Project Proposals for AGAR ASSOP Data

Project 1: Genomic Epidemiology of *S. aureus* bacteraemia in Australia

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Required Data:

1. *S. aureus* clinical and microbiological data (2013-2016)
2. *S. aureus* typing data (2013-2014)
3. Raw MRSA whole genome sequence data (2015-2016 – when available)

Background:

We are currently conducting a genomic study of the combined multicentre VANESSA/ANZCOSS cohorts (846 samples from 749 patients with *S. aureus* bacteraemia [SAB]) with four purposes:

1. Develop a high-resolution model of the population structure of SAB in Australia during the two study periods (2007-2008 and 2011-2012). Additionally, investigate the presence of clonal population at both a state- and institution-level with the goal of establishing a phylogeographic model to study *S. aureus* transmission.
2. Generate a comprehensive database for antimicrobial resistance elements associated with SAB in Australia, and assess changes in this pool of resistance genes over time. In particular, looking into the genetic context of resistance elements amongst isolates that display phenotypic co-resistance to multiple antimicrobials. We also want to investigate prevalence of mobile genetic elements carrying multiple resistance elements and there contribution to o-resistance in this population
3. Explore potential molecular determinants of clinical outcomes, specially looking at the association between genotype and 30-day mortality or persistent bacteraemia.
4. Study within-host evolution of *S. aureus* isolates in persistent bacteraemia, if multiple isolates are available from the same clinical case.

Preliminary results indicate that the proportion of ST239 among all MRSA blood isolates declined from 59% in 2007 to 15% in 2012, while ST22 and ST45 became the most frequent clones, accounting together for 45% of cases in 2012 (15% in 2007). Data from this cohort and the Victorian Hospital Pathogen Surveillance Study (VHPSS) show that there was not only a reduction in the proportion of methicillin-resistant *S. aureus* (MRSA) cases, but also a decline of co-resistance to non-βlactam antibiotics among MRSA isolates. Patients with ST239 bacteraemia were more likely to die, as compared to all other ST, after correcting for age and comorbidities.

Proposal:

The AGAR data would largely be used as a validation dataset for the hypothesis and genomics models generated in our current work. Preliminary analysis of the 2013-2014 ASSOP cohorts had detected similar trends to the observed in the VANESSA/ANZCOSS cohorts. For example, the proportion of ST239 bacteraemia was 16.0% and 10.7% in 2013 and 2014, respectively. Additionally, our analysis of 334 MRSA bacteraemia episodes from the ASSOP 2013 database for which both ST type and mortality were available shows that ST239 again had the highest mortality at 30 days (35%), while mortality for non-ST239 MRSA bacteraemia was 17%. Furthermore, the extension of the time period being studied (2007-2016) will enable more sophisticated temporal modelling to be performed.