BIOLOGY
BLUE ASH

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PROJECT TITLE: Pharmacological studies of kinase inhibitors for Naegleria species, the cousin of the brain-eating amoeba, Naegleria fowleri

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Project Description

The long-term goal of the project is to develop drugs to fight against infectious diseases caused by eukaryotic cells such as amoeba, algae, and fungi. The specific aim of the summer proposal is to design and construct such potential drugs that specifically target and inhibit the brain-eating amoeba, Naegleria fowleri (N. fowleri).

Naegleriasis has been reported in every continent, except Antarctica. The causative agent N. fowleri is a unicellular amoeba found in freshwater or wet soil. When contaminated water enters the nasal cavity, the amoeba gains access to the organs of the central nervous system through the olfactory nerves. Although it is a rare infectious disease (145 cases in the U.S. between 1962 and 2018), the death rate exceeds 97% in the U.S. Unfortunately, the victims are typically young children (median age is 12). Because Naegleria species is thermophilic, the infection typically happens in the southern states, but cases of Naegleriasis were recently reported in northern states such as Minnesota, Indiana, and Maryland. One of the reasons for the extremely high fatality comes from the fact that effective treatment has not been established. Moreover, the most commonly used drug, amphotericin B, is highly toxic not only to the amoeba but also to humans, severely damaging the liver and kidneys (potentially fatal). Therefore, the project aims to develop new effective and less-toxic antibiotics against N. fowleri.

Using non-pathogenic species of Naegleria (N. gruberi) as a model organism, our students discovered that the amoeba is resistant to certain anti-mycotic drugs but sensitive to another class of a kinase inhibitor. Therefore, we want to design derivatives of the anti-mycotic drugs to make them effective against the amoeba and test the efficacy of other kinase inhibitors that we have not explored yet.