The Type V secretion pathway: a premium source of virulence factors?

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recombination intermediate known as a double Holliday junction.

In this study, the synthetic double Holliday junction substrate was designed so that one DNA molecule was radiolabelled, enabling any changes to be measured by a change in electrophoretic mobility. Additionally, any crossing-over could be detected by following the fate of unique restriction sites on the DNA sequences flanking the double Holliday junction.

Intriguingly, the authors observed that BLM and hTOPIIIα together resolved the double Holliday junction, whereas neither BLM nor hTOPIIIα could achieve this alone. Furthermore, this always occurred without any crossing over of genetic material. This might help explain the high sister chromatid exchange frequency seen in Bloom's syndrome cells, as recombination intermediates might be processed aberrantly in the absence of BLM resulting in abnormally high levels of crossing over. These findings also suggest that suppression of crossing over during homologous recombination is important for maintenance of genomic stability and cancer prevention in normal cells.

2 Wu, L. and Hickson, I.D. (2003) The Bloom's syndrome helicase suppresses crossing over during homologous recombination. *Nature* 426, 870-874

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Live action telomeres

Telomeres, at the ends of eukaryotic chromosomes, consist of multiple tandem copies of the hexanucleotide, TTAGGG, together with a complex of associated proteins. These structures perform essential roles for the cell, including maintaining chromosome stability and regulating proliferative life span. In addition, they are responsible for silencing telomere-adjacent genes (by means of their localized heterochromatin structure) and are thought to influence specific chromosome positioning in the nucleus, through their firm attachments to the nuclear matrix. Despite this attachment, new research now reveals that some telomeres, at least, can be surprisingly mobile.

To study telomere movement, Molenaar *et al.* [3] have now established a method of visualizing telomeres in live cells. Using a fluorescent peptide-nucleic acid probe (PNA) the team targeted telomeric repeat sequences in human osteosarcoma cells and studied their motion over time. They observed three different modes of telomere movement. First, the majority of telomeres showed slow (average: 1.8 x 10^{-4} μmetre^2 per s) and constrained diffusion (radius of constraint 0.5 mm), as might be expected for matrix attached DNA. The second group, however, making up about 10% of telomeres, moved considerably faster (average: 5.8 x 10^{-4} μmetre^2 per s) and had a larger radius of confinement (1.2 mm). The third and smallest population moved faster still, with an average speed of 1.9 x 10^{-3} μmetre^2 per s and in the time period analysed had moved so far that a radius of constraint could not be calculated.

The authors suggest that the finding that some telomeres are relatively free from constraint might indicate their dissociation from the nuclear matrix. The authors further suggest that this dissociation might be coupled with transcriptional derepression of telomere-silenced genes. Both of these speculations, however, remain to be tested.

3 Molenaar, C. *et al.* (2003) Visualizing telomere dynamics in living mammalian cells using PNA probes. *EMBO J.* 22, 6631–6641

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Bacteriology

The type V secretion pathway: a premium source of virulence factors?

Since its discovery in the late 1980s, the family of secreted proteins termed the autotransporters has been expanding continuously to become the largest group of secreted proteins in Gram-negative bacteria. The type V secretion pathway, which includes the autotransporters, can be defined by secreted proteins that are: (i) translocated across the outer membrane via a transmembrane pore formed by a β-barrel; and (ii) contain all the information required for translocation through the cell envelope.

The autotransporters are restricted to the phylums Proteobacteria and *Chlamydiae*. By characterizing the polymorphic membrane protein PmpD from *Chlamydophila pneumoniae*, Wehrl *et al.* [5] demonstrate that it is a truly autotransporter protein. The neosynthetised PmpD is exported from the cytoplasm to the periplasmic space by the Sec apparatus with the concomittant cleavage of the N-terminal signal sequence. The C-terminal part of the protein then forms a β-barrel in the outer membrane allowing secretion of the N-terminal passenger domain outside the cell. It was hypothesized that the protein would interact with some components of the outer membrane.

All autotransporter proteins characterized thus far act as virulence factors. PmpD shares homology with some adhesins; this is supported by the presence of a highly repetitive tetra-amino acid motif involved in adhesion to membranes of different host cell types. Such a function is suggested experimentally by neutralizing chlamydial infectivity with anti-N-pmpD antibodies. However, this finding does not discriminate between an inhibition of binding and uptake/invasion, and a negative effect of bound antibodies on the course of chlamydial development after entry into the eukaryotic cell.

Although further work is needed to clarify this, the direct interaction of PmpD with the host cells and the subsequent mediation of immunostimulatory events demonstrate its role as a key virulence factor. From a therapeutic point of view, it demonstrates further that PmpD is an important target for anti-chlamydial vaccination.

5 Wehrl, W. *et al.* (2004) From the inside out - processing of the Chlamydial autotransporter PmpD and its role in bacterial adhesion and activation of human host cells. *Mol. Microbiol.* 51, 319–334

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