Rational design of an antifungal polyacrylamide library with reduced host-cell toxicity.

Schaefer S, Pham TTP, Brunke S, Hube B, Jung K, Lenardon MD, Boyer C (2021) Rational design of an antifungal polyacrylamide library with reduced host-cell toxicity. *ACS Appl Mater Interfaces* 13(23), 27430-27444.

Abstract

Life-threatening invasive fungal infections represent an urgent threat to human health worldwide. The limited set of antifungal drugs has critical constraints such as resistance development and/or adverse side effects. One approach to overcome these limitations is to mimic naturally occurring antifungal peptides called defensins. Inspired by their advantageous amphiphilic properties, a library of 35 synthetic, linear, ternary polyacrylamides was prepared by controlled/living radical polymerization. The effect of the degree of polymerization (20, 40, and 100) and varying hydrophobic functionalities (branched, linear, cyclic, or aromatic differing in their number of carbons) on their antifungal activity was investigated. Short copolymers with a calculated log P of ~1.5 revealed optimal activity against the major human fungal pathogen Candida albicans and other pathogenic fungal species with limited toxicity to mammalian host cells (red blood cells and fibroblasts). Remarkably, selected copolymers outperformed the commercial antifungal drug amphotericin B, with respect to the therapeutic index, highlighting their potential as novel antifungal compounds.

Involved units

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