

Homonucleotide stretches in chromosomal DNA of *Campylobacter jejuni* display high frequency polymorphism as detected by direct PCR analysis

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Abstract

Homopolymeric nucleotide tracts have been previously identified in the genome sequence of *Campylobacter jejuni* 11168 [Parkhill et al., Nature 403 (2000) 665–668]. These tracts are believed to regulate contingency genes but as yet no phenotypic variation has been identified associated with many of these genes. To investigate homopolymeric tracts for genes for which there is no observable phenotype, a method was designed to visualise profiles of the various tract lengths directly at the genomic level by means of PCR and denatured polyacrylamide gel electrophoresis. Six of the seven contingency genes investigated displayed variation in the length of the respective homonucleotide tracts. Surprisingly, each contingency gene gave a typical peak profile that represented a conserved size distribution of polymorphic forms. For each gene studied, peak profiles were conserved between strains of *C. jejuni*. Duplicated genes, containing homonucleotide stretches, displayed locus-specific peak distributions for each gene copy. Contingency genes were polymorphic within single colonies, and the observed complex peak profiles suggested a frequency of slippage several orders of magnitude higher than reported for other organisms. No G7 (or C7) stretch was ever observed, and their absence from the complete genome suggests strong selection against their presence. In view of the predictable outcome of the process leading to these polymorphisms, it is hypothesised that the formation and/or selection of these tracts is not a random process, but is driven by as yet unknown mechanism(s). High-frequency polymorphism of these genes may be a mechanism by which *C. jejuni* survives selection bottlenecks between opportunities for growth within a host. © 2002 Published by Elsevier Science B.V. on behalf of the Federation of European Microbiological Societies.

Keywords: Contingency gene; Homopolymorphic repeat; Phase-variable gene

1. Introduction

Campylobacter jejuni is a major cause of human acute bacterial enteritis worldwide [1]. This pathogen also colonises the gastrointestinal tracts of a wide variety of domestic and wild animals and birds. Contaminated meat products are considered a major source of human infection. To survive a wide range of habitats, campylobacters must

have evolved mechanisms to respond to various environmental stresses.

Several bacterial species use binary switches (phase variation) of gene expression mediated by changes in polymeric DNA repeat sequences [2,3]. Their single units may consist of up to seven nucleotides and are repeated in variable numbers, or, in the case of homonucleotide tracks, comprise runs of a single nucleotide. Variation in the number of repeat units, present within or upstream of a gene, results in variable expression of so-called contingency genes. Such variation is introduced by slippage during replication, and phenotypic selection can result in adaptation for best-fit survival as an alternative to transcriptional regulation. In most recognised cases, contingency genes result in antigenic or phase variation to escape

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