NEONATAL IMMUNE DYSFUNCTION AND RISK OF SEPSIS OF PREMATURE INFANTS IN A MALARIA ENDEMIC AREA

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Background
Human newborns are bombarded with multiple pathogens on leaving the sterile intra-uterine environment, and yet have suboptimal innate immunity and limited immunological memory, thus leading to increased susceptibility to infections in early life. Toll-like receptors (TLRs) represent one of the first lines of defence against microorganisms and play an important role in the orchestration between innate immunity responses, regulatory and inflammatory responses to pathogens. Measurement of these biomarkers in a newborn population could provide new indicators of immune system dysfunction and thus determine the depth of immunosuppression.

Methods
The study is part of the ongoing SEPSIS project conducted in Benin on a cohort follow-up of 240 newborns from birth to 3 months with clinical data collected. Newborns from pregnant women with infection risk factors or prematurity at delivery are enrolled in the study. Immunological analysis is performing in cord blood and peripheral blood at 3 months. Ex vivo functionality of the innate response via TLRs after stimulation of whole blood with different agonists from TLR1 to TLR9 (LPS, FSL1, Pam3CSK4, Flagellin, PolyI: C, CPG-ODN, Imiquimod and Resiquimod) are performing. Cytokine/chemokine pro and anti-inflammatory will be quantified in culture supernatants using CBA technique by flow cytometry. Mononuclear cells are cryopreserved in liquid nitrogen to investigate immune system dysfunction with Treg and Breg cells phenotyping by flow cytometry.

Results
We have actually enrolled 100 newborns and performed the stimulations on whole blood for cytokine assays and cryopreserved CBMC/PBMC for phenotyping. Immunological tests are ongoing and preliminary results will be presented. Analysis will be performed to evaluate the impact of an *in utero* contact with a soluble malaria/bacterial antigen or prematurity on the newborn immune system.

Conclusion
We hope from this study to better understand the consequences of prematurity or pregnancy maternal infections on immune mechanisms (Treg / Breg lymphocytes, and TLRs functions) involved in the control of neonatal infections.

Keywords: Toll-Like receptors (TLR), Treg, Breg, newborn, infection