

**Mining of two major medical fungal culture collections enables the identification of the genetic diversity of the agents of cryptococcosis in 55 countries.**

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**Abstract:**

Members of the *C. neoformans/C. gattii* species complex are the second most common cause of life-threatening human/animal mycoses. To enable a timely response to the emergence of highly virulent strains it is important to understand the global cryptococcal genotype structure. Using either URA5-RFLP, PCR-fingerprinting, AFLP or MLST analysis 3203 isolates from 55 countries were grouped into eight major molecular types, VNI-VNIV for *C. neoformans* and VGI-VGIV for *C. gattii*, and their global distribution was determined. The data were collected from 2 culture collections, Pathogenic Fungal Collection – FIOCRUZ, Brazil and Australian Medical Fungal Collection - The University of Sydney, Australia, as well as from published studies. *C. neoformans* VNI was the most prevalent molecular type, causing 68% of all infections and making up 58% of all isolates. Analyses of the environmental samples alone suggested that both species are equally present, and VNI and VGII are the most prevalent molecular types. An environmental shift was identified for *C. gattii*, having a much wider distribution and being not restricted to tropical and subtropical regions. The AD hybrid (VNIII), previously thought to be restricted to Southern Europe, was also found in the Americas. For the first time a correlation between molecular types and serotypes has been conducted based on 2574 isolates, confirming that in *C. neoformans* serotypes A and D correspond with the molecular types, VNI/VNII and VNIV, respectively. In *C. gattii* both, serotypes B and C, are found in all four molecular types, with serotype B being predominant in VGI and VGII, and serotype C in VGIII and VGIV. All molecular types of *C. neoformans* and the molecular type VGIV of *C. gattii* predominated in immunocompromised hosts, while *C. gattii* VGI-VGIII predominated in immunocompetent hosts. The global network of cryptococcal culture collections established as part of these study and the obtained genotyping data enable the understanding of the global spread of a major human/animal pathogen, which is forming the basis for prediction and response to possible outbreaks.

**Key words:** Biodiversity, *Cryptococcus gattii*, *Cryptococcus neoformans*