

Coordinated modulation of multiple processes through phase variation of a c-di-GMP phosphodiesterase in *Clostridioides difficile*

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The opportunistic nosocomial pathogen *Clostridioides difficile* exhibits phenotypic heterogeneity through phase variation, a stochastic, reversible process that modulates expression. In *C. difficile*, multiple sequences in the genome undergo inversion through site-specific recombination. One such loci lies upstream of *pdcb*, which encodes phosphodiesterases (PDEs) that degrade the signaling molecule c-di-GMP. Expression of *pdcb* has been shown to be heterogeneous and the orientation of the invertible sequence, or 'pdcb switch', determines expression. In this study, we aimed to identify the full mechanism of *pdcb* regulation. The *pdcb* switch contains a promoter that when properly oriented promotes *pdcb* expression. Expression is augmented by an additional promoter upstream of the *pdcb* switch. Additionally, an element near the left invertible repeat of the invertible element modulates transcription from the upstream promoter. Overall, complex transcriptional regulation takes place to control the phase variation of *pdcb* and further work is needed to investigate the mechanisms behind expression.