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Paper Poster Session

Fungal diagnosis: from culture to molecular techniques

Molecular characterization and azole susceptibility of *Aspergillus flavus* species complex clinical isolates

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Background: Section Flavi is one of the most significant sections in the genus *Aspergillus*, and species of this section *can cause* invasive aspergillosis as well as allergic diseases in humans. The high number of species belonging to the Flavi section, and their morphological similarity make their precise identification difficult by phenotypic methods. In this study, we present data on molecular characterization and antifungal susceptibility profile of French clinical isolates of *Flavi section*.

Material/methods: Eighty fungal isolates, reported as *A. flavus*, were included in the study. These clinical isolates were recovered from several specimens over a 15-year period (2001-2015). The isolates were initially identified by morphological characteristics. After subculture, each isolate was identified to the species level by sequencing a locus/region of the β -tubulin and calmodulin genes. The isolates were also screened for their susceptibilities to azoles antifungal agents on 3-sectors agar plates containing itraconazole, voriconazole and a drug-free control. Azole resistance was confirmed by evaluating the MIC using Etest® on RPMI 1640.

Results: Among the 80 isolates, molecular analysis of the partial β -tubulin and calmodulin sequences showed that 78 isolates were *A. flavus sensu stricto* and 2 isolates were identified as *A. parasiticus* and *A. tamarii*, respectively. These 2 strains were isolated from sputa and were not resistant to azole antifungal drugs. Among the *A. flavus sensu stricto* isolates, a limited polymorphism was observed for the partial β -tubulin gene: for 75 isolates (96%), sequences were identical to the reference sequence. For partial calmodulin gene, a higher degree of polymorphism was observed with sequences identical to the references sequences found in only 14 isolates (18%). Moreover, 2 strains of *A. flavus sensu stricto* were resistant to voriconazole but not to itraconazole. Analysis of *CYP51A* gene polymorphism for these isolates is in progress.

Conclusions: For the first time in France, we molecularly characterized a large collection of clinical isolates belonging to *A. flavus* section. Most of the isolates were identified as *A. flavus sensu stricto* and were susceptible to azole antifungal drugs. Nevertheless, the occurrence of a few resistant isolates highlights the importance of antifungal susceptibility testing.