Horizon Scanning Series
The Future of Precision Medicine in Australia

Malaria and Disease Vectors

This input paper was prepared by Dr Alyssa Barry and Professor Karen Day (The University of Melbourne)

Suggested Citation

Barry, A, Day, K (2017). The Future of Precision Medicine in Australia: Malaria and Disease Vectors. Input paper for the Horizon Scanning Project "The Future of Precision Medicine in Australia" on behalf of the Australian Council of Learned Academies, www.acola.org.au.

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The spread of vector-borne diseases can be influenced by drivers including movement of both the human host and vector (Lum *et al.* 2004), however it is difficult to understand their impact on the pathogen using the current gold standard epidemiological data on disease or infection prevalence. Pathogen genomics on the other hand, connects individual infections and pathogen populations on the basis of similarities or relatedness amongst different isolates and populations. Combining this information with epidemiological metadata helps to identify the source of outbreaks and corridors of transmission and understand how pathogens are evolving in response to intervention(Grad & Lipsitch 2014). Using malaria as an example, with declining transmission, the genetic exchange between individual parasites and populations leads to more fragmented, less diverse populations (Anderson *et al.* 2000) including in response to intervention (Anthony *et al.* 2005; Daniels *et al.* 2015). This spatial clustering then requires a switch from broad ranging to more targeted approaches. Population genetic analysis informs targeted control efforts by defining clusters as potential units of elimination, and how they connect to each other, informing on the risk of reintroduction and disease spread. Genetic analysis can also determine whether infections are predominantly locally acquired or imported from other endemic areas which can help to make decisions around maintaining local control or focusing resources elsewhere(Obaldia *et al.* 2015). Likewise, genetic analysis can also track the origins of imported infections (Rodrigues *et al.* 2014) and drug resistance (Roper *et al.* 2004)

Unlike genotyping approaches targeting specific regions of the genome, whole genomic sequencing provides complete information about pathogens that along with epidemiological 'metadata' can greatly enhance control efforts(Grad & Lipsitch 2014). Indeed, pathogen genomic surveillance has tracked the source and spread of pathogens in real time(Quick *et al.* 2016), the emergence of drug resistance(Miotto *et al.* 2013), response to intervention(Croucher *et al.* 2013) and informed vaccine design(Russell *et al.* 2008). It also future proofs a dataset against emerging questions such as those pertinent to a specific geographic area or transmission setting, as they arise.

The advent and reducing cost of high throughput NextGen sequencing technologies, allowing whole genome analysis, makes it a realistic goal to aim for implementation of genomic surveillance in infectious disease control and elimination. We now have the technology to conduct these types of investigations however a major challenge is how to progress from sample collection to data output in a time frame that allows data to influence control programs and patient treatment. Real time portable sequencing platforms, such as the pocket-sized Oxford Nanopore MinION, can generate enough sequence data to cover an entire pathogen genome within hours as shown for Zika (Quick *et al.* 2017) and Dengue viruses (Yamagishi *et al.* 2017). However, approaches that translate complex genomic data into information that can guide control programs are needed and will require novel methodology to take advantage of the full genomic information in an efficient, adaptive and user-friendly manner(Kwiatkowski 2015). Importantly, this data must be widely accessible to research, public health and clinical settings and produce interpretable output able to guide control strategies. This requires major efforts from computer scientists and bioinformaticians to develop simple to use computational tools to make full use of the data being generated.

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