Genomic Epidemiology of bla-KPC Klebsiella pneumoniae (KPC-Kp) in a High-Transmission Long-Term Acute Care Hospital (LTACH)

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Introduction
An outstanding question in the field of healthcare epidemiology is why some patients-admissions lead to outbreaks while others do not. Identification of drivers of transmission requires knowing which patients are linked by transmission within the facility.

High prevalence of MDRO and low resolution of traditional molecular epidemiology methods hinders efforts to identify pathways of nosocomial transmission.

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Methods
1. Perform WGS on KPC-Kp isolates.
2. Leverage WGS and surveillance data to develop a phylogenetic approach to identify transmission clusters.
3. Analyze transmission clusters in context of patient location and movement to determine routes of transmission.

Figure 2. Longitudinal dataset tailored to address specific epidemiological transmission linked to imported cases in an LTACH.

Whole-genome sequencing (WGS) can be used to overcome barriers

Objectives
1. Evaluate genetic factors associated with the size of transmission clusters.
2. Identify and evaluate clusters without temporal overlap between putative donor colonization, or an unidentified environmental, common location, or inter-floor healthcare worker source.

Figure 3. Patient bed trace ordered by WGS phylogeny of patient isolates. Throughout the study, there were numerous importations and conversions, as well as extensive spatio-temporal overlap between patients with closely related strains.

Hypothesis: Whole-genome sequencing (WGS) can be used to overcome barriers of lower resolution methods of sample collection, metadata, and analysis strategies are tailored to specific epidemiological questions.

Objective: Apply genomics to identify pathways of KPC- Klebsiella pneumoniae (KPC-Kp) transmission linked to imported cases in an LTACH.

Figure 4. Schematic of phylogenetic method to detect transmission clusters. Transmission clusters are defined as the maximum subtree that contains a single index patient. Clusters can contain multiple index patients in cases where isolates from multiple index patients are identical.

Figure 5. Example of epidemiologically plausible phylogenetically defined transmission cluster. The cluster detection method is based only on genetic distance, and not temporal or location tracking.

Results
Phylogenetically defined transmission clusters have a range of genetic diversity, arguing against application of a strict genetic distance based cutoff.

Figure 6. Distribution of transmission cluster size by sequence-type. A box plot indicates distribution of epidemiologically plausible transmission clusters stemming from index cases, defined by MLST. Numbers of isolates that are not part of transmission clusters by MLST shown 3 sequence-types (134, 36, 1168 that are not involved transmission, suggesting these STs may be less transmissible in this setting. ST15 and ST20 were found only in transmission clusters. Percentages show the proportion of ST observed that was not in a cluster.

Figure 7. Example cluster with serial overlap in common location.

Future directions
1. Evaluate genetic factors associated with the size of transmission clusters.
2. Evaluate transmission clusters for evidence of an environmental reservoir for KPC-Kp.

Figure 8. Examination of spatio-temporal overlap between putative donors and recipients in transmission clusters shows that 88% of acquisitions are explained by overlap within the facility, while only 61% are explained by floor overlap.

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