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## HIV-1 gp41 enhances CD44-mediated monocytes migration across Cryptococcus-infected brain endothelial cells

H. Cao*, L.-K. Zhang, X.-L. He, M. Long, Y. Li, S.-H. Huang

*Southern Medical University, Guangzhou, China*

**Background:** Transmigration of monocytes across the blood-brain barrier (BBB) is a critical event in Cryptococcal meningitis (CM) as the main complications in patients with AIDS, which has a high mortality rate. It has been reported that the invasion of BBB by Cryptococcus neoformans(CN) was dependent on CN binding to CD44, a primary hyaluronic acid (HA) receptors onthe brain microvascular endothelial cell (BMEC) for CN's major virlence factor HA adhesion, and HIV-1 gp41 ectodomain enhanced CN binding to BMEC,but the exact relationship between HIV-1 gp41 ectodomain and monocytes migration into the brain induced by CN are not yet understood.

**Methods & Materials:** In order to examine the role of HIV-1 gp41 ectodomain in the CD44-mediated monocyte THP-1 transmigration across BMEC, the transmigration assay with transwell filter (12.0-μm pore size, 12-mm diameter,Millipore) covered byconfluent BMEC monolayers was utilized.

**Results:** The result showed that the number of THP-1 migration was remarkably increased in response to higher concentrations of Gp41 ectodomain in a dose-dependent manner. A maximum migration (about 28.4% higher than control) of THP-1 could be induced with 200 μg/mL of Gp41 ectodomain at 24 h. Further more, The studies demonstrated that Bikunin,the inhibitor of CD44, markedly blocked THP-1 transendothelial migration when compared tothe PBS control ($P<0.01$) in a dose-dependent way, in which the maximum dose (1200 μg/mL) of Bikunin to BMEC significantlyreduced the THP-1 transmigration by46.6% as compared with the control at 3 h.

**Conclusion:** Taken together,our data suggested that CD44 was impotant forCN-induced THP-1 transmigration across BMEC, and CN-induced THP-1 transmigration across BMEC is significantly enhanced in the presence of HIV-1 gp41 ectodomain via the interaction between CN and CD44. *(Acknowledgments: This study was supported by the National Natural Science Foundation of China, No. 81171644 to H.C.)*

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## Phenotypic and molecular antifungal susceptibility of yeast isolates from Pretoria, South Africa

Y. Dangor*, M. Hyana, R. Lekalakala, N. Mbelle

*University of Pretoria, Pretoria, South Africa*

**Background:** The distribution of yeast isolates and antifungal susceptibility patterns show marked variation between different geographic areas. Thus, it is necessary to monitor the local antifungal susceptibility profiles and understand the mechanism of resistance among yeasts.

**Methods & Materials:** A total of 250 yeast isolates were collected from the diagnostic laboratory in the Department of Medical Microbiology at the University of Pretoria-National Health Laboratory Services. The antifungal susceptibility of 87 isolates was determined by the Etest for three azole antifungals (fluconazole, posaconazole and voriconazole), amphotericin B and caspofungin. Polymerase chain reaction was performed on *C. albicans* isolates to amplify the *ERG11* gene and the *FKS1* gene. Sequencing was done for the amplification products and the sequence data were analyzed by the CLC genome workbench software.

**Results:** *Candida* species accounted for 82.8% and *C. neoformans* accounted for 17.2% of the isolates. *C. albicans* was the most commonly isolated (76.8% of *Candida* species), of which 30% were resistant to caspofungin. Fluconazole resistance was detected in 56.7% of *C. parapsilosis* isolates. Cross-resistance was found between fluconazole and voriconazole.

Resistance to posaconazole was detected in 66.7% of *C. glabrata* isolates. Other *Candida* species and *C. neoformans* isolates were fully susceptible. *C. neoformans* var. *gattii* isolates were less susceptible to azole antifungal agents than *C. neoformans* var. *neoformans* isolates.

Point mutations were frequently observed among the *ERG11* gene of both azole resistant and azole susceptible isolates, but amino acid substitutions were detected in only one azole resistant and in two azole susceptible isolates. The amino acid substitutions D116E and K128T were found simultaneously in fluconazole and voriconazole susceptible isolate and V437I was found in another susceptible isolate.The S642L substitution was detected in the *FKS1* gene of all the isolates that were caspofungin resistant and caspofungin susceptible.

**Conclusion:** Cross-resistance was detected between fluconazole and voriconazole with *Candida albicans*. Resistance to azole and caspofungin antifungal agents existed without the previously described molecular alterations in the *ERG11* and *FKS1* genes of resistant isolates. Further studies are required to explain the role of new amino acid substitutions, as well as the involvement of other mechanisms in resistance to antifungal drugs

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