Characterisation of key bio-nano interactions between organosilica nanoparticles and *Candida albicans*

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Candida albicans (*C. albicans*), a commensal microorganism in healthy individuals, is capable of causing life-threatening infections in immunocompromised patients. Known as the fourth most common hospitable-acquired pathogen, many of these infections are caused by drug-resistant biofilms on implantable devices such as a catheter, which are difficult to treat and diagnose [1, 2]. Mortality rates from systemic infections are between 10-47% despite the availability of antimicrobial therapy and current diagnostic measures [3]. Hence, novel materials need to be explored for the development of new therapeutic, diagnostic or theranostic tools in an effort to combat nosocomial infections caused by *C. albicans*.

Fundamental interactions between mammalian cells and silica nanoparticles focusing on cytotoxicity, cell association and imaging have been investigated for applications such as drug delivery, diagnostics and imaging [4]. While it is widely accepted that a range of inorganic nanoparticles including silver, gold and zinc oxide are inherently cytotoxic to microbial cells [5], the bio-nano interactions between silica nanoparticles and pathogenic fungi have not been well characterised.

In this study, we investigated the interactions between *C. albicans* and organosilica nanoparticles, which are highly tuneable and coated with the antifouling polymer, PEG, to provide an additional functional handle for drug conjugation. We found that size and PEGylation of the nanoparticles had minimal effect on the growth and viability of *C. albicans*. Yet, association between the nanoparticles and the pathogen was found to be size and concentration-dependent. We then employed a whole blood assay to further study how PEGylated organosilica nanoparticles of different sizes and concentrations associate with human immune cells, which are the first cell types nanomaterials are likely to encounter *in vivo* or during an infection. This provided us with an insight into the likely behaviour of the nanoparticles *in vivo*. Lastly, we attached the clinically relevant drug, caspofungin, on the surface of PEGylated nanoparticles to switch the surface interactions between *C. albicans* and organosilica nanoparticles from benign to antifungal, without impacting the viability of primary human neutrophils. Our results illuminate how organosilica nanomaterials could be used as scaffolds for designing biomaterials for detecting or preventing *C. albicans* infections.

References

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Figures

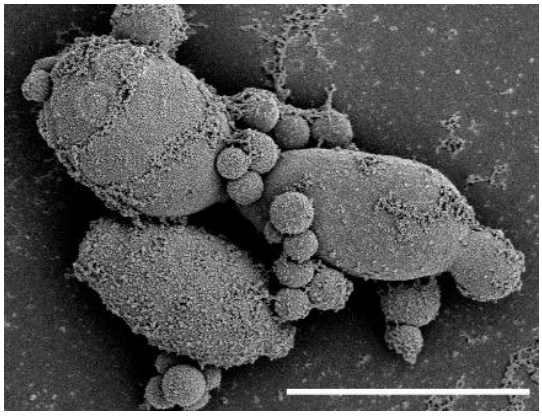

Figure 1. SEM image of ~800 nm PEGylated organosilica nanoparticles associating with *C. albicans*. Scale bar represents 5µm.