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Next-gen sequencing of multi-drug resistant *Acinetobacter baumannii* to determine antibiotic resistance genotypes

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Background

Multi-drug resistant (MDR) *Acinetobacter baumannii* is an important cause of hospital acquired infection and often increases mortality and length of stay[1-3]. The mechanisms of resistance include: (1) antimicrobial-inactivating enzymes such as □-lactamases, (2) alteration of membrane porin channels, and (3) mutations that change cellular functions [4]. Accurate genotyping and correlation to antimicrobial susceptibility will help prevent and treat outbreaks of Acinetobacter.

The genome of *A. baumannii* ranges from 3.2 Megabases (Mb) in the drug sensitive SDF strain up to 3.9 Mb in the MDR AYE strain. A surprisingly high proportion of *baumannii* ORFs, (15%-20%), are located in resistance islands or "alien islands" - long stretches of DNA acquired from a foreign source. The MDR AYE strain has an 86Kb island containing 45-50 drug resistance genes located in an insertion hotspot [5]. Our study aims to sequence several A. *baumanni*i isolates from Metro Nashville General (NGH) Hospital and conduct a strain-to-reference genomic characterization of clinical virulence factors.

Materials and methods

A retrospective review of the NGH hospital epidemiology data base included 247 isolates of *A. baumannii* from 164 patients (submitted, *BMC Infectious Disease*). Cluster Software version 2.11 and TreeView software grouped resistance phenotypes into six categories (see Figure 1) [6].

1.Pan resistant
2.Pan sensitive
3.Sensitive to meropenem /imipenem only.
4.Sensitive to meropenem/imipenem and aminoglycoside only.
5.Sensitive to cephalosporins only.
6.Resistant to aminoglycosides only.

We chose a meripenum/imepenum and aminoglycosides sensitive *baumanii* isolate for strain-to-reference sequencing on an Illumina Genome Analyzer II system at the Vanderbilt University Genome Technology Core (https://gtc.vanderbilt.edu/gtc/tech).

Conclusion

Initial sequencing yielded 5,250,420 reads of 43bp each, yielding 225.76 Mb of total sequence. The reads from our isolate were aligned to MDR *baumannii* reference strain ACICU (NC_010611.1). Alignment was done with the Bowtie Aligner [7]. Of the 5.2 million total reads, 4,004,012 (76.26%) aligned to AICIU, with a mean coverage depth of 43.96 fold. Roughly 58% of the ACICU genome was covered by at least one read. We will next align the reads further with other *baumannii* reference strains including MDR AYE (NC_010410) and non-resistant strain SDF (NC_010400) in order to further characterize and annotate our isolate at the genomic level.

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Sequencing and alignment was performed at the Vanderbilt University Genome Technology Core (https://gtc.vanderbilt.edu/gtc/tech).

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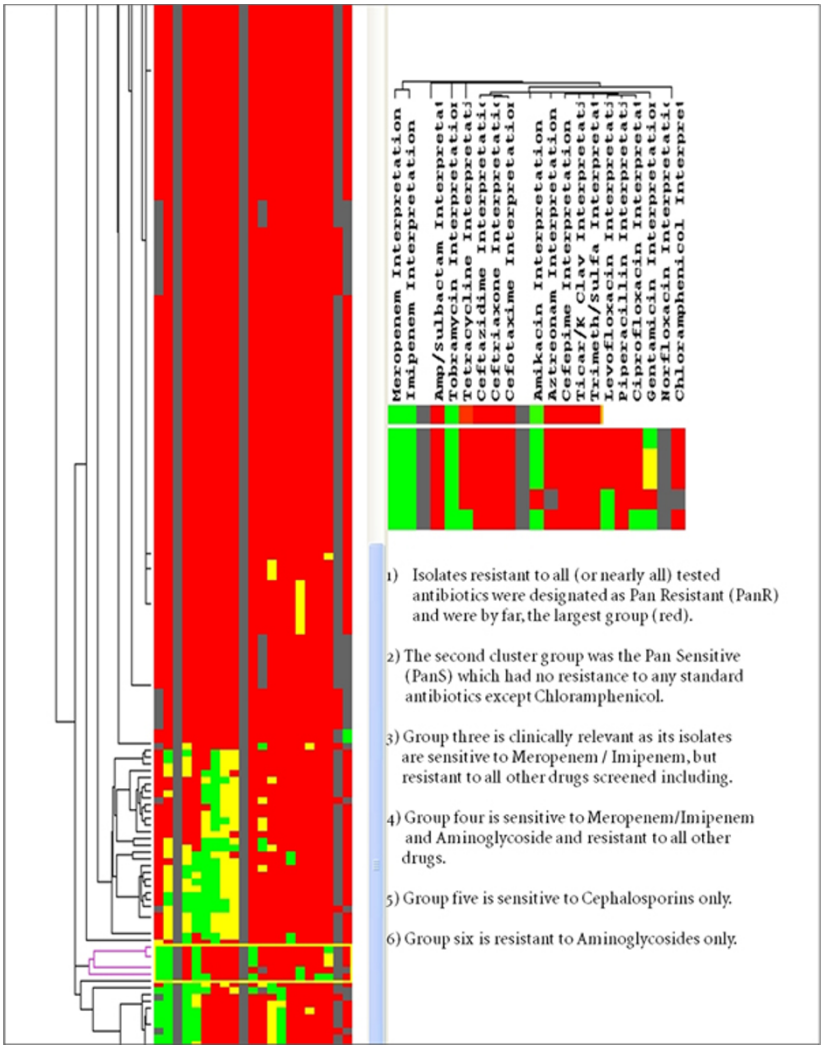

Figure 1 Clustered *baumannii* groups. Left Side: full clustergram of all isolate phenotypes. Right Side: zoom in of resistance group 4: meripenem/imipenum and aminoglycoside sensitive. **Legend:** red = resistant, green = sensitive, yellow = intermediate, black/gray = no data.

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