Susanne Harris

BACTERIAL PATHOGENESIS

Chlamydia gets a NUE look

Chlamydia trachomatis encodes a type III secretion system (T3SS), through which it secretes effectors into the host cell. Writing in PLoS Pathogens, Pennini *et al.* now show that one of the T3SS effectors produced by *C. trachomatis* is a histone methyltransferase that is targeted to the nucleus of the host cell.

Epigenetic regulation of gene expression in eukaryotic cells relies on a system of enzymes that control the post-translational modification of histones, leading to alterations in the overall chromatin structure. Several viral and bacterial pathogens co-opt host epigenetic regulatory mechanisms, either by interfering with the signalling pathways that regulate histone-modifying enzymes or by producing their own versions of these

enzymes. However, for most bacteria, little is known about the function of secreted effectors in general.

Analysis of the genome sequence of *C. trachomatis* revealed an ORF that is conserved among Chlamydiae and is predicted to encode a SET domain-containing histone methyltransferase. Consistent with this protein having a role as an effector, Pennini *et al.* found that the amino-terminal region was sufficient to direct T3SS-dependent export of a reporter protein in the heterologous host *Shigella flexneri*. In HeLa cells infected with *C. trachomatis*, the protein was secreted from the bacterium and then translocated into the nucleus, leading the authors to name the protein NUE (for 'nuclear effector'). Furthermore, a GFP-tagged

version of NUE was found in the chromatin-associated fractions of HeLa cell nuclear extracts. *In vitro* methyltransferase assays revealed that NUE could methylate histones H2B, H3 and H4 but had no activity towards the chlamydial histone H1-like protein Hc1.

These findings represent the first description of a bacterial effector that is targeted to the host cell nucleus and acts directly on mammalian histones. However, the host genes for which expression is altered by NUE remain to be identified.

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ORIGINAL RESEARCH PAPER Pennini, M. E., Perrinet, S., Dautry-Varsat, A. & Subtil, A. Histone methylation by NUE, a novel nuclear effector of the intracellular pathogen *Chlamydia trachomatis*. *PLoS Pathog.* **6**, e1000995 (2010)

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