TARGETING GLYCAN-MEDIATED ADHESION IN FUNGAL INFECTION

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Chronic fungal infections affect over 150 million individuals. These infections can have a huge impact on immunocompromised and vulnerable populations [1]. Yeasts from the *Candida* spp. are opportunistic fungal pathogens, some of which like *C. albicans* and *C. auris* have been classified as critical priority pathogens by the World Health Organization. Adherence to host tissue is critical to their ability to colonise and infect the host. We have designed and evaluated carbohydrate-based anti-adhesion compounds as inhibitors of *C. albicans* adherence to exfoliated buccal epithelial cells (BECs). A small library of aromatic glycoconjugates were synthesised using synthetic carbohydrate chemistry and Copper-Catalyzed Azide-Alkyne Cycloaddtion (CuAAC) chemistry. These were evaluated as anti-adhesion ligands and it was found that a divalent galactoside (Figure 1) showed the best anti-adhesive properties, capable of displacing over 50% of yeast cells already attached to the BECs [2].
To optimise the activity of this lead compound, several strategies have been explored: we have carried out Structure-Activity Relationship (SAR) studies, where we have investigated alternative scaffolds and glycomimetic compounds. We have also considered different multivalent presentations, where the lead compound was graphed numerous times onto a common scaffold to enhance binding affinity [3,4]. Our results pave the way for the identification of new carbohydrate-binding adhesins involved in fungal pathogenesis.

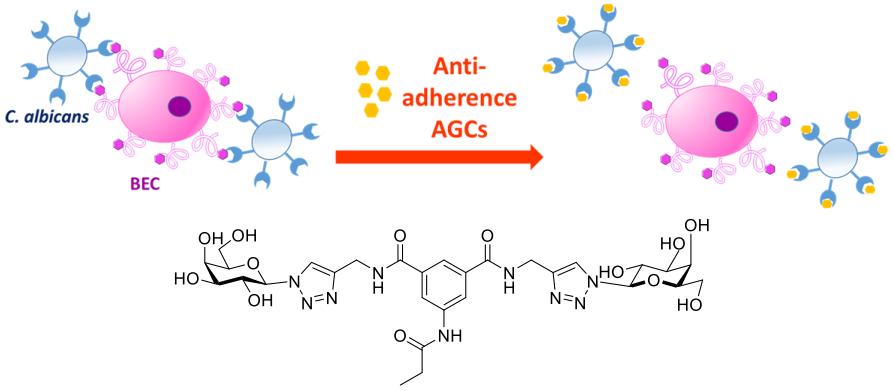

Figure 1. Graphical representation of the anti-adhesion approach (top) and the structure of lead compound divalent galactoside (bottom).

References:
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