

Expression of bacterial flagellin, TLR5 and interleukin-22 are significantly associated with oral rotavirus vaccine take among south African infants

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Abstract

Background: Bacterial flagellin, a potent intestinal innate immune activator, has been shown to prevent and cure rotavirus infection in mice, independent of interferons. Its signalling occurs via Toll-like receptor (TLR5) and Nod-like receptor C4 (NLRC4) whose activation elicit the production of interleukins 22 (IL-22) and IL-18, respectively. Changes in abundance of flagella-producing bacteria in the gut may influence the luminal concentration of flagellin, thereby altering the threshold of intestinal immune activation. Here, we assessed whether a high abundance of flagellin at the time of vaccination would negatively affect the oral Rotavirus (RV) vaccine take.

Methodology: Stool and saliva specimen were collected from infants attending a routine rotavirus immunization programme at a healthcare clinic, in Brits, north of Pretoria. Stool samples were divided into vaccine shedders ($n = 50$) and non-vaccine shedders ($n = 44$) based on the shedding of the vaccine virus. Quantitative real-time PCR was used to determine both the abundance of bacterial flagellin in stool DNA samples and expression of TLR5, NLRC4, IL-22 and IL-18 encoding genes between the two study groups.

Results: There were no significant differences in the abundance of bacterial flagellin between vaccine shedders and non-shedders ($p = 0.15$). However, the expression of flagellin-encoding *fliC* was increased 7.5-fold in non-shedders compared to shedders, $p = 0.001$. Similarly, TLR5 ($p = 0.045$), and IL-22 ($p = 0.054$) were significantly expressed in non-shedders versus shedders. The expression of NLRC4 ($p = 0.507$,) and IL-18 dependent NLRC4 ($p = 0.650$), were, on the other hand, not different between the two study groups.

Conclusion: Collectively, our observations suggest a possible negative impact of the abundance of viable flagellated bacteria at the time of vaccination on the replication and therefore the performance of oral RV vaccines.