

Rotavirus vaccine shedding is associated with increased frequency of circulating T follicular helper and T helper 2 cells in Malawian infants

Chikondi A. Malamba^{1,2,3}, Esther Thaulo¹, Jonathan Mandolo^{1,2}, Chimwemwe Mhango¹, Immaculate Mhango¹, Prisca Benedicto^{1,2,3}, Leonard Mvaya¹, Miren Iturriza-Gomara², Kondwani C. Jambo^{1,2,4},
Khuzwayo C. Jere^{1,2,3}

¹Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Blantyre, Malawi, ²University of Malawi, College of Medicine, Blantyre, Malawi, ³University of Liverpool, UK, ⁴Liverpool School of Tropical Medicine, UK

Background

Rotavirus causes severe gastroenteritis amongst infants and young children. Malawi introduced Rotarix rotavirus vaccine (RV1) in 2012, but its effectiveness is lower compared to developed countries. RV1 replication is thought to be an important step in induction of rotavirus-specific neutralising antibodies. Induction of these high affinity neutralising antibodies is dependent on CD4⁺ T cell help provided by T follicular helper (Tfh) and T helper 2 (Th2) cells. We investigated whether RV1 shedding is associated with induction of circulating Tfh and Th2 cells in Malawian vaccinated infants.

Methods

Peripheral blood and stool samples were collected at week 6 (before vaccination) and week 14 of age (4 weeks post-second dose). Flow cytometry-based immunophenotyping was used to characterize T-cell subsets in peripheral blood samples. Rotavirus-specific VP6 quantitative Real-Time Polymerase Chain Reaction (qRT-PCR) and Rotarix-specific NSP2 RT-PCR assays were used to measure vaccine shedding in stool samples, a surrogate of vaccine replication.

Results

The frequency of cTfh and Th2 cells was similar between vaccine shedders ($n=8$) and non-shedders ($n=7$), before RV1 vaccination (cTfh 0.59 vs. 0.37, $p=0.17$; Th2 0.5 vs. 0.4, $p=0.78$). However, four weeks post-second dose, the frequency of cTfh and Th2 cells was higher in vaccine shedders than non-shedders (cTfh 1.7 vs. 0.84, $p=0.01$; Th2 0.84 vs. 0.14, $p=0.04$). In contrast, the frequency of Th1 cells was similar in vaccine shedders compared to non-shedders, before and after vaccination (all $p>0.05$).

Conclusion

Our findings show higher frequencies of cTfh and Th2 in vaccine shedders compared to non-shedders following RV1 vaccination in Malawian infants. These findings support the critical role of vaccine replication as an important driver for inducing robust cellular immunity. Further ongoing work will characterise phenotype and functional capacity of RV1-specific T cells in Malawian infants.