Transcription analysis of the genes tcdA-E of the pathogenicity locus of Clostridium difficile

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To analyse the transcription pattern of the five tcdA-E genes of the pathogenicity locus (PaLoc) of Clostridium difficile a protocol was established to purify RNA from strain VPI10463. Transcription analysis of the five tcdA-E genes showed that they were all transcribed. In the early exponential phase, a high level of tcdC and low levels of tcdA,B,D,E transcripts were detectable; this was inverted in the stationary phase, suggesting that TcdC might have a negative influence on transcription of the other genes. Three transcription initiation sites, one for tcdA and two for tcdB were determined by primer extension analysis. Readthrough transcripts from outside the locus were not obtainable, so that parts of the transcription of tcdD, tcdB, tcdA and tcdC must occur by monocistronic transcription. Within the locus all possible intergenic readthrough transcripts were detectable except that between tcdC and tcdA, a stretch of DNA interrupted by a functional transcription terminator. Thus we found mono- and polycistronic transcription of tcdA and tcdB to occur which should lead to production of a surplus of tcdA over tcdB transcripts. This would explain the surplus of TcdA over TcdB expression observed in vitro. Due to its basic nature and similarity to BcnA of Clostridium perfringens and to Orf-22 of Clostridium botulinum, TcdD is most probably a regulatory protein with DNA-binding properties. On the basis of the presented study we discuss a model for the growth-phase-related, coordinate regulation of toxin expression wherein tcdC has a negative and tcdD a positive regulatory function on transcription of the tcdD,B,E and tcdA genes.

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