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Isolation and characterization of fungal secondary metabolites with anti-*Naegleria fowleri* (brain eating amoeba) activity

Kristóf B. Cank[1], Tyler N. Graf[1], Christopher A. Rice[2], Dennis E. Kyle[2], Cedric J. Pearce[3] and Nicholas H. Oberlies[1]

[1] Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, USA
[2]Center for Tropical & Emerging Global Diseases, University of Georgia, Athens, GA, USA
[3]Mycosynthetix, Inc., Hillsborough, NC, USA

E-mail: k_cank@ung.edu

Naegleria fowleri, commonly known as "brain eating amoeba" is a free-living amoeba, which is responsible for primary amoebic meningoencephalitis (PAM). This is a very rare but severe human disease that is rapidly fatal leading to death in approximately one week or less [1]. Due to the low number of infections, to date, there are no clinical trials addressing the efficacy of one treatment over another. The lack of effective treatments as well as the 95% mortality rate creates an urgent need for new and more effective therapeutics [2,3]. Our goals is to address this compelling need by exploring the vast untapped biodiversity in the fungal kingdom. We have screened over 4000 fungal extracts in a single point assay at 50 µg/mL concentration. For elimination of cytotoxic fractions, we tested the samples against four different human cancer cell lines including melanoma, breast, ovarian, and lung carcinoma cell lines. To exclude the already known compounds, the active samples were evaluated by using our in-house developed UPLC-PDA-HRMS-MS/MS dereplication method. Bioactivity directed isolation and structure elucidation of secondary metabolites, resulted in several compounds with notable activity against *Naegleria fowleri*. The characterization of additional fractions is currently ongoing. This study shows that the inherent structural diversity of fungal secondary metabolites indicates that fungi can be a promising source for new anti-*Naegleria* therapeutics.

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