

## Use of Toxin-Specific Single Domain Antibodies to Treat C. difficile Infections

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#### Technology description

Clostridium difficile is a gastrointestinal pathogen that is a leading cause of hospital-related infections in developed nations. It is responsible for C. difficile-associated disease (CDAD) in humans, with symptoms ranging in severity from mild cases of antibiotic associated diarrhea to fatal colitis. The recent emergence of hypervirulent, antibioticresistant, C. difficile strains with increased morbidity, mortality and recurrence rates have warranted the development of novel, non-antibiotic, treatment regimes. The development of antibodies targeting virulence factors - such as bacterial toxins - would help reduce the selection pressure that antibiotics place upon pathogensand also be useful to control the infection' s recurrence. Clostridium difficile is a Gram-positive pathogen that produces two primary virulence factors, enterotoxins A and B, which are responsible for CDAD. Monoclonal antibodies specific for toxin A and toxin B have been shown to effectively treat CDAD and prevent disease relapse in animal models and in humans. A superior alternative to monoclonal antibodies for antitoxin immunotherapy is to use variable heavy-chain single-domain antibodies (VHHs) isolated from Camelidaespecies. These VHHs maintain many characteristics of conventional mAbs, including high target affinity and specificity, with the added advantages of small size (~15 kDa), easy genetic manipulation, amenable to library screening and selection, inherent thermal and proteolytic stability, and high-yield, low-cost recombinant production in bacteria, yeasts, plants, and mammalian cells. In particular, toxin-specific VHHs engineered to resist theacidic pH and proteases of the gastrointestinal tract would make these VHHs efficacious oral therapeutics.

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