Dectin-3-targeted antifungal liposomes efficiently bind and kill diverse fungal pathogens

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Abstract

DectiSomes are anti-infective drug-loaded liposomes targeted to pathogenic cells by pathogen receptors including the Dectins. We have previously used C-type lectin (CTL) pathogen receptors Dectin-1, Dectin-2, and DC-SIGN to target DectiSomes to the extracellular oligoglycans surrounding diverse pathogenic fungi and kill them. Dectin-3 (a.k.a. MCL, *CLEC4D*) is a CTL pathogen receptor whose known cognate ligands are partly distinct from other CTLs. We expressed and purified a truncated Dectin-3 polypeptide (DEC3) comprised of its carbohydrate recognition domain and stalk region. We prepared amphotericin B (AmB)-loaded pegylated liposomes (AmB-LLs) and coated them with this isoform of Dectin-3 (DEC3-AmB-LLs), and we prepared control liposomes coated with Bovine Serum Albumin (BSA-AmB-LLs). DEC3-AmB-LLs bound to the exopolysaccharide matrices of *Candida albicans*, *Rhizopus delemar* (f.k.a. *R. oryzae*), and *Cryptococcus neoformans* from one to several orders of magnitude more strongly than untargeted AmB-LLs or BSA-AmB-LLs. The data from our quantitative fluorescent binding assays were standardized using a CellProfiler program, AreaPipe, that was developed for this purpose. Consistent with enhanced binding, DEC3-AmB-LLs inhibited and/or killed *C. albicans* and *R. delemar* more efficiently than control liposomes, which significantly reduced the effective dose of AmB. In conclusion, Dectin-3 targeting has the potential to advance our goal of building pan-antifungal DectiSomes.

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