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Paper Poster Session

Update in fungal resistance and susceptibility

Whole-genome sequencing of multidrug-resistant *Candida auris* isolates demonstrates clonal strains in Indian hospitals

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Background: Multidrug resistant *Candida auris* reported from Asia, Middle East and South Africa is an important nosocomial agent causing fungemia and deep seated tissue infections. Recently, the genetic and proteomic profiles of global *C.auris* isolates from India,Brazil,South Africa,Korea and Japan determined by MLST, AFLP and MALDI-TOF MS identified geographical clustering in this yeast. Further, *C. auris* exhibits high MICs of fluconazole and amphotericin B associated with clinical failure and limited options for antifungal therapy. The study aimed to investigate the clonal mode of transmission and intra species variation in *C.auris* isolates among patients from different hospitals located in different geographic regions in India using Whole Genome Sequencing.

Material/methods: A total of 5 clinical *C. auris* strains from individual patients in 3 hospitals in Delhi, North India and single centre in Kerala, South India were undertaken for whole genome analysis using Illumina MiSeq (n=4) and a solitary isolate was sequenced using Ion Torrent PGM318 platform. Of the 5 strains, 3 were from patients with candidemia and the remaining isolates were from patients with invasive candidiasis. Antifungal susceptibility testing of *C. auris* isolates was determined by CLSI microbroth dilution method. The whole genome data was analyzed using GeneMark-ES2,RNAmmer, tRNAscan-SE v1.21 and UnifiedGenotyper. The functional annotation was done using COG database and average nucleotide identity (ANI) was calculated using JSPECIES package. A phylogenetic network was constructed using SplitsTree based on concatenated alignment of the core genes.

Results: *Candida auris* genome is diploid comprising of 12.3 Mb with a G+C content of 44.8% and 6,675 coding sequences. The assembled draft genome of the five *C. auris* isolates suggested them to be highly related among each other with only 0.2% variation among genomes. Interestingly, all the related *C. auris* strains were from hospitals that had geographic distance ranging from 50-2081Km.

Although, all *C. auris* isolates were resistant to fluconazole, one was resistant to voriconazole and amphotericin B and the other isolate was resistant to voriconazole, flucytosine and all the echinocandins. Low diversity was observed among the *C. auris* isolates irrespective of the AFST pattern. *C. auris* *ERG3*, *ERG11*, *FKS1*, *FKS2* and *FKS3* genes in single copy number were observed and exhibited 78-85% similarity with *C. albicans* and *C. glabrata*. A phylogeny based on the concatenated sequences of 136 conserved core genes confirms that the isolates are more similar to each other than to *C. albicans*, *C. glabrata*, *S. cerevisiae* and *C. guilliermondii*. Although, *Clavispora lusitaniae* is closely related to *C. auris* strains, the low ANI value (<95%) among other *Candida* species and *C. auris* suggested divergence.

Conclusions: The present study highlights clonal expansion of *C. auris* isolates in India as highly related population was observed in clinical specimens irrespective of geographic location or AFST pattern.