TITLE: IDENTIFICATION OF POTENTIAL VACCINE CANDIDATES FOR *TRICHOSPORON ASAHII* AND *CRYPTOCOCCUS* SPP. BY REVERSE VACCINOLOGY

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ABSTRACT:

Together with *Cryptococcus* spp., *Trichosporon* spp. is classified within the Basidiomycota phylum and is emerging as an opportunistic pathogen of invasive infections. *T. asahii* is the most clinically relevant species, mainly due to its resistance against antifungals and the high mortality rates of infected immunocompromised patients (up to 80%). To prevent fungal infections, inactivated fungal cells, protein and sugar-conjugated vaccines are being explored. Thus, our aim was to identify potential vaccine candidates within the *T. asahii* proteome with cross-protection against *C. neoformans* using reverse vaccinology. *In silico* analyzes were performed using the predicted proteome of *T. asahii* CBS2479 deposited in the NCBI. Prediction of extracellularity was performed in CELLO v.2.5 and PSORT II programs, and immunogenicity, in Vaxijen v2.0. Comparisons to human and *Cryptococcus* spp. proteomes were performed in the NCBI-BLASTp. Protein candidates were selected according to criteria: no similarity with human proteins, description of functional characterization and similarity/coverage with *Cryptococcus* spp. proteins ≥50%. Immunogenic epitopes were mapped in Tepitool and 3D models were generated in the I-TASSER. Population coverage of HLA alleles were performed in the Population Coverage-IEBD tool. From 8,300 proteins analyzed, 268 were predicted as extracellular by both programs but 205 exhibited immunogenic potential (score ≥ 0.5). Only 137 had no similarity with human proteins. To identify candidates that could induce cross-protection with *Cryptococcus* spp., by applying the inclusion criteria, four proteins were selected with similarity (52 to 60%) and coverage (82 to 100%) between *T. asahii* and *Cryptococcus* spp. proteins. Immunogenic epitopes were found externally to the 3D model of the proteins as: 18 epitopes in the Major allergen Asp F2 (NCBI accession number XP_014180978.1), 23 in the Alpha-1,3-glucanase (XP_014180398.1), 40 in the Glyoxal oxidase precursor (XP_014180666.1) and 29 in the Chitin deacetylase-like mannoprotein MP98 (XP_014180616.1). Considering the HLA population coverage, epitopes from the first protein exhibited median coverage of 79,73%, the second, 77,85%; third, 69,69%; and the last, 68,52%. By using reverse vaccinology, we were able to identify 110 immunogenic epitopes to create a vaccine with potential cross protection against *T. asahii* and *Cryptococcus* spp., with a global coverage rate from HLA alleles of 99.98%.

Keywords: Reverse vaccinology, *Cryptococcus* spp., *Trichosporon* spp., protein vaccine

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