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Assessment of host innate immunity in the pathogenesis of the hemolytic-uremic syndrome

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Abstract

Shiga toxins (Stx1 and Stx2) are a major pathogenic factor in enterohaemorrhagic Escherichia coli O157: H7 infections that cause haemolytic-uremic syndrome, a serious extraintestinal complication[1]. Shiga toxins consist of a a globotriaosylceramide (Gb(3))-binding B subunit pentamer and an enzymic A subunit[2]. The ability for Shiga toxins to bind to the surface of human neutrophils, a potential mediator for toxin translocation and HUS pathogenesis, has been the object of controversy. It is demonstrated in this study that Stx2 elicits a reproducible and consistent effect on isolated human neutrophils which do not express Gb3, confirming previous work that Stx2 binds in a non-classic mechanism to these cells. Stx2 induced a greater increase in the expression of a specific inflammatory profile than Stx1 alone, particularly in TNF-alpha expression ($P<0.05$, Student's t-test). Moreover, co-stimulating neutrophils with LPS appeared to nullify the Stx2 affect. In contrast, co-stimulating neutrophils with Stx1 and LPS appeared to increase the expression of IL-8 ($P<0.05$, Student's t-test). This observed activation of neutrophils and subsequent inflammatory profile provides a better understanding of the role of host innate immunity in the pathogenesis of HUS.

References

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