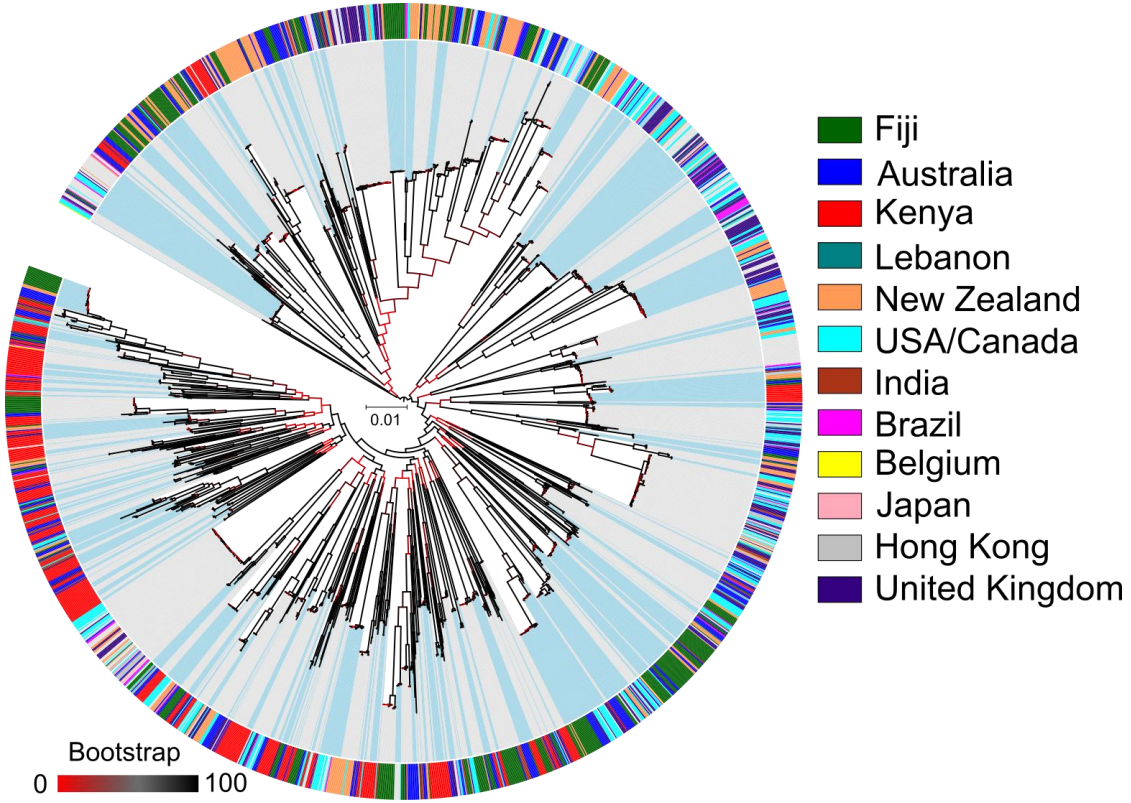
Global database of 2,083 GAS genome sequences



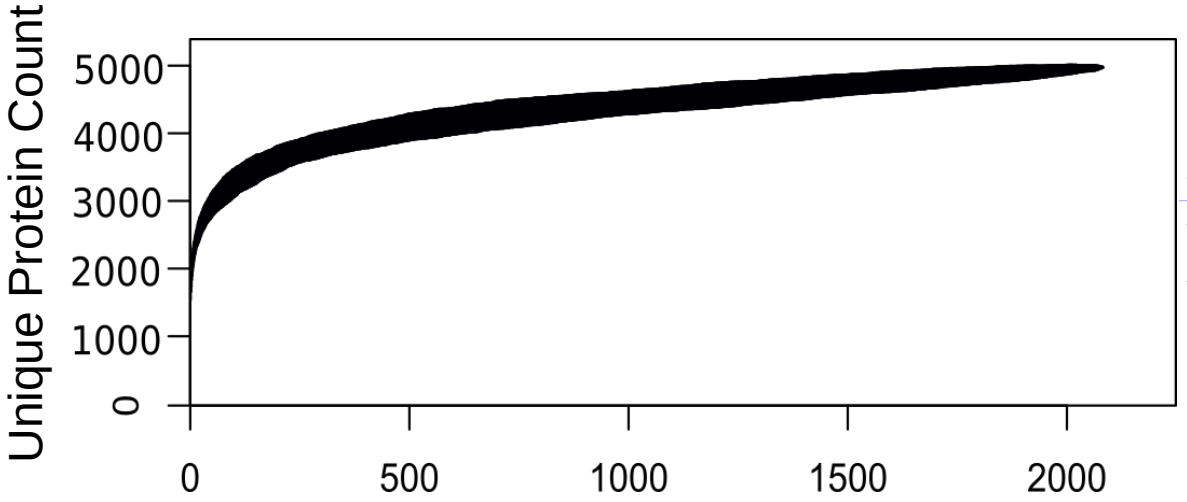
150 *emm*
247 *emm* subtypes
37* M-clusters
484 MLST

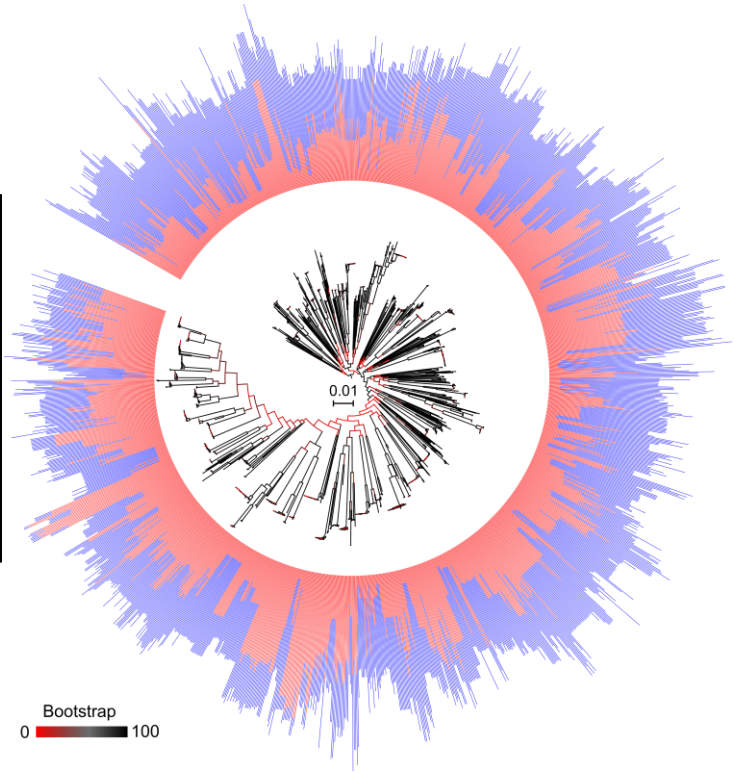
‘Global’ GAS Population Genomics

~300 evolving lineages



Gene Content of GAS in Constant Flux

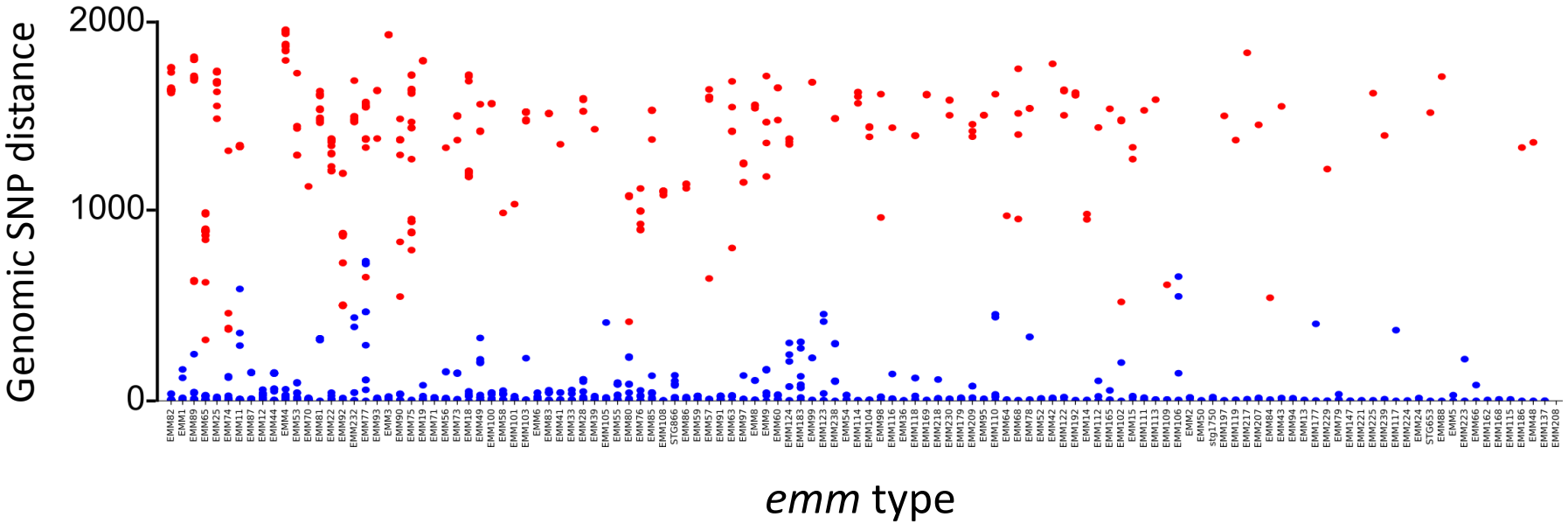




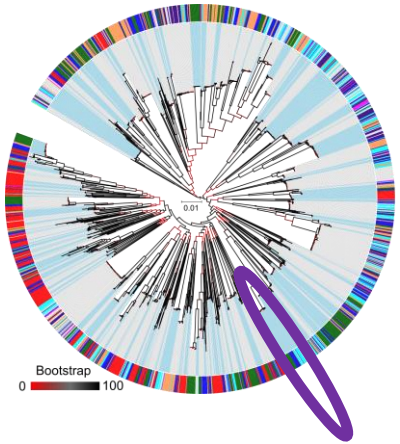
‘Global’ GAS Population Genomics

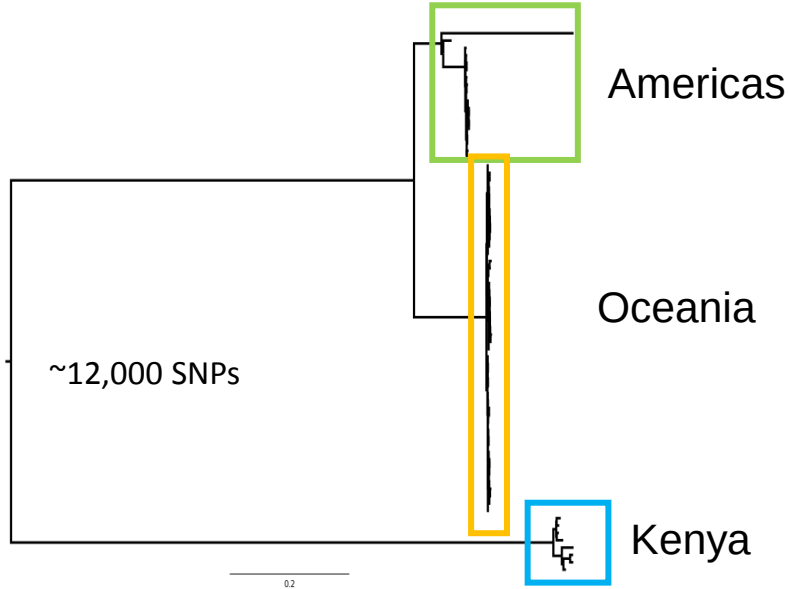
Extensive sequence variation in genomes exhibiting the same *emm* type

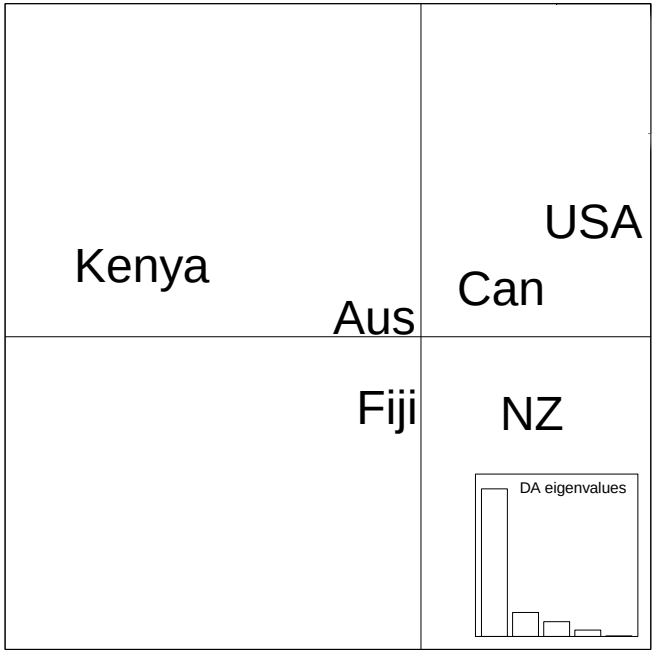
> Caution when using *emm* as a marker of ‘relatedness’



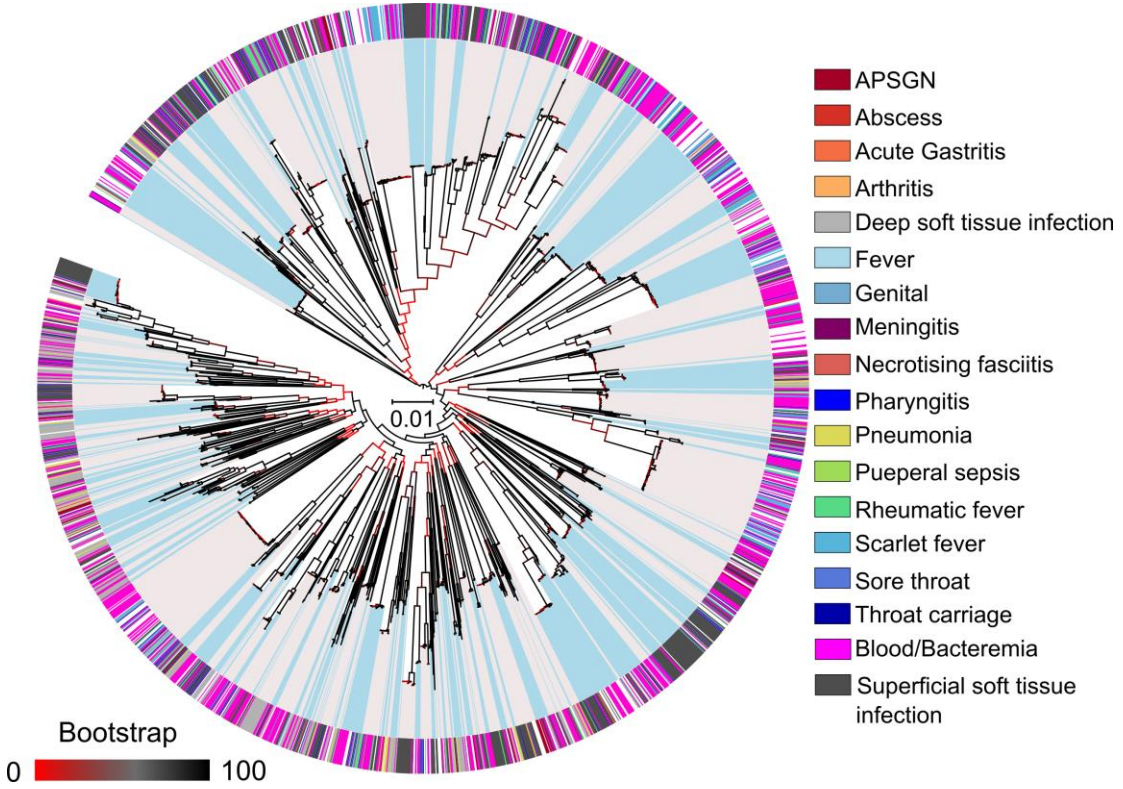
Accessory Genome as a Geographical Marker







Disease is Not Evolutionary Restricted



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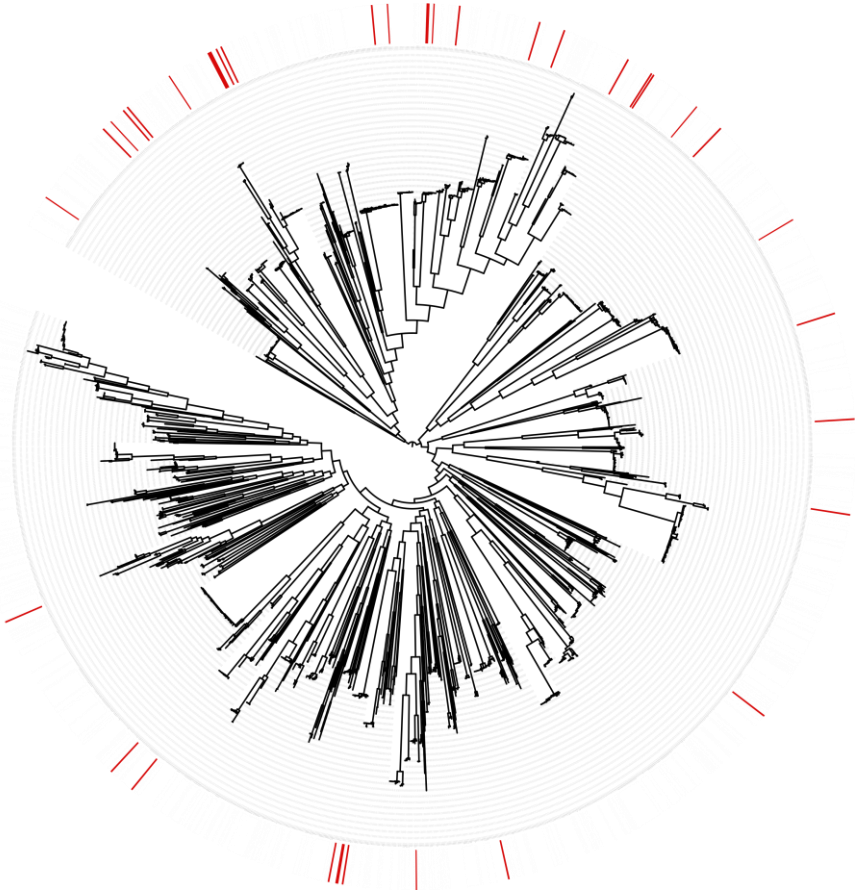
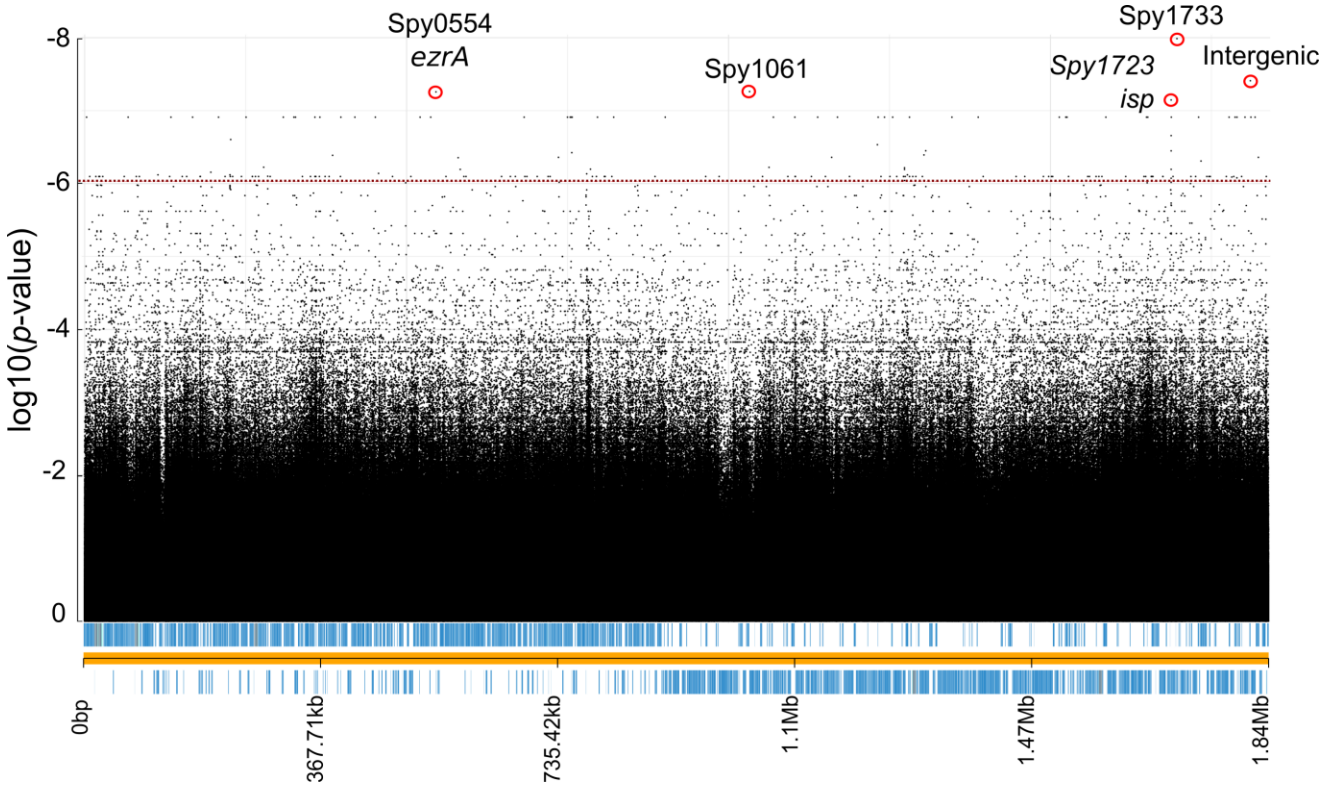
23rd PUBLIC HEALTH SUMMER SCHOOL
UNIVERSITY OF OTAGO, WELLINGTON

No Single Rheumatogenic Lineage



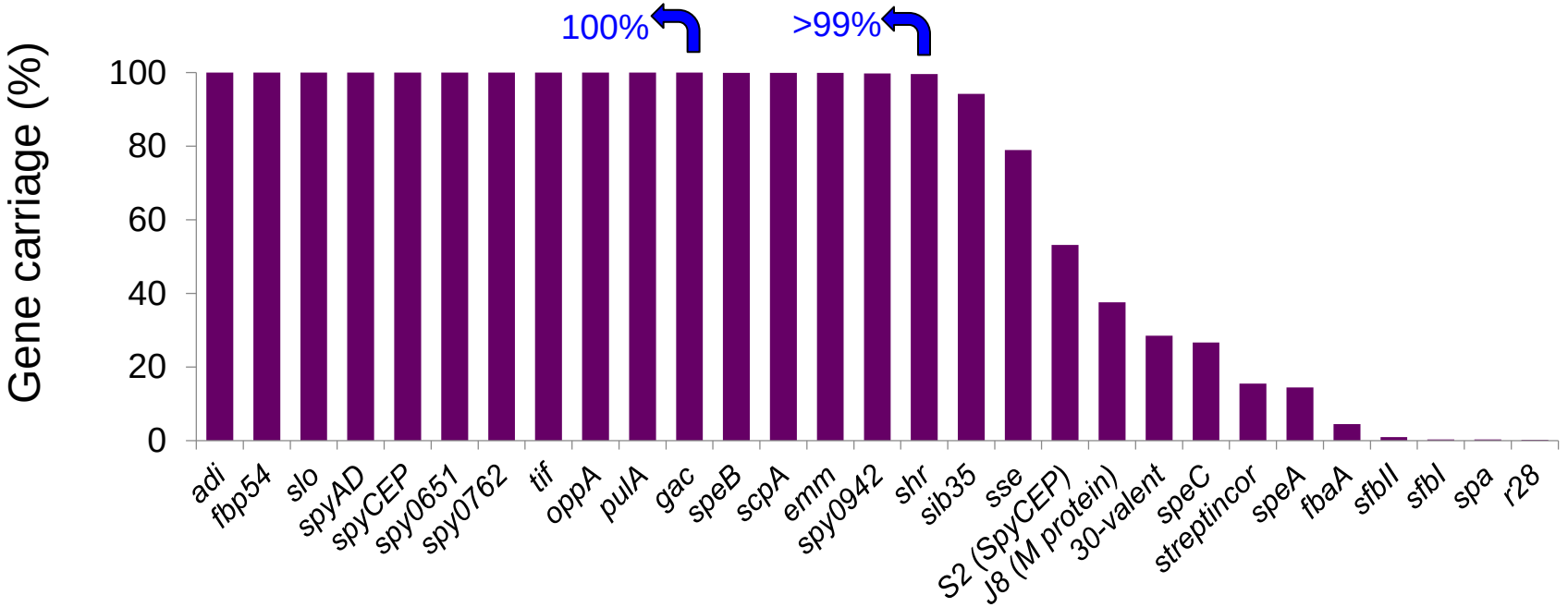
Searching for Global Disease Signatures



Advancing Vaccine Design Through Population Genomics

- Extensive genotypic and serotypic diversity (e.g. >200 *emm* types)
- Vaccine safety concerns due to the autoimmune disease caused by repeated GAS infection
- Antigen gene carriage is not universal
- Extensive antigenic variation also reported

Global Vaccine Antigen Carriage



Only 16 candidate vaccine antigens provide >99% global coverage

Global Multicomponent Vaccine Formulation

Vaccine	Vaccine antigens	Europe	Oceania	North America	South America	Asia	East Africa	*TOTAL*
GSK (3-valent)	SLO; SpyCEP; SpyAD	**>99%**	**>99%**	**>99%**	**>99%**	**>99%**	**>99%**	***>99%***
Spy7 (7-valent)	Spy0651; Spy0762; Spy0942; PulA; OppA; SpyAD; ScpA	**>99%**	**>99%**	**>99%**	**>99%**	**>99%**	**>99%**	***>99%***
Combo #5 (5-valent)	TF; ScpA; SpyCEP; ADI; SLO	**>99%**	**>99%**	**>99%**	**>99%**	**>99%**	**>99%**	***>99%***
StreptInCor	M-protein eptiope	**39%**	**26%**	**15%**	**12%**	**34%**	**17%**	***23%***
MJ8VAX	J8 (M-protein) - DT	**45%**	**41%**	**31%**	**31%**	**57%**	**25%**	***37%***
S2-J8	S2 (SpyCEP); J8	**>99%**	**>99%**	**>99%**	**>99%**	**>99%**	**>99%**	***>99%***
30-valent	30 M-protein	**71%**	**33%**	**75%**	**53%**	**73%**	**28%**	***48%***
30-valent with Mrp	30 M-protein with Mrp	**77%**	**51%**	**83%**	**59%**	**83%**	**33%**	***60%***

Summary

- Genomics is a key technology in current/future public health
  - Diagnostics
  - Surveillance
  - Vaccine design
  - Identify molecular markers of disease
- The ability to maximise the utility of genomics relies on comprehensive sampling and routine surveillance
- Bacterial evolution is dynamic and an ongoing process

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