TITLE: Surveillance of the 2016 state of Maine clinical resistome by whole genome sequencing

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BACKGROUND: Current national surveillance methods for identifying the prevalence of novel resistant strains of multidrug resistant organisms, such as carbapenem or colistin resistance do not tend to capture isolates from Maine. The goal of this project was to determine what novel resistant strains of multidrug resistant organisms and genes may be present in the State of Maine.

METHODS: The Maine Center for Disease Control worked to seek voluntary submission of antibiotic resistant *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii* from clinical laboratories across the state. Upon isolate receipt, total chromosomal and plasmid nucleic acid were extracted via the Qiagen DNA mini kit. Genomic material from gram-positive bacteria was extracted using an in-house method. Whole genome sequencing (WGS) was performed on the Illumina MiSeq sequencing platform using Illumina's NexteraXT protocols and reagents. Paired FastQ files were assembled by the PATRIC (https://www.patricbrc.org/) bioinformatics webportal using the MiSeq assembly default parameters. *In silico* analysis of assembled sequences was accomplished via the Comprehensive Antibiotic Resistance Database (CARD, https://card.mcmaster.ca/), the Center for Genomic Epidemiology (http://www.genomicepidemiology.org/) and The Centre for Genomic Pathogen Surveillances' Whole Genome Sequence Analysis (https://www.wgsa.net/).

RESULTS: Antibiotic resistance and strain typing was conducted on 395 isolates. The KPC-2 gene was found in one isolate of *K. pneumonia* and the KPC-3 gene was found in three *K. pneumonia* isolates and one *E. coli* isolate. The carbapenase genes NDM, OXA-48, IMP, and VIM, the colistin resistance gene *mcr-1*, and the novel methicillin resistance gene *mecC* were not found in any isolates tested. Multiple variants of CTX, CMY, SHV and TEM and other OXA genes were sequenced and found in various species. Four vancomycin resistant *Enterococcus* were sequenced with one of the isolates harboring both VanA and VanB type resistance mechanisms. *Staphylococcus aureus* strain typing revealed that MRSA subtype/MLST USA300_FPR3757/ST-8 and JH1/ST-5 dominate Maine.

CONCLUSIONS: This is the first report of using WGS to provide a molecular epidemiological analysis of the antibiotic resistance mechanisms present within the State of Maine. The prevalence of emerging pathogens is low in the densest areas of Maine both in patient population and in hospital numbers. The emergence of WGS changes the traditional paradigm of public health infectious disease surveillance. With a single data file, resistance genes, virulence factors, metabolic pathways, serogrouping, point mutations, phylogenetic tree creation can be reported out, directly influencing infection control and patient care, and outbreak analysis.