The Role of the st313-td Gene in Virulence of Salmonella Typhimurium ST313

Multidrug-resistant Salmonella enterica serovar Typhimurium ST313 has emerged in sub-Saharan Africa causing severe infections in humans. Therefore, it has been speculated that this specific sequence type, ST313, carries factors associated with increased pathogenicity. We assessed the role in virulence of a gene with a yet unknown function, st313-td, detected in ST313 through comparative genomics. Additionally, the structure of the genomic island ST313-GI, harbouring the gene was determined. The gene st313-td was cloned into wild type S. Typhimurium 4/74 (4/74-C) as well as knocked out in S. Typhimurium ST313 02-03/002 (Delta st313-td) followed by complementation (02-03/002-C). Delta st313-td was less virulent in mice following i.p. challenge than the wild type and this phenotype could be partly complemented in trans, indicating that st313td plays a role during systemic infection. The gene st313-td was shown not to affect invasion of cultured epithelial cells, while the absence of the gene significantly affects uptake and intracellular survival within macrophages. The gene st313-td was proven to be strongly associated to invasiveness, harboured by 92.5% of S. Typhimurium blood isolates (n = 82) and 100% of S. Dublin strains (n = 50) analysed. On the contrary, S. Typhimurium isolates of animal and food origin (n = 82) did not carry st313-td. Six human, non-blood isolates of S. Typhimurium from Belarus, China and Nepal harbouring the gene and belonged to sequence types ST98 and ST19. Our data showed a global presence of the st313-td gene and in other sequence types than ST313. The gene st313-td was shown to be expressed during logarithmic phase of growth in 14 selected Salmonella strains carrying the gene. This study reveals that st313-td plays a role in S. Typhimurium ST313 pathogenesis and adds another chapter to understanding of the virulence of S. Typhimurium and in particular of the emerging sequence type ST313.

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