

TITLE: KERATITIS DUE TO EMERGING OPPORTUNISTIC HUMAN PATHOGENS IN THE *FUSARIUM OXYSPORUM* SPECIES COMPLEX.

AUTHORS: MONTEIRO, R.C.¹, ZORAT YU, M.C.², DOS SANTOS, M.C.³; CARVALHO, J.A.¹; PINHEIRO, B.G.¹; COLOMBO, A.L.³; DE CAMARGO, Z.P.^{1,4}, HÖFLING-LIMA, A.L.², RODRIGUES, A.M.^{1,4}

INSTITUTION: ¹DEPARTAMENTO DE MICROBIOLOGIA, IMUNOLOGIA E PARASITOLOGIA, DISCIPLINA DE BIOLOGIA CELULAR, PROGRAMA DE PÓS-GRADUAÇÃO EM MICROBIOLOGIA E IMUNOLOGIA, UNIVERSIDADE FEDERAL DE SÃO PAULO, SÃO PAULO, SP (RUA BOTUCATU, 862, EDIFÍCIO DE CIÊNCIAS BIOMÉDICAS, 8º ANDAR, CEP 04023-901, SÃO PAULO – SP, BRASIL); ²DEPARTAMENTO DE OFTAMOLOGIA E CIÊNCIAS VISUAIS, UNIVERSIDADE FEDERAL DE SÃO PAULO, SÃO PAULO, SP (RUA PEDRO DE TOLEDO, 669, EDIFÍCIO DE PESQUISA II, 4º ANDAR FRENTE, CEP 04021-001, SÃO PAULO – SP, BRASIL);

³DEPARTAMENTO DE MEDICINA, PROGRAMA DE PÓS-GRADUAÇÃO EM INFECTOLOGIA, UNIVERSIDADE FEDERAL DE SÃO PAULO, SÃO PAULO, SP (RUA BOTUCATU, 669, EDIFÍCIO DE PESQUISA II, 5º ANDAR, CEP 04021-001, SÃO PAULO – SP, BRASIL);

⁴DEPARTAMENTO DE MEDICINA, PROGRAMA DE PÓS-GRADUAÇÃO EM INFECTOLOGIA, UNIVERSIDADE FEDERAL DE SÃO PAULO, SÃO PAULO, SP (RUA BOTUCATU, 862, EDIFÍCIO DE CIÊNCIAS BIOMÉDICAS, 8º ANDAR, CEP 04023-901, SÃO PAULO – SP, BRASIL);

ABSTRACT:

Members of the *Fusarium oxysporum* species complex (FOSC) are ubiquitous in the environment. Several isolates can cause diseases of many plant species of economic importance or develop opportunistic infections in animals and immunosuppressed humans. FOSC is known by clonal spread of sequence types related to humans in several environments. Here we described four cases of ocular fusariosis due to FOSC without a previous report in Brazil, with molecular track haplotypes for human-related in FOSC. All patients were undergoing treatment with amphotericin B and fluconazole and evolved to cure. Isolates were cultured in malt extract agar (MEA) for DNA procedures. Sequencing of partial genes *tef1α*, *rpb2*, *cal*, β -*tub*, and rRNA 28s, besides MALDI-TOF, were carried out for identification. Sequences of *tef1α* were retrieved from Genbank to carry out haplotypic network analysis. Additionally, susceptibility tests were performed according to CLSI (M38-A2). Samples were identified as *F. veterinarium* (n=2), *F. contaminatum* (n=1), and *F. curvatum* (n=1) by MLSA. According to these results, MALDI-TOF could identify the two samples of *F. veterinarium* but failed for the other samples, mistaken by *F. oxysporum*. Haplotype network analysis involving 1,316 sequences revealed a clonal spread of *tef1α*-related genotypes (H2) associated with *F. veterinarium*, with a high representative of clinical samples from the database. In contrast, few isolates were related to human infections to clades bearing *F. contaminatum* (H1, and H99) and *F. curvatum* (H3, H26, and H122). Isolates showed higher MIC for itraconazole (>16,0 µg/mL), posaconazole (>8-16,0 µg/mL), and voriconazole (1µg/mL), while they showed relatively reduced MIC for amphotericin B, as expected. Human pathogens in FOSC are significant emerging pathogens in clinical mycology because they are very refractory to treatment and have reduced susceptibility to antifungals, as demonstrated here. *F. veterinarium* is the major pathogen in FOSC, although other species can cause infections. Genetic approaches are critical to recognize and speciate members of the FOSC of medical relevance. The study of how fusariosis spread has loomed large in the struggle to understand, contain, and respond to emerging *Fusarium* species.

Keywords: *Fusarium oxysporum*, keratitis, sequencing, MALDI-TOF

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