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Kinetics of myeloid derived suppressor cells (MDSC) and their effect on vaccine-specific responses during the first year of life

Ana Gervassi[1], Elvis Kidzeru[3], Leesa Kim[1] Soren Gantt[4], Heather Jaspan[2, 3] and **Helen Horton[5]**
[1]Center for Infectious Disease Research, USA
[2]Seattle Children's Hospital, USA
[3]University of Cape Town, South Africa
[4]University of British Columbia, Canada
[5]Janssen Pharmaceuticals, Belgium

MDSC are a heterogeneous population of immature myeloid cells with suppressive function. MDSC are normally present at low frequency in healthy individuals but their frequencies increase in settings of persistent inflammation, such as chronic infection, autoimmunity and malignancy. MDSC suppress T cell activation and have been shown to decrease efficacy of dendritic cell vaccines. MDSC have also been shown to skew immunity to a Th2 response, which is a well-known characteristic of the infant immune response. We have demonstrated that healthy neonates possess increased frequencies of granulocytic-MDSC. These neonatal G-MDSC suppress both CD4+ and CD8+ T cell proliferative responses, decrease T cell IFN- cytokine production and inhibit NK cell cytotoxicity in a contact-dependent manner. Their ability to suppress immune responses is STAT-3 dependent. In order to evaluate if MDSC reduce vaccine-specific responses during the first year of life, we have been conducting a longitudinal study in Khayelitsha, Western Cape Province, South Africa since March 2013. Ninety-one mother-infant pairs have been enrolled in the study. T-cell and B-cell vaccine-specific responses were measured at birth, 6, 10, 14- weeks of age, and 6, 9, 12- months of age and will be correlated to the frequencies of MDSC at the time of vaccination. At birth, MDSC frequencies were significantly higher compared to other time points, but rapidly decreased to healthy adult levels by 6-weeks of age. There was a trend towards increased MDSC frequency in HIV-exposed infants and a significantly higher MDSC frequency in HIV+ mothers compared to their uninfected counterparts at one year postpartum, but not at delivery. Neonates and young children are known to respond poorly to infection and sub-optimally to most vaccines. The immunologic mechanisms involved in these sub-optimal responses have only begun to be elucidated and the ability to understand these mechanisms will form the basis for the development of adjuvants specifically designed for infant vaccines and for therapeutic interventions after infection.

Biography

Ana Gervassi completed her MSc and PhD at the University of Washington and her Post-doctoral studies at Seattle Biomedical Research Institute. She is a Staff Scientist at the Center for Infectious Disease Research in Seattle, WA. Her research interests are focused on immune regulation of both vaccine responses as well as during chronic viral infections. She has a broad experience in antigen discovery, T cell immunology, and development of assays to measure T cell responses (e.g. multi-parameter flow cytometry and functional immunoassays). Additionally, she has developed assays to measure specific T cell responses to vaccine antigens, in *vitro* prime CD8+ T cells for antigen discovery. Currently, she is most interested in understanding the immune regulatory mechanisms that lead to poor immune responses and T cell exhaustion.

ana.gervassi@cidresearch.org

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