A privileged lead series of orally active, GI-restricted compounds for the treatment of Gram-positive infections of the colon such as *C. difficile* infections.

- Potent MIC activity (low µg/ml) with small molecule lead series having “first-in-class” potential
- Anti-sporulation activity to prevent re-infection
- Fast time-to-kill
- Acting in the colon – low intestinal permeability
- Active against epidemic strain
- Simple structure – low COGS
- In vivo studies underway

**THE CHALLENGE**

*Clostridium difficile* is a Gram-positive, anaerobic, spore-forming bacterium that is one of the most common causes of infectious diarrhea in hospital patients worldwide. Infection by *C. difficile* can result in a disease state referred to as *Clostridium difficile* infection (CDI), which may present as mild to severe diarrhoea that can lead to potentially fatal complications such as toxic mega-colon and pseudomembranous colitis. *C. difficile* has been declared as an urgent threat to public health by the US Centers for Disease Control and Prevention. Changes in CDI epidemiology have been driven by the emergence of epidemic strains with novel virulence factors and antibiotic resistance. In 2015, it was reported that there were nearly 500,000 CDIs in the US alone, with ~20% recurrence and 30,000 associated deaths each year.

Current treatment options for CDIs are becoming increasingly restricted. Metronidazole (MTZ) has limited concentrations at the required site of action (colon), due to high systemic availability, and its effectiveness is limited. The GI-restricted vancomycin (VAN), while effective, has detrimental effects against intestinal microflora and is expensive to produce. Both drugs are associated with significant recurrence of infection, and resistance is also an issue.

**THE TECHNOLOGY**

Researchers at Monash Institute of Pharmaceutical Sciences (MIPS) led by Prof. Jonathan Baell in collaboration with Dr Glen Carter at the Peter Doherty Institute have developed a series of novel molecules with potent and rapid-acting (MIC low µg/ml) activity against *C. difficile*. These molecules are designed specifically to reach the colon in high concentrations to impart oral efficacy. In addition, they have demonstrated activity against *E. faecium*, another important pathogen that colonises the gut under dysbiotic conditions.

Importantly, these compounds have also demonstrated potent anti-sporulation activity against an epidemic NAP1/027 *C. difficile* isolate. This finding is of utmost importance, since very few *C. difficile* therapeutics display any sporulation inhibitory activity.

Initial Caco-2 studies have indicated that this series is impermeable to the intestine, supporting the potential for high colon concentrations, the desired site of action. Selected compounds are currently being evaluated in vivo in the gold standard hamster CDI model.

**Intellectual Property**: Provisional patent application relating top new compositions - in draft.

**Reference**


**THE OPPORTUNITY**

Monash is seeking a partner to advance this lead series to lead candidate. MIPS researchers and colleagues have strengths in medicinal chemistry, activity studies and preclinical profiling. The ideal partner will be able to take this technology through clinical studies.

**CONTACT US**

Monash Innovation
P: +61 3 9905 9910
E: innovation@monash.edu