Metabolomic screening of cerebrospinal fluid from Human Immunodeficiency Virus - infected patients with cryptococcal meningitis under treatment with Fluconazole

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ABSTRACT

Introduction: *Cryptococcus neoformans* is the main cause of fungal meningitis in HIV-infected patients. In addition to a long treatment period, the incidence of mortality and recurrence of this disease are especially alarming. Therefore, better understanding the molecular conditions surrounding target locations in the body can be of assistance for the management and control of this disease. Herein, we present a study with an approach based on metabolomics that presents the metabolic fingerprint of the cerebrospinal fluid (CSF) of patients with meningitis receiving fluconazole, in a fast strategy that requires minimal sample preparation.

Materials and Methods: CSF samples of control and disease groups are directly infused and analyzed by high-resolution mass spectrometry (HRMS) on mass range of 500-2000 *m/z*. The analyses of *m/z* ratio versus intensity of FT-HRMS signals were performed by Principal Component Analysis (PCA) to discriminate and select characteristic signals for each group. Databases were consulted to elect potential pathophysiological biomarkers.

Results: Statistical analysis shows great accuracy (88%) to discriminate samples between control and disease groups, but low accuracy between samples of the same group. Control group presented markers that can be related to normal composition of CSF. Disease group showed molecules closely related to the host's immune response and modulation caused by yeast. The identified compounds can be associated with a potentially increased activity in metabolic pathways of the yeast and treatment-related markers.

Conclusion: These findings demonstrate that metabolic fingerprinting can be an useful tool for treatment monitoring in immunocompromised patients, as well as serve as the starting point of further developments on more accurate and fast diagnostic methods.

Keywords: *Cryptococcus neoformans*, cerebrospinal fluid, HR-FTMS, metabolomic profile.