

Publication

Bacterial persistence within erythrocytes: a unique pathogenic strategy of Bartonella spp

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Keywords Bartonella, arthropod vector, erythrocyte, cell invasion, persistence, type IV secretion The genus Bartonella comprises human-specific and zoonotic pathogens responsible for a wide range of clinical manifestations, including Carrion's disease, trench fever, cat scratch disease, bacillary angiomatosis and peliosis, endocarditis and bacteremia. These arthropod-borne pathogens typically parasitise erythrocytes in their mammalian reservoir host(s), resulting in a long-lasting haemotropic infection. We have studied the process of Bartonella erythrocyte parasitism by tracking green fluorescent proteinexpressing bacteria in the blood of experimentally infected animals. Following intravenous infection, bacteria colonise a yet enigmatic primary niche, from where they are seeded into the blood stream in regular intervals of approximately five days. Bacteria invade mature erythrocytes, replicate temporarily and persist in this unique intracellular niche for the remaining life span of the infected erythrocytes. A triggered antibody response typically results in an abrogation of bacteremia within 3 months of infection, likely by blocking new waves of bacterial invasion into erythrocytes. The recent establishment of genetic tools for Bartonella spp. permitted us to identify several putative pathogenicity determinants. Application of differential fluorescence induction technology resulted in the isolation of bacterial genes differentially expressed during infection in vitro and in vivo, including an unknown family of autotransporter proteins as well as a novel type IV secretion system homologous to the conjugation system of E. coli plasmid R388. Mutational analysis of a previously described type IV secretion system displaying homology to the virB locus of Agrobacterium tumefaciens provided the first example of an essential pathogenicity locus in Bartonella. Though required for establishing haemotropic infection, it remains to be demonstrated if this type IV secretion system is necessary for colonisation of the primary niche or for the subsequent colonisation of erythrocytes.

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