BACTERIAL PATHOGENESIS

Channelling the host epigenome

“the *P. aeruginosa* T3SS translocon is a genuine effector that functions as a pore-forming toxin

The Gram-negative bacterium *Pseudomonas aeruginosa* causes clinically relevant infections, including pneumonia, urinary tract infections and wound infections. The bacterium uses a type III secretion system (T3SS) to inject effectors into host cells that manipulate cellular pathways. Previous reports suggested that bacteria, mostly intracellular bacteria, can affect the chromatin structure and the transcriptional programme of host cells, for example by inducing histone modifications. Here, Dortet *et al.* show that the T3SS of *P. aeruginosa* causes histone modifications in eukaryotic cells, independent of secreted effectors.

The authors first showed that HeLa cells or A549 epithelial lung cells that were infected with *P. aeruginosa* had decreased levels of phosphorylation of serine 10 of histone H3 compared with uninfected cells

2 hours post-infection. Moreover, a *P. aeruginosa* strain that lacked the T3SS did not induce significant dephosphorylation of serine 10 of histone H3, which suggests a role for the T3SS in the dephosphorylation of this residue.

The T3SS comprises an export apparatus, a basal body, a needle and a translocation pore (also known as the translocon), and it transports effector proteins that are injected into the target cells through the translocon. The authors examined which component induces the observed histone modification and found that the *P. aeruginosa* effectors ExoS, ExoT, ExoU and ExoY are not required for the T3SS-dependent dephosphorylation of serine 10 of histone H3. Instead, they showed that the PopB–PopD translocon causes dephosphorylation of the residue. PopB and PopD are secreted by the needle complex and form a membrane pore that delivers effector proteins across the host cell plasma membrane. The addition of the purified PopB–PopD translocon, but not purified PopB or PopD alone, induced dephosphorylation of serine 10, which suggests a direct role of the heterodimeric complex. Thus, in addition to forming a channel in the host membrane, the PopB–PopD translocon functions as a virulence factor that triggers the modification of histone H3.

Moreover, the PopB–PopD translocon was shown to induce K⁺ efflux and fragmentation of the mitochondrial network within 2 hours

post infection, an effect that was previously shown to be induced by cholesterol-dependent pore-forming toxins. On the basis of their observations, the authors propose that the T3SS of *P. aeruginosa* functions as a pore-forming toxin that subverts host cell functions independent of the presence of any T3SS effectors.

Finally, the authors showed that the PopB–PopD translocon remains anchored in the host membrane after the bacterium leaves the site of contact, and they propose two models whereby the PopB–PopD complex can either be released by the bacterium into the cellular milieu and become spontaneously inserted into the host membrane to form the pore, or the complex could be inserted directly by the T3SS during bacterial infection.

In summary, the data suggest that the *P. aeruginosa* T3SS translocon is a genuine effector that functions as a pore-forming toxin. Ion flux that is induced following pore formation leads to the modification of histone H3 and host cell subversion. Future studies will be required to elucidate the pathway that links K⁺ efflux and the modification of the host chromatin.

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ORIGINAL ARTICLE Dortet L. *et al.* Pore-forming activity of the *Pseudomonas aeruginosa* type III secretion system translocon alters the host epigenome. *Nat. Microbiol.* <http://dx.doi.org/10.1038/s41564-018-0109-7> (2018)

FURTHER READING Deng, W. *et al.* Assembly, structure, function and regulation of type III secretion systems. *Nat. Rev. Microbiol.* **15**, 323–337 (2017)