Meningococcal disease: a paradigm of type-IV pilus dependent pathogenesis

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Neisseria meningitidis (meningococcus) is a cause of meningitis and of rapidly progressing fatal septic shock. A crucial step in the pathogenesis of invasive meningococcal diseases is the adhesion of bloodborne meningococci to both peripheral and brain endothelia, leading to major vascular dysfunctions.
Our team has developed interdisciplinary approaches to elucidate the intricate network of interactions and molecular strategies selected by this bacterial pathogen to colonize human peripheral and brain vasculature and get access to the brain. We have demonstrated that the capacity of *N. meningitidis* to bind to peripheral and brain endothelial cells relies on the interaction between their type IV pili (Tfp) and a complex formed by the endothelial cell receptor CD147 and the b2-adrenergic receptor. More recently, we have demonstrated that meningococcal Tfp recognize specific glycan determinants exposed on these host cell receptors. Using a humanized mouse model of infection, we have revealed that Tfp-mediated interaction with vascular wall provides a niche for bacterial replication, triggering purpuric lesions, sustained bacteraemia and mice lethality. Finally, we have identified compounds, previously used in human medicine, that induce the disassembly of type IV within minutes. In the humanized mice model, these compounds reduce meningococcal colonization of the human vessels, reduce vascular dysfunctions, intravascular coagulation and inflammation, and they improve mouse survival. Targeting Tfp thus appears as particularly promising strategy to reduce virulence and combat infection diseases.

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