

# High-throughput sequencing to explore the extrachromosomal plasmid rDNA of *Naegleria fowleri* AY27 genotype II: A human brain-eating Amoeba

Syed Shah Hassan<sup>1</sup>, Muhammad Aurongzeb<sup>1</sup>, Muhammad Jahanzaib<sup>1</sup>, Hafiz Muhammad Talha Malik<sup>2</sup>, Zarrin Basharat<sup>1</sup>, Asad Karim<sup>1</sup>, and Yasmeen Rashid<sup>3</sup>

<sup>1</sup>Dr Panjwani Center for Molecular Medicine and Drug Research

<sup>2</sup>23rd Pair Lab Service (Private) Limited

<sup>3</sup>University of Karachi Faculty of Science

April 16, 2024

## Abstract

*Naegleria fowleri* is the only known *Naegleria* spp. that cause acute, fulminant, and rapidly fatal infection in the central nervous system of humans called primary amebic meningoencephalitis (PAM). We report a 28 years-old suspected PAM patient hospitalized in Karachi, Pakistan, with no earlier memoir of recreational activities but daily ritual ablution. Wet film observation of CSF showed amoebic trophozoites and confirmation of *N. fowleri* was done using Internal Transcribed Spacers detection method ((ITS-PCR). Clinical isolate of *N. fowleri* from patient CSF was sequenced for circular extrachromosomal ribosomal DNA (CERE - rDNA). The CERE contains 18S, 5.8S and 28S ribosomal subunits separated by internal transcribed spacers, 5 open reading frames (ORF's), and mostly repeat elements comprising 7268bp out of 15786bp (46%). A wide variety of variations and recombination events were observed. Finally, the ORF's that comprised of only 4 hypothetical proteins were modelled and screened against Zinc drug-like compounds. Two compounds [ZINC77564275 (ethyl 2-(((4-isopropyl-4H-1,2,4-triazol-3-yl)methyl)(methyl)amino)oxazole-4-carboxylate) and ZINC15022129 (5-(2-methoxyphenoxy)-[2,2'-bipyrimidine]-4,6(1H,5H)-dione)] were finalized as potential druggable compounds based on ADME toxicity analysis. We propose that the compounds showing least toxicity would be potential drug candidates after laboratory experimental validation is performed.

## Hosted file

Plasmid-Nf\_Manuscript\_\_31-12-21.docx available at <https://authorea.com/users/514173/articles/713063-high-throughput-sequencing-to-explore-the-extrachromosomal-plasmid-rdna-of-naegleria-fowleri-ay27-genotype-ii-a-human-brain-eating-amoeba>



