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Poster abstract submission

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Poster title

Monoclonal antibodies targeting the fungal cell surface: next generation antifungal therapeutics

Poster abstract

Invasive fungal infections represent a critical unmet medical need, responsible for >2.5 million global deaths annually. There are several major challenges complicating the treatment of fungal infections. These include a concerning rise in antifungal drug resistance, the emergence of multidrug resistant species, drug toxicities and drug-drug interactions. In parallel there is an ever-increasing number of immunocompromised patients and those undergoing complex treatments, at high risk of invasive infections. Mortality rate associated with these infections is unacceptably high, >40% even with treatment. We leveraged our fungal cell wall expertise to identify novel, surface-exposed peptide targets that are more abundant in drug-resistant fungi and become upregulated in response to treatment with current antifungals. The peptides belong to cell wall proteins that are critical for cell wall remodelling and pathogenicity and are expressed during infection. The selected drug targets are required for cell wall robustness, Pga31 is pan-Candida and Utr2 is pan-fungal belonging to a chitin:glucan crosslinking enzyme family.

A panel of fully human monoclonal antibodies (mAbs) targeting these cell wall proteins are at late stage of preclinical development leading to candidate nomination. With strong affinity to their peptide targets , our mAbs have demonstrated recognition of clinically significant Candida species, including drug-resistant and drug-susceptible isolates of Candida albicans, C. auris, C. parapsilosis and C. tropicalis, as well as Aspergillus fumigatus. mAb binding was enhanced when cells were stressed with antifungal agents, caspofungin and fluconazole, due to increased expression of the mAb targets. There was preferential binding to the invasive hyphal morphology of C. albicans even without antifungal treatment. Enhanced antibody-mediated opsonisation was detected, the binding of antibodies significantly induced phagocytosis of fungal cells by murine J774.1 macrophages compared with controls. The mAbs have proven in vivo efficacy in clinically predictive murine invasive candidiasis models that represent the immunocompetent and immunosuppressed status of patients.

Novel approaches are desperately needed to tackle invasive fungal infections. There is huge potential for

unique, fungal-specific cell wall-targeting mAbs to improve clinical outcomes in complex patients and, either as monotherapy or co-therapy with existing antifungals.

Research topic

Biological therapeutics