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Antifungal and Antiparasitic Indoloquinoline Derivatives

Patent No. 8,158,646 B2

New indoloquinolinium salts and their derivatives have been obtained and have been shown to demonstrate potent anti-infective actions against opportunistic pathogens associated with HIV AIDS, cancer chemotherapy, organ transplant and other immune compromised conditions and could serve as replacement therapies for amphotericin B without the associated toxicity.

Florida A&M University
Division of Research

Contact:
Rose Glee, Ph.D.
Director
Office of Technology
Transfer, Licensing &
Commercialization
660 Ardelia Court
Tallahassee, FL-32307
Phone: 850-412-7232
rose.glee@famu.edu

Inventors:
Seth Y Ablordeppey, Ph.D.
seth.ablordeppey@famu.edu

Key Features:
Potential replacements for current anti-opportunistic infection agents with minimal side-effects.

Field:
Pharmaceutical

Technology:
Drug treatment of OIs

Stage of Development:
Pre-clinical studies involving animal studies

Status:
Seeking research support to escalate animal studies, establish metabolic stability & pharmacokinetic profiles

Patent Status:
Issued

Background:

Opportunistic Infections (OIs) caused by pathogenic microorganisms such as *Cryptococcus neoformans, Candida albicans* and *Aspergillus fumigatus* are growing medical concerns for immuno-compromised patients such as those with AIDS, diabetes, organ transplant patients, patients on cancer chemotherapy, and several others. The burden imposed by these infections is staggering, both in terms of economic loss and human suffering. In sub-Saharan Africa for example, 15-30% of all patients with AIDS develop cryptococcal disease and cryptococcal meningitis occurs in 30% of these individuals. If not properly treated, these OIs are often fatal.

Statement of Problem:

1.3 million people in the US are living with HIV, with 20% unaware of their status. With their immune systems compromised, up to 90% will experience an OI episode. The medications available for treating OIs are limited because they were not important prior to the AIDS epidemic. Unfortunately, even the limited numbers are further limited by resistance development, drug interactions and toxicity. Amphotericin B, the gold standard for OI treatment produces nephrotoxicity in patients on the drug.

Potential Solution:

Our invention comprises the discovery and *in vivo* validation of the efficacy of natural product-derived agents with potent, less toxic and overall better therapeutic profiles than Amphotericin B. **For example, one of the discoveries decreased brain *C. neoformans* infections 50% more than Amphotericin B in animal models of the infection**. Because they have different mechanisms of action, these compounds will be complementary to those currently on the market and might be useful in treatment-resistant cases especially. Another exciting aspect is that unlike the drugs on the market, external application of the new compounds would have limited capacity to cause systemic toxicity.

The Benefits:

- The new drugs are effective against a broad spectrum of opportunistic infections
- They will treat opportunistic infections without nephrotoxicity.
- These drugs should be complementary to the drugs currently available and thus might be useful in treatment-resistant cases.

Commercialization Status:

Indoloquinolinium salts and their derivatives are currently in the pre-clinical development stage. This research has been funded by the National Institutes of Health, NIAID/NCRR. Validation of the observed activities in larger animal models is planned along with additional pharmacokinetic studies. We seek venture capitalists and partners or licensees with interest in small molecule drug development in the Biotechnology and/or Pharmaceutical Industries.