



Uncovering the Secrets of Fungal Cell Wall Architecture

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Life-threatening fungal infections affect more than two million people worldwide but effective antifungal medications are very limited, thus resulting in high mortality. The fungal cell wall is a promising target for future antifungal drugs as it contains polysaccharides that are absent in humans. However, our knowledge of the fungal cell wall architecture remains ambiguous due to technical constraints of traditional experimental techniques.

Experiments on the high-field magnets at the MagLab provide unprecedented NMR resolution from a variety of polysaccharides and proteins (Figs. 1a,b). Magic Angle Spinning (MAS) Dynamic Nuclear Polarization (DNP) provides a 30-fold sensitivity enhancement (Fig. 1c), which enabled this collaboration to determine the spatial proximities between different biomacromolecules (Fig. 1d). This information on intermolecular packing, together with site-specific information on molecular hydration and dynamics, lead to a new structural model of the fungal cell wall that substantially differs from any preceding impressions of the structure of fungal cell walls.

The revised model will serve as the structural basis for designing better antifungal drugs that inhibit a broader spectrum of infectious fungi. The methods highlighted in this experiment can be widely applied to a variety of carbohydrate-rich biomaterials, such as the cell walls in plants, bacteria and algae.

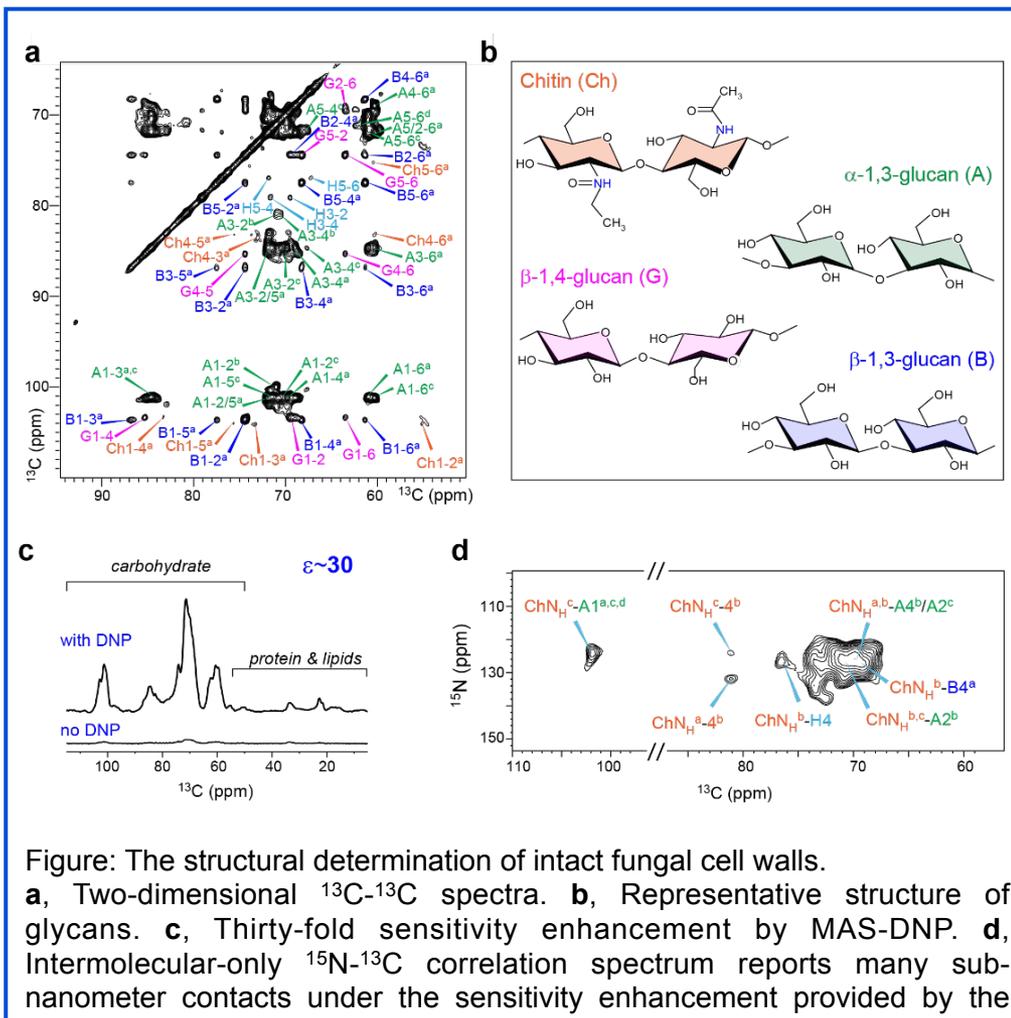


Figure: The structural determination of intact fungal cell walls. **a**, Two-dimensional ^{13}C - ^{13}C spectra. **b**, Representative structure of glycans. **c**, Thirty-fold sensitivity enhancement by MAS-DNP. **d**, Intermolecular-only ^{15}N - ^{13}C correlation spectrum reports many sub-nanometer contacts under the sensitivity enhancement provided by the

MagLab's MAS-DNP.

Facilities and instrumentation used: 800 MHz solid-state NMR and the 600 MHz/395 GHz DNP system at the MagLab's NMR facility.

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