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Whole Genome Sequencing is Unable to Track *Candida auris* Transmission

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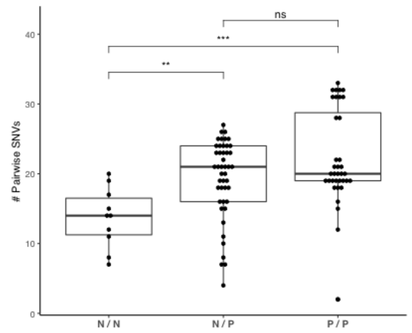
Background

- *Candida auris* is a novel emerging fungal species capable of both antifungal resistance and outbreaks in healthcare settings
- Surging *C. auris* cases at our institution prompted whole genome sequencing (WGS) of patients inside and outside of nosocomial transmission, with comparison to regional and international strains

Methods

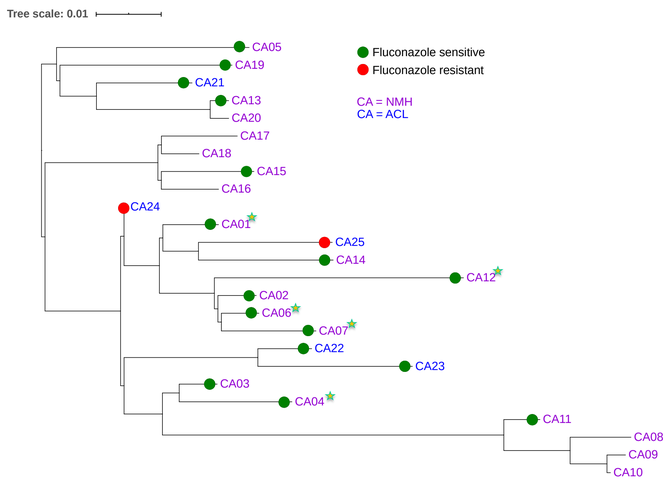
- *C. auris* isolates from patient who received inpatient care at Northwestern Memorial Hospital (NMH) in Chicago, IL from June 2018 to December 2019 were identified
- Strains were classified as nosocomial (detected > 48 hours after admission) or present on admission (POA)
- Internal strains were identified via Vitek MS/Vitek 2 through 18S rRNA sequencing using ITS1/ITS4 primer sets and D1/D2 DNA sequencing with phenotypic characterization, species were then matched through ITS sequencing to known isolates in GenBank
- Genome sequences were compared against isolates from other institutions in the Chicagoland area obtained from a reference lab (ACL) with samples from facilities separated by a minimum and maximum distance of 5.5 and 25.2 miles, and from the CDC
- Susceptibilities were performed with Thermo Sensitre YeastOne IO3IVD
- Fluconazole MIC values from ACL and the CDC were obtained through written report and the CDC & FDA Antibiotic Resistance Isolate Bank
- DNA was isolated with the Qiagen Genomic DNA extract kit and libraries prepared with the Nextera Illumina kit
- WGS was performed with the Illumina MiSeq platform to generate paired-end 300 bp reads
- Two isolates underwent long-read sequencing on the Oxford Nanopore GridION platform to obtain closed genome

Figure 1. Pairwise SNV differences



*Pairwise SNV differences between nosocomial and POA isolates. N, nosocomial isolates; P, isolates from POA patients; ns, no significant difference. Statistical analysis performed with unpaired Wilcoxon tests. ** p < 0.01, *** p < 0.001*

Figure 2. Phylogenetic tree of local isolates



Midpoint-rooted maximum likelihood phylogenetic analysis of all NMH and ACL isolates with corresponding fluconazole sensitivity profiles, when known. Strains with a star are nosocomial strains.

Results

- Twenty isolates from NMH (five nosocomial and fifteen POA), five from ACL, and two from the CDC underwent WGS to yield 12.6 Mb genomes
- SNV counts were lower among nosocomially acquired cases when compared to *C. auris* isolates present on admission (Figure 1)
- Phylogenetic analysis of nosocomial and POA isolates failed to separate the two groups (Figure 2)
- Two patients thought to be part of a transmission cluster (isolates CA06 and CA07), differed by 7 SNVs
- Isolates from room surfaces from a *C. auris* patient differed by 1-6 SNVs from each other and from 7-8 SNVs from the patient isolate
- Samples taken from different body sites of another patient differed by 4-9 SNV
- All NMH isolates were fluconazole sensitive, but a fluconazole resistant ACL isolate differed from a sensitive NMH isolate by only 4 SNVs

Limitations

- Phylogenetic observations are limited due to low sample size
- Heterogenous loci were removed and non-haploid sites were not analyzed

Conclusions

- All Chicagoland area isolates showed low levels of variation and no difference in overall pairwise SNV across hospital systems
- No distinct cluster of nosocomial isolates identified, but the average number of SNV between nosocomial isolates was less than POA/POA or nosocomial/POA
- Genomic variations associated with intra- or inter-host suggests recovering all the colonized and infecting genomes for comparison are required for outbreak investigation

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