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Functional characterization of a putative Type IV pilus gene cluster in *Clostridium difficile*

Yi-Tzu Lin and **I-Hsiu Huang**
National Cheng Kung University, Taiwan

Clostridium difficile is a Gram-positive anaerobic human pathogen capable of withstanding multiple antibiotics. C. difficile infections (CDIs) are the leading cause of antibiotic-associated diarrhea worldwide. *C. difficile* exerts its action through the production of two glycosylating toxins, Toxin A and Toxin B. Similar to many other pathogens, *C. difficile* has the ability to bind and colonize the intestinal epithelium, however little is known about cell surface proteins that contributes to its adherence. Genome analysis of multiple *C. difficile* strains revealed a putative Type IV pilus gene cluster. Type IV pilus (TFP) is a unique bacterial appendage that has been reported in many gram-negative bacteria to play an important role in motility, adherence and biofilm formation. In our study, we aim to characterize the role of TFP in *C. difficile* pathogenesis. Results indicated that the TFP gene cluster was expressed constitutively in two toxin-encoding strain of *C. difficile*. To further investigate the functionality of TFP in *C. difficile*, insertional mutations were made in pilA which encodes for putative pilin subunits of TFP and in pilT which encodes for a putative retraction ATPase associated with TFP disassembly. Interestingly, unlike previously reported in Clostridium perfringens, TFP in *C. difficile* did not appear to be involved in twitching motility. We further demonstrated that TFP was expressed on the *C. difficile* surface and was involved in biofilm formation. Unexpectedly, preliminary animal studies indicated that *C. difficile* mutants lacking TFP was more virulent. We anticipate this study will reveal the function of TFP in *C. difficile* and provide alternative target for developing a rapid *C. difficile* detection method in the future.

Biography

Yi-Tzu Lin works at Department of Microbiology and Immunology, National Cheng Kung University, Taiwan.

beatrice1991930@hotmail.com

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