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Altered spore cortex impairs virulence in C. difficile

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Spores are produced by many organisms as the result of a survival mechanism, triggered under several types of adverse environmental conditions. They are multi-layered structures, composed of a compressed dehydrated inner core, surrounded by the inner membrane, a germ cell-wall, a peptidoglycan layer known as the cortex, an outer membrane, a proteinaceous external coat, and for some species the outermost layer called the exosporium. This study focuses on the spore cortex of *Clostridium difficile*, a Gram-positive spore-forming, toxin-producing anaerobic bacterium that can colonize the intestinal tracts of humans, considered as the leading cause of hospital and community-acquired antibiotic-associated diarrhea. Given the highly original structure described for the vegetative cell peptidoglycan of *C. difficile*, and notably the particularly high level of N-deacetylation and its impact on host-pathogen interactions, we focused on the cortex N-deacetylases, and especially the N-deacetylase responsible for muramic lactam synthesis in *C. difficile*. Moreover, given the central role of spores in the physiopathology of *C. difficile* infection, we also investigated the contribution of cortex structure in *C. difficile* virulence, presenting the first study connecting cortex structure and virulence. In this context, we provide the fine structure of *C. difficile* cortex and the characterization of *pdaA* as the N-deacetylase responsible for muramic lactams synthesis.