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***B. fragilis* sequence:**
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BACTERIAL PATHOGENESIS

Bacteroides inverts for success

A DNA invertase that can modulate gene expression at multiple loci scattered throughout the genome has been identified in the human commensal bacterium *Bacteroides fragilis*.

B. fragilis encodes eight known extracellular polysaccharides (PSA–PSH). The genes encoding seven of these polysaccharides can be switched on and off by DNA inversions in the promoter regions. This process, which alters the bacterial surface structure, is known as phase variation and is an important bacterial virulence factor. In *B. fragilis* this phase variation is controlled by a DNA invertase.

To identify putative DNA invertases, Coyne *et al*. made use of the publicly available genome sequence of the type strain *B. fragilis* NCTC9343. In prokaryotes, DNA invertases segregate into two evolutionarily distinct families of site-specific recombinases — tyrosine-specific recombinases (Tsrs) and serine site-specific recombinases (Ssrs). Sequence analysis revealed 28 Tsrs and two Ssrs with putative DNA invertase activity. Of these, nine Tsrs and only one Ssr were shown to be conserved in *B. fragilis*. A plasmid containing an invertible *B. fragilis* polysaccharide promoter (the PSA promoter) was used to detect which, if any, of the putative invertases were able to perform the inversion in a related *Bacteroides* species. Of the ten candidate proteins, only one — Ssr2 — was able to invert the *B. fragilis* promoter sequence.

To probe the function of Ssr2, allelic exchange was used to construct *ssr2* deletion mutants, and the inversion of the polysaccharide promoter regions was analysed. The deletion of *ssr2* 'locked' the seven invertible polysaccharide promoters in one conformation and if Ssr2 was added *in trans*, inversion was restored. This indicates that gene expression at all of the invertible polysaccharide biosynthesis loci can be controlled by Ssr2. This was confirmed when the plasmid assay was extended and Ssr2 was shown to act directly on all six remaining invertible polysaccharide promoters. Coyne *et al*. therefore changed the name of Ssr2 to Mpi, for multiple promoter invertase.

Analysis of the polysaccharide expression patterns in the *mpi* deletion mutants indicated that the regulation of polysaccharide expresssion is complex, and also indicated that Mpi can act both directly and indirectly. The effects of this newly identified invertase are not limited to extracellular polysaccharides. By using a consensus sequence from the inverted repeats flanking the polysaccharide promoters to search the *B. fragilis* genome sequence, six other potential target loci for Mpi were identified. Further analysis confirmed that these additional loci were definite sites of action for Mpi.

As well as being a component of the intestinal microflora, *B. fragilis* is frequently isolated from intra-abdominal abscesses. The Mpi protein affords *B. fragilis* economical yet highly flexible control over its surface structures, an attribute that could have contributed to the success of this bacterium's dual identity: a commensal inhabitant of the intestine on the one hand and opportunistic pathogen on the other.

Sheilagh Clarkson

References and links

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