



INVESTIGATING NEW DRUG LEADS FOR FUNGAL INFECTIONS

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Aspergillus fumigatus and *Candida albicans* are fungal species that can cause serious, often fatal, disease in the vulnerable, especially cancer and AIDS patients. Current medicines to treat these infections have many drawbacks including serious side effects and limited effectiveness. This project aims to find new leads in the fight against these kinds of infection. A molecular approach has been used to find proteins that are essential for the survival of both *A. fumigatus* and *C. albicans*. The theory is that if these essential proteins are disabled the fungal cells will die. Therefore it is hoped that finding chemicals that disrupt these proteins will provide chemical leads for antifungal drug discovery. To date 3 proteins have been identified that are essential for the survival of both types of fungi. The 3 essential proteins have been made in large quantities using bacterial cells and screens are being developed to test for activity of the protein. Measuring activity of the protein in the presence of a library of small molecule compounds will enable identification of chemical inhibitors. Chemicals that disrupt both *A. fumigatus* and *C. albicans* proteins will be analysed in further detail to identify the best starting points for drug design. It is important that a new drug has the ability to enter cells in order to disrupt the protein inside the cell and cause cell death. This will be tested by mixing the chemicals of interest with whole cells to see if they can enter and then kill the cells. It is also important that the chemicals are not toxic to human cells. One way of testing this is to grow mammalian cells in a test tube in the presence of the chemicals and see if the cells stay alive. Other considerations are how easily the drug compounds can be manufactured, costs and intellectual property surrounding the work.

This study should result in new broad-spectrum antifungal drug leads to fight two of the most medically important fungi. Newer, effective antifungal medicines will result in huge benefits to human health.