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Molecular mechanisms of phage MDAΦ entry in Neisseria meningitidis

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Background

Neisseria meningitidis is a commensal bacterium that colonizes the human nasopharyngeal mucosa. Under ill-defined circumstances, the bacterium crosses the nasopharyngeal barrier and spreads in the bloodstream. A filamentous phage, designated MDAΦ (Meningococcal Disease Associated), has been associated with invasive meningococcal diseases in young adults [1,2]. This phage can infect different meningococcal strains using their type IV pili (TFP) and hijacks the TFP secretin PilQ to be extruded without damaging the host [3]. Biofilm analysis revealed that colonization of epithelial cells by N. meningitidis promotes phage secretion, in place of TFP, maintaining bacteria-bacteria interactions and bacterial colonization of epithelial cells. This suggest that MDAΦ increase the occurrence of diseases by increasing bacterial colonization in the mucosa at the site-of-entry [4].

Aim/Methods

Here, our aim was to understand the molecular mechanism by which MDAΦ infects N. meningitidis. We focused on the first step of phage interaction with bacteria and examined the interplay between phage and TFP.

Results

Investigations with deletion mutants of genes involved in the TFP machinery have shown that phage entry requires a functional and retractable TFP. This result is consistent with the literature on Ff, Pf4, or CTXΦ phages that interact directly with the pili tip and require retractable pili for infection. However, we found no evidence here for the interaction of MDAΦ with the TFP tip. We therefore focused on the possible interaction between PilE, the major pilin forming the TFP fiber, and the phage capsid. Since PilE is subjected to antigenic variation, we evaluated the possibility that different variants of PilE allow different phage entry. We identified PilE variants associated with MDAΦ entry suggesting a direct interaction between PilE and phage particles. Then, we have shown that the purified TFP and MDAΦ form bundles together. Finally, structure prediction and analysis of the charged amino acids of TFP and those of MDAΦ capsid coat supported our hypothesis.

Conclusions

Together, our data support a new model of interaction between filamentous phages and type IV pili. [1] Bille, et al., JEM (2005) [2] Bille, et al., PLoS ONE (2008) [3] Meyer, et al., Microbiology (2016) [4] Bille, et al., PLOS Pathog. (2017)