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Heterologous production, purification and crystallization of sterol 24C-methyltransferases from opportunistic pathogenic fungi

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Opportunistic pathogenic fungi cause infectious fungal disease with extremely high mortality rates, especially in immune-compromised patients [1]. Antifungal resistance and multi-drug resistance have emerged against the limited number of clinically used antifungals. Because of the high HIV/AIDS incidence in Sub-Saharan Africa [2], anti-fungal drug resistance is specifically of concern; therefore, there is an urgent need to develop novel therapies.

In this study, sterol C24-methyltransferase (SMT) has been identified as a novel target for anti-fungal drug development. An expression vector library was prepared with SMT genes from four opportunistic pathogenic fungi, heterologously expressed in *Escherichia coli* and the SMT proteins purified with affinity chromatography. The SMT from *Candida albicans* was crystallised and diffraction data was collected at the Diamond Light Source synchrotron.

Expression of truncated SMT genes from all four fungi was successful, and the SMT from *C. albicans* was successfully purified and crystallised; however, diffraction was only observed at low resolution (~7Å). Purification of the SMTs from the other three pathogens is ongoing, and crystallisation of the *C. albicans* SMT is currently being optimised.

[1] Denning DW (2024) Global incidence and mortality of severe fungal disease. *Lancet Infectious Diseases*. 24(7):e428-e438.
[2] Dos Santos Abrantes PM, McArthur CP & Africa CWJ (2014). Multi-drug resistant oral *Candida* species isolated from HIV-positive patients in South Africa and Cameroon. *Diagnostic Microbiology and Infectious Disease*. 79(2), 222–227.

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