Highly branched poly(N-*iso*propyl acrylamide) responsive to fungi

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Fungal diseases are a growing problem in the tropics and can be fatal for patients with supressed immune systems. Treatment often requires the use of relatively toxic drugs such as amphotericin B. Therefore, increasing the efficacy of this and similar drugs addresses a significant need. On the otherhand detection of fungal infections and differentiation from bacteria is a key goal in the fight against antimicrobial resistance. Here we describe a branched polymer with amphotericin end groups. We show how the polymer binds to its usual target, ergosterol, and retains antifungal activity. The polymer responds to the binding of the target by desolvation of polymer chain segments and we report early indications of increased activity against some strains of fungi. The MIC against two strains of *Candid albicans* were 1.23 (SC5314) and 1.0 (ATCC90028) µmol of amphotericin mL^{-1} compared to MICs against the same strains of 0.48 amd 4.76 µmol of amphotericin mL^{-1} for amphotericin B not attached to the polymer. The action of the polymer against fungi is in contrast to our previously reported work on similar polymers, which respond to bacteria (by desolvation) but did not kill the organisms. We tentatively propose that the maintenance of the efficacy is associated with increasing local concentration of the amphotercin ligands and the potential for the desolvated globule to disrupt the cell membrane. Importantly the polymer showed no toxic effects to corneal epithelial cells even at concentrations as high as 5 mg ml^{-1}. In contrast amphotericin B was toxic at and above 10 µg ml^{-1}.

Improved and faster diagnosis can inform treatment and negate strategies such as polypharmacy.

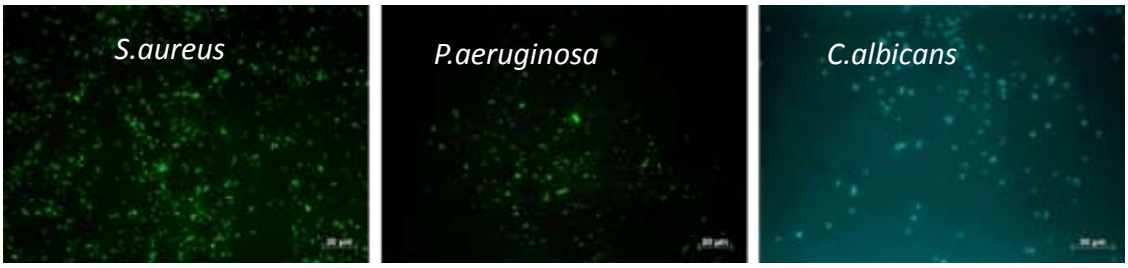

Figure 1 Bacteria and fungi attached to hydrogel functionalzed with H-PNIPAM carrying ligands each class of organism

We have, therefore, developed a diagnostic device that carries three HB-PNIPAM polymers functionalized with ligands for Gram-negative, Gram-positive or fungal infections. Each of these polymers is attached to a methacrylic hydrogel membrane. These three classes of organism can then be attached the membrane as shown in Figure 1. Importantly in this immobilized format the amphotericin HB-PNIPAM does not kill fungi. The device has been sown to be effective for sampling infections in *in vivo.*