**Novel Hit Compounds as Putative Antifungals**

**Technology Description**

Researchers have discovered novel scaffolds which could serve as starting structures to develop new drugs with antifungal activity. They have identified eight (8) compounds that exhibit antifungal activity against two strains of *Aspergillus fumigatus* targeting the fungal cytochrome P450 dependent lanosterol 14-α demethylase (CYP51A) enzyme. These compounds can serve as new starting scaffolds for further hit-to-lead optimization.

In recent decades, fungal infections have been one of the most common and serious health problems worldwide causing over one million human deaths each year. One of the most common airborne fungal pathogens, causing serious and usually fatal invasive infections, is *Aspergillus fumigatus.* The disease caused by fungi of the Aspergillus genus is known in the literature as aspergillosis. This disease is generally separated into three categories, based mainly on the range of symptoms it causes, namely allergic bronchopulmonary aspergillosis (ABPA), chronic necrotizing aspergillosis, and invasive aspergillosis (IA).



Figure 1. Compounds identified and selected from the pharmacophore-based virtual screening and docking studies. Zinc IDs: (1) ZINC02414861, (2) ZINC08765786, (3) ZINCE09152123, (4) ZINC09517045, (5) ZINC12729365, (6) ZINC12996228, (7) ZINCE13779062, and (8) ZINC4613236

**Stage of Research**

The researchers evaluated the compounds docking scores and the presence of crucial binding interactions to a homology model of the CYP51A enzyme. They have performed *in vitro* assays to determine the antifungal activity of the compounds against *Aspergillus fumigatus* (ATCC 204305) and *Aspergillus fumigatus* (human clinical isolate). Additionally, the researchers have identified the minimal inhibitory concentrations (MIC) and minimal fungicidal concentrations (MFC) for the compounds compared to reference azole drugs, econazole, and ketoconazole.

**Applications**

Treating invasive infections caused by *Aspergillus fumigatus*:

* allergic bronchopulmonary aspergillosis
* chronic necrotizing aspergillosis
* invasive aspergillosis

**Key Advantages**

* Scaffolds differentiate from classical azoles which exhibit high toxicity, unfavorable side effects, and a plethora of interactions with other drugs
* Drugs based on the new scaffolds will be less prone to resistance