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“Comparative epitope binding of parental, recombinant, and single-chain variable fragment formats of the anti- β -1,2-mannotriose monoclonal antibody C3.1 across medically important *Candida* species”

Candida species are opportunistic fungal pathogens responsible for severe, invasive bloodstream infections. *C. auris* has established itself as a ‘superbug’ due to its multidrug resistance, ease of nosocomial transmission, and high mortality rate, especially in immunocompromised and hospitalized patients. *C. auris* has emerged as a serious global public health threat, underscoring the urgent need for novel therapeutic approaches.

Our research has previously identified monoclonal antibodies (mAbs) as a promising approach to treating *Candida* infections. mAb C3.1 is an IgG3 antibody specific for β -1,2-mannotriose, a conserved cell-surface glycan epitope expressed by many medically important *Candida* spp. C3.1 has been shown to enhance survival and reduce fungal burden in mouse models of both disseminated and vaginal candidiasis. mAb C3.1 is thought to confer protection through rapid complement activation, leading to enhanced opsonization and phagocytic killing.

This study focused on comparing the original mouse parental C3.1 with three engineered formats — recombinant mouse IgG3, recombinant human IgG1, and a single-chain variable fragment (scFv) — to determine which format is most suitable for future therapeutic use in humans.

Recombinant mouse C3.1 IgG3 and human IgG1 were engineered to improve complement activation in humans while retaining epitope specificity. An scFv was also generated to define the minimal binding unit of C3.1. Enzyme-linked immunosorbent assay (ELISA) was used to compare the binding of all four formats to the β -1,2-mannotriose epitope. In addition, immunofluorescence assays (IFA) were performed to assess whole-cell binding and surface distribution in five medically important *Candida* species: *C. auris*, *C. albicans*, *C. tropicalis*, *C. glabrata*, and *C. parapsilosis*. All four formats bound β -1,2-mannotriose by ELISA and showed surface binding across all five species by IFA, with profiles comparable to the parental C3.1.

Findings from this study will identify the most effective format for future clinical use of mAb C3.1 in treating *Candida* infections.