Structure of fungal cell wall immune epitopes - the origins of immunity

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For a fungus, there may be nothing as biologically variable and highly regulated as the glycans in its cell wall. This makes the wall challenging to study, but worth the effort because of the potential to reveal novel targets for antifungal drugs and mechanisms that are important for immune recognition. But the outer cell wall is a moving target for efficient immune recognition because the chemistry of the surface is not fixed and responds and changes according to environmental conditions. How does immune recognition cope with this extreme biological variability?

We have used a variety of microscopic, forward and reverse genetic and immunological tools to generate a new spatially accurate model of the cell wall and to explore how dynamic changes in the wall influence immune surveillance. As a model system we have been exploring the immunology or mannan recognition in *Candida* species.

We have also demonstrated that immune relevant epitopes can be diffused or clustered, superficial or buried in the cell wall and they changed during batch culture and between different cellular morphologies. Unbiased screening of a haploid mutant library has revealed gene sets for both predicted (e.g. cell wall mannosylation) and novel processes that are important for the assembly of the cell wall immune epitope. This suggests that the C-type lectin immune receptors Mannose Receptor, DC-SIGN and Dectin-2 recognise different mannan species that are present on different components of the outer wall *N*-linked mannans. This work demonstrates recent advances that have generated a scaler and dynamic model of the cell wall that illuminates mechanisms of immune recognition and cell wall homeostasis.

Reference: Gow, N.A.R. & Lenardon, M.D. (2022). Architecture the dynamic fungal cell wall. *Nature Reviews Microbiology* https://doi.org/10.1038/s41579-022-00796-9. PMID 36266346