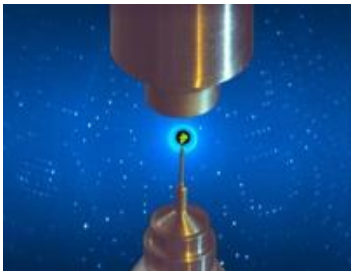

Contribution ID: **10** Type: **Poster**

Linking genes and membrane lipid composition to insights of the antifungal mechanism of Amphotericin B provided by neutron reflectometry

Wednesday 9 June 2021 13:40 (20 minutes)

Candida glabrata has been known as a non-pathogenic yeast found in healthy humans, but the number of infections caused by it has increased, making understanding its virulence an urgent task. In our multidisciplinary effort, we combine methods to produce *C. glabrata* strains with well-defined genetic modifications of virulence/resistance factors(1) with characterization of their membrane lipid composition and structure and interaction mechanism with the antifungal drug Amphotericin B (AmB). AmB, being a WHO essential medicine, has a broad spectrum and has been used against systemic fungal and parasitic infections. It is often a last line of defense, but despite its long track record, its mechanism of action and how resistance can evolve is not well understood. We use neutron reflection to study the AmB mechanism in model(2) and in membranes from *C. glabrata* strains with increased or decreased AmB resistance due to a defined change in gene expression. Hereby we have observed that resistance is related to increased AmB membrane insertion and decreased sterol extraction while high susceptibility to AmB correlates with a higher sterol extraction and lower insertion. Our integrative approach demonstrates how neutron techniques can provide insight into the molecular basis of antifungal activity and resistance with the aim to improve therapies, find better drugs and new drug targets.

1 Ishchuk et al. Front Microbiol, 2019. 10: 1679
2 Delhom et al. Nanomaterials, 2020. 10(12)

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