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View Abstract

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TITLE: BCG INDUCES GESTATIONAL AGE-INDEPENDENT INNATE IMMUNE STIMULATION IN NEONATES: A VALIDATION OF FUNCTIONAL IMMUNOLOGIC BATTERY WITH SMALL VOLUME BLOOD (SVB) SAMPLING

PRESENTATION TYPE: Oral or Poster

PREFERRED TOPIC: Immunology/Inflammation

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ABSTRACT BODY:

Introduction: Despite its significance as a leading cause of infant mortality, improving outcomes in neonatal sepsis has lagged behind adults. While increased infectious susceptibility in early life may be partly due to a tolerogenic immune phenotype, investigations of neonatal immune function are largely understudied. For preterm infants, the limitations caused by low blood volume (80-100mL in a typical 1000 gram neonate) have largely contributed to the paucity of research on their immune function. This study aims to 1) establish a protocol for a functional immunologic testing battery using peripheral blood (PB) microsampling, and 2) to test for age-dependent effects of BCG stimulation, a known immunoadjuvant, on innate immune function.

Methods: Preterm (PT) and full term (FT) infants were recruited in addition to healthy adults (HA). A 250-300μL blood sample was obtained, of which 50μL were allocated for innate immune function testing. TNFα-secreting cells were quantified using enzyme-linked immunosorbent (ELISPOT) assays, and LPS, BCG, or a combination were used as innate immune stimulants. After 24-hour incubation, ELISPOT supernatants were collected from two subjects per group, and ELISA (Milliplex) was performed for additional cytokine quantification. Remaining samples were used for PBMC isolation to quantify HLA-DR expression, myeloid-derived suppressor cell (MDSCs) and subpopulation proportions via flow cytometry.

Results: 10 HA, 14 FT and 9 PT blood samples were obtained. BCG stimulation resulted in significant increases in TNFα spot count, size and intensity in FT infants ($p<0.05$). Co-stimulation with BCG+LPS, and LPS alone also resulted in significant increases in these parameters across age groups ($p<0.05$). Further cytokine analysis showed BCG stimulation and LPS co-stimulation led to higher concentrations of pro-inflammatory cytokines, including TNFα, IL-12p70, and CXCL8 compared to unstimulated or LPS-stimulated samples, regardless of age. Flow analysis revealed similar mHLA-DR expression levels, with significantly higher proportions of total and granulocytic MDSCs in PT and FT subjects compared to HA, with elevated proportions of early MDSCs in HA subjects ($p<0.05$).

Conclusions: Our results confirm elevated total and granulocytic MDSC proportions in peripheral blood in PT/FT compared to HA, which may contribute to the overall immunotolerant phenotype seen in early life. BCG stimulation augmented the pro-inflammatory innate immune response in PT/FT, and shows promise as a potential future therapy for neonatal sepsis prevention. Furthermore, our findings demonstrate successful implementation of a novel battery of functional immune assays utilizing microsampling of PB, with the potential for broadening functional testing capabilities to broaden our understanding of the unique complexities of the neonatal immune system.

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TABLE TITLE: (No Tables)

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Disclosure: NO, there are no relationships to disclose.

Submission Rules Confirmation: I confirm that I have read and complied with the submission guidelines.

ARE YOU A MEMBER?:

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