276

PHENOTYPE AND ACTIVATION LEVELS OF DENDRITIC CELLS (DC) AND MONOCYTES IN PREGNANCY-ASSOCIATED MALARIA DURING A FOLLOW-UP IN BENIN

Samad Ibitokou[1], Nadine Fievet[2], Bertin Vianou[1], Carine Agbowai[1], Sem Ezinmegnon[1], Mayke Oesterholt[3], Achille Massougbodji[1], Thor Theander[4], Stefania Varani[5], Marita Troye-Blomberg[6], Adrian J.F. Luty[3], Philippe Deloron[7]

[1]University of Abomey Calavi, Faculté des Sciences de la Santé, Cotonou, Benin, [2]IRD UMR216, Mother and Child Health in the Tropics, Cotonou, Benin, [3]Department of Medical Microbiology, Radboud University, Nijmegen Medical Centre, Nijmegen, The Netherlands, [4]Department of International Health, Institute of International Health, Immunology and Microbiology, University of Copenhagen, Copenhagen, Denmark, [5]Department of Laboratory Medicine, Division of Clinical Microbiology, Karolinska University Hospital, Huddinge, Sweden, [6]Department of Immunology, Wenner-Gren Institute, Stockholm University, Stockholm, Sweden, [7]Université René Descartes, Faculté de Pharmacie, Paris, France

Dendritic cells (DC) are important both in amplifying the innate immune response, and in initiating adaptive immunity and shaping the type of T helper (Th) response. Although the role of DC in immune responses to many intracellular pathogens has been delineated and research is underway to identify the mechanisms involved, relatively little is known concerning the role of DC in immunity to malaria. We evaluated the immunophenotype of antigen presenting cells (APC) in peripheral blood of pregnant Beninois women from the area of Come, southwestern Benin, where we are conducting a longitudinal prospective study of 1000 mothers. Pregnant women are enrolled ≤ 24 weeks of pregnancy and followed at each ante-natal visit until delivery. Cellular immunological assessments have been performed with samples from a subgroup of 149 women at enrolment and 106 at delivery, with or without active *Plasmodium falciparum* infection detected by a rapid diagnostic test. Immunophenotyping of APC and their level of activation (HLA-DR, CD86 expression) are being evaluated using flow cytometry. *P. falciparum* infection was associated with DC altered maturation in pregnant women, as reflected by lower frequencies of MDC and PDC and their downregulated expression of HLA-DR but not CD86, whether in early pregnancy or at delivery. DC of pregnant women with anaemia were present at low frequency during pregnancy. In conclusion, HLA class II expression on DC is fundamental for presenting antigens to T cells and inducing their activation. Therefore, impaired DC activation upon malaria infection in pregnant women may result in a deficient and delayed adaptive immune response to the parasite and/or to other pathogens. Therefore, through an inhibitory effect on DC, *P. falciparum* may impair cell mediated immunity in pregnant women leading to a reduce response against the parasite itself and possibly rendering pregnant women more susceptible to other infections.

277

INHIBITORY HUMORAL RESPONSES TO THE *PLASMODIUM FALCIPARUM* VACCINE CANDIDATE EBA-175 ARE LINKED TO ERYTHROCYTE RECEPTOR USAGE

Aida S. Badiane[1], Amy Bei[2], Ambroise Dioum Ahouidi[3], Nichole Salinas[4], Daouda Ndiaye[1], Ousmane Sarr[1], Omar Ndir[1], Niraj Tolia[4], Souleymane Mboup[1], Manoj Duraisingh[5]

[1]Cheikh Anta Diop University and Le Dantec Hospital, Dakar, Senegal, [2]Harvard School of Public Healt, Boston, MA, United States, [3]Cheikh Anta Diop University, Dakar, Senegal, [4]Washington University School of Medicine, St. Louis, MO, United States, [5]Harvard School of Public Health, Boston, MA, United States

Plasmodium falciparum utilizes multiple ligand-receptor interactions for invasion. The invasion ligand EBA-175 is being developed as a major blood-stage vaccine candidate. It is located in the apical micronemes of merozoites and mediates parasite invasion of host erythrocytes in a sialic acid dependent manner. In this study, we seek to address the ability of naturally acquired antibodies raised against the EBA-175 RII erythrocyte binding domain to inhibit parasite invasion, in relationship to its sialic acid dependence. To address this hypothesis, we have taken two primary approaches. We have determined the presence of antibodies to the PfEBA-175 RII domain by ELISA in individuals from malaria endemic areas of Senegal with high or low transmission. We have tested the plasma of those individuals for their specific EBA-175 inhibitory potential by performing invasion assays using *P. falciparum* EBA-175 KO transgenic parasites. We have also affinity purified antibodies to the EBA-175 RII domain from pooled patient serum for the invasion inhibition of uncultured Senegalese parasite isolates in *ex vivo* assays. Our results suggest that naturally acquired anti-EBA-175 RII antibodies significantly inhibit invasion of Senegalese parasites and this inhibition is dependent on the sialic acid dependence of the parasite strain. This work has implications for vaccine design based on EBA-175 in the context of alternative invasion pathways.

278

IMPACT OF MATERNAL CYTOKINE GENE POLYMORPHISMS ON MOTHER AND FETUS BIOLOGICAL AND IMMUNOLOGICAL PARAMETERS IN THE CONTEXT OF PLACENTAL MALARIA

Adjimon Gatien Lokossou[1], Célia Dechavanne[1], Aziz Bouraïma[2], David Courtin[2], Agnès Le Port[1], Rodolphe Ladékpo[2], Julien Noukpo[2], Désiré Bonou[2], Claude Ahouangninou[2], Franck Loumedjinon[2], Messanh Daoudou[2], André Garcia[1], Florence Migot-Nabias[1]

[1]Research Institute for Development, Paris, France, [2]Research Institute for Development, Cotonou, Benin

Some single mutations in cytokines genes are related to modifications of the protein production. For cytokines involved in the regulation of the antibody production, particular gene polymorphisms influence the antibody levels. We investigated the consequences of some cytokine gene polymorphisms on the antibody levels of mothers at delivery, and on fetal immunity, in the context of *P. falciparum* placental malaria infection. We hypothesized that if some maternal cytokine gene polymorphisms lead to an increased production of maternal specific antibodies, they could help to lower the *in utero* sensitization of the fetus to plasmodial antigens, and contribute to delay the occurrence of the first malaria attack in early life. Six-hundred pairs of mothers and children were recruited in south-west Benin, where malaria is endemic. At delivery, peripheral blood was drawn from mothers, as well as corresponding cord blood. Eleven percent of mothers had a placenta infected with *P. falciparum*. From the maternal genomic DNA, 5 mutations occurring in genes coding for IL-4, IL-10 and IL-13 were genotyped by quantitative PCR. High frequencies were observed for genotypes IL-4-590 TT (61.8%), IL-4 +33 CT (50.5%), IL-10-1082 AA (52.5%), IL-10-592 AC (51.3%) and IL-13-1055 CT (51.0%). We evaluated the influence of these mutations on the ability of maternal mononuclear cells to produce the cytokines of interest, following stimulation by mitogens. Finally, we determined maternal and fetal plasmatic levels of IgM, IgG and cytophilic isotypes IgG1 and IgG3 directed against recombinant proteins from the MSP1, MSP2, MSP3, AMA1 and / or GLURP antigens, which are candidates for inclusion into a multivalent vaccine against malaria. The analysis of the relationships between i) maternal cytokine gene polymorphisms, ii) maternal cytokine and related antibody production, and iii) fetal specific antibody production, may help to understand the strength of the mother and child immunological interactions during pregnancy, depending on the presence or not of a plasmodial placental infection.

Supplement to
THE AMERICAN JOURNAL OF
Tropical Medicine and Hygiene
Official Journal of the American Society of Tropical Medicine and Hygiene

Volume 83 November 2010 Number 5 Supplement

Abstract Book

American Society of Tropical Medicine and Hygiene

59th Annual Meeting

59
ASTMH fifty-ninth
ANNUAL MEETING

November 3–7, 2010

Atlanta Marriott Marquis

Hilton Atlanta

Atlanta, Georgia, USA

Supplement to

The American Journal of
Tropical Medicine and Hygiene