Microbial and inter-kingdom interactions: how extracellular vesicles from *Candida* and *Cryptococcus* induce specific responses

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Extracellular vesicles (EVs) play a crucial role in fungal cell communication and in modulating the host immune system. Understanding their involvement in fungal virulence could uncover novel targets for treating fungal infections. In this study, we investigated the role of EVs in both intra- and interspecies communication among fungi from the genera *Candida* and *Cryptococcus*. We cultured *Candida albicans, Candida auris, Cryptococcus neoformans,* and *Cryptococcus gatti* to isolate and characterize their EVs using Nanoparticle Tracking Analysis, Zeta potential measurements, and Transmission Electron Microscopy. To verify EVs internalization, we labeled them with Vibrant Dil® and incubated them with fungal cells. We introduced EVs from *C. albicans* and *C. auris* into *C. albicans* biofilms to assess their impact on biofilm adhesion, dispersion, and antifungal susceptibility. Additionally, we used EVs from *C. neoformans* and *C. gattii* to evaluate the transfer of the key virulence factor glucuronoxylomannan (GXM) to a non-encapsulated *C. neoformans* mutant strain (*Cap67*Δ). We also investigated the immunomodulatory effects of fungal EVs on THP-1 human macrophages by analyzing cell viability, performing qPCR, and conducting ELISA assays. Our results indicate that EV internalization can enhance biofilm formation and increase antifungal drug tolerance. Furthermore, we found that fungal EVs exert significant immunostimulatory effects, prompting human macrophages to produce

predominantly pro-inflammatory cytokines and the upregulation of genes associated with the immune response.

POSTER PRESENTATION TO BE JUDGED FOR THE STUDENT AWARDS

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