

Whole genome sequencing of multi-drug resistant bacteria causing bloodstream infections

The MERINO study was an international multi-centre randomized controlled trial (RCT) comparing antibiotic treatment options for bloodstream infections caused by extended-spectrum beta-lactamase (ESBL) and AmpC-producing *E. coli* and *K. pneumoniae*. The trial recruited more than 380 patients from centres within Australia, New Zealand and Singapore as well as hospitals in Europe, the Middle East, South Africa and Canada. The trial demonstrated that piperacillin-tazobactam, even when testing susceptible in vitro, was not as effective as meropenem and was associated with increased mortality at 30 days. This finding has significant implications for clinical practice. The RCPA Foundation helped to support whole genome sequencing (WGS) of the bacterial isolates from patients enrolled in the trial. This allowed us to characterise the range of antimicrobial resistance genes and explore the relationship between these factors and clinical outcomes.

The study was published in JAMA in 2018 (Harris PNA, et al. *JAMA*. 2018;320:984–994), where it has received considerable attention (Page views >100,000; 25 Citations, Altmetric score 591). WGS helped us to understand the molecular basis of the observed resistance and is now one of the largest collections of genomes from ESBL and AmpC producing Enterobacteriaceae from our region; all the sequences are now publicly available on NCBI (Bioproject Accession no. PRJNA398288). This collection is likely to be an invaluable bio-bank for future in vitro work and will help support further research in this area.

Research output from the project

Published manuscripts

1. **Harris PNA**, et al. Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality for Patients With *E coli* or *Klebsiella pneumoniae* Bloodstream Infection and Ceftriaxone Resistance: A Randomized Clinical Trial. *JAMA*. 2018 Sep 11;320(10):984-994. *Citations (36 citations, Scopus)*
2. **Harris PNA**, et al; Whole genome analysis of cephalosporin-resistant *Escherichia coli* from bloodstream infections in Australia, New Zealand and Singapore: high prevalence of CMY-2 producers and ST131 carrying *bla*_{CTX-M-15} and *bla*_{CTX-M-27}. *J Antimicrob Chemother*. 2018 Mar 1;73(3):634-642. *(9 citations, Scopus)*

Manuscript in preparation

1. Henderson A, Paterson DL & **Harris PNA**. Association between piperacillin-tazobactam MIC and mortality in patients treated with piperacillin-tazobactam from the MERINO study.