

IMPACT OF MYELOID DERIVED SUPPRESSOR CELLS ON ANTIBODY RESPONSES TO VACCINE STIMULATIONS IN INFANTS

*Elvis Kidzeru^{1,7,8}, *Ana Gervassi², Nicholas Lejarcegui², Enock Havyarimana¹, Sandra Dross^{2,3}, Grace Itaya², Kevin Urdahl², Soren Gantt⁴, **Helen Horton^{2,3,6}, **Heather Jaspan^{1,3,5}

¹ Division of Immunology, Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa

² Seattle Biomedical Research Institute, Seattle, Washington, United States of America (USA)

³ University of Washington Department of Global Health, Seattle, Washington, USA

⁴ University of British Columbia Department of Paediatrics and Child and Family Research Institute, Vancouver, Canada

⁵ University of Washington, Seattle Children's Hospital, Seattle, Washington, USA

⁶ Janssen Pharmaceutical, Department of Infectious Diseases, Beerse, Belgium

⁷ Department of Radiation Oncology, University of Cape Town/ Groote Schuur Hospital, Cape Town, South Africa

⁸ Centre for Medical Research, Institute of Medical Research and Medical Plant Studies, Ministry of Scientific Research and Innovation, Yaoundé, Cameroon

*, ** contributed equally

Background

Vaccination is no news till date, the most successful public health and cost-effective way of combatting infectious diseases that cause morbidity and mortality in children in the first few years of life. Young infants respond poorly to vaccines, but cause of reduced immunity is not clear. We hypothesized that myeloid-derived suppressor cells (MDSC) that might be induced during gestation, would suppress infant's antibody-immune responses.

We evaluated the impact of MDSC on infant-specific antibody responses to Hepatitis B (Hep B), Tetanus toxoid (TT), *Bordetella pertussis* (BP), and *Haemophilus influenzae* type b (Hib) antigens in South African infants.

Methods

In -80°C stored plasma samples, we measured antibody-specific levels of Hep B, TT, BP and Hib responses using ELISA. MDSC frequencies were quantified using multiparameter flow cytometry in whole PBMC.

Results

At birth (n=21), infants had low levels of specific antibodies than at 6 months (n=32) post immunization to Hep B (0.6898 [interquartile range {IQR}, 0-1.175] mIU/mL, vs 16.12 [IQR, 0-62.75] mIU/mL; p=0.0060), TT (0.1138 [IQR, 0.0423-0.2245] IU/mL, vs 1.663 [IQR, 0.9980-2.910] IU/mL; p<0.0001), BP (20.98 [IQR, 12.35-45.19] IU/mL, vs 109.9 [IQR, 87.12-149.6] IU/mL; p<0.0001), Hib (0.2098 [IQR, 0.0305-0.9352] mg/L, vs 2.680 [IQR, 0.8962-6.151] mg/L; p=0.0087). Level of antibodies were significantly higher at 14 weeks (n=32) than at birth to TT (0.1138 [IQR, 0.0423-0.2245] IU/mL, vs 2.142 [IQR, 0.5106-3.303] IU/mL; p<0.0001) and BP (20.98 [IQR, 12.35-45.19] IU/mL, vs 104.0 [IQR, 70.86-133.1] IU/mL; p<0.0001), but not for Hep B and Hib between birth and 14 weeks. At birth, HIV-exposed uninfected (HEU) infants had lower Hib specific antibody levels than unexposed (HU) infants (0.1260 [IQR, 0-0.2923] mg/L, vs 0.6965 [IQR, 0.1340-12.96] mg/L; p=0.0256), but not to other antigens. There was no correlation between specific antibody responses in infants and MDSC frequency measured either at the time at which responses were measured or time at which the first vaccine dose was administered for all the antigens (6 weeks).

Conclusion

Antigen-specific antibody responses increased with time post vaccination as MDSC frequency dropped immediately by 6 weeks after birth reflecting the lack of correlation between antibody responses and MDSC frequency. Therefore, MDSC had little effect on vaccine specific antibody responses.