a major role in the observed microbe-mediated *Plasmodium* refractoriness but large populations of replicating bacteria are required. Physical interaction between bacteria and parasite were not observed following oral co-introduction in mosquitoes and supplementing nutrients required for parasite development do not rescue infection. We are currently using biochemical and continued phenotypic analyses to elucidate the mechanism of inhibition, which could lead to the identification of novel anti-*Plasmodium* molecules.

871

ANTIBODIES PRODUCED AGAINST RECOMBINANT SIX-CYSTEINE GAMETE SURFACE HOMOLOGY FRAGMENTS FROM *PLASMODIUM FALCIPARUM* PFS48/45 AND PFS230 RECOGNIZE SEXUAL STAGES AND MAY BLOCK TRANSMISSION

Raul Herrera, Marian Ortiz, Christopher Rowe, Vu Nguyen, Richard L. Shimp, Karine Reiter, Lynn Lambert, Louis H. Miller, Patrick E. Duffy, Nicholas J. MacDonald, Yimin Wu, David L. Narum

Laboratory of Malaria Immunology and Vaccinology, Rockville, MD, United States

The development of a *falciparum* malaria transmission blocking vaccine is being evaluated as a complement to a pre-erythrocytic vaccine. Antibodies against the sexual stage protein, Pfs25, significantly inhibit oocyst development when assessed by a membrane feeding assay, though it requires higher antibody titers in humans to achieve complete blocking in transmission. In order to evaluate whether the transmission blocking activity of Pfs25 may be enhanced by the inclusion of additional sexual stage antigens, we aimed to produce two recombinant forms of the cysteine-rich *Plasmodium* gamete surface homology fragments derived from Pfs48/45 and Pfs230. Using a modified *Pichia pastoris* host that overexpresses protein disulfide isomerase, multiple forms of Pfs48/45 have been expressed and purified that contain 8 to 10 cysteines, which form a "double domain". An amino-terminal region of Pfs230 containing a single "double domain" was expressed and refolded from inclusion bodies derived from *Escherichia coli*. Antibodies generated in rabbits against both of these recombinant forms of Pfs48/45 and Pfs230 recognized unfixed gametes by indirect immunofluorescence. In contrast, only rabbit antisera against Pfs230 inhibited oocyst development by greater than 97% (reduction in oocyst prevelance was 50 to 90%) using neat sera in the presence of complement. The failure of the Pfs48/45 antisera to inhibit oocyst development may be the result of a poorly folded immunogen or that the Pfs48/45 "double domain" is not a significant biological target. Now that a recombinant form of Pfs230 has been produced using a scalable system that induces inhibitory antibodies, pre-clinical studies evaluating Pfs25 and Pfs230 may be performed.

872

HUMAN ANTIBODY RESPONSE TO *ANOPHELES* SALIVARY GSG6-P1 PEPTIDE: NEW IMMUNO-EPIDEMIOLOGICAL TOOL FOR EVALUATING THE EFFICACY OF INSECTICIDES TREATED NETS (ITNS) IN MALARIA VECTOR CONTROL

Papa M. Drame[1], Anne Poinsignon[2], Patrick Besnard[3], Sylvie Cornelie[2], Jacques Le Mire[3], Filomeno Fortes[4], Jean-Claude Toto[5], Mbacke Sembene[6], Francois Simondon[7], Pierre Carnevale[2], Franck Remoue[1]

[1]Institut de recherche pour le Developpement, Cotonou, Benin, [2]Institut de recherche pour le Developpement, Montpellier, France, [3]Malaria Control Program, Medical Service of ACERGY-SONAMET, Lobito, Angola, [4]National Malaria Control Program, Ministry of Health, Luanda, Angola, [5]Laboratoire de Recherche sur le Paludisme, OCEAC, Yaoundé, Cameroon, [6]Department of Animal Biology, Faculty of Sciences and Technics, Cheikh Anta Diop University, Dakar, Senegal, [7]Epidemiology Department of Sanofis-Aventis, Lyon, France

To optimize malaria control, WHO has emphasized the need for new indicators to evaluate the efficacy of vector control strategies. Previous studies have shown that the quantification of human antibody (Ab) response to *Anopheles* salivary proteins represent an epidemiological biomarker of exposure to *Anopheles* bites and malaria risk. In particular, only one salivary peptide, the gSG6-P1, is one clear candidate to evaluate the level of exposure to *An. gambiae* and *An. funestus* bites. The aim of the study was then to validate this peptide as a new tool to evaluate the efficacy of ITNs use. One longitudinal study, concerning individuals (n=108) living in malaria endemic area was performed from March 2005 to January 2007 (Angola). The cohort was followed for parasitological, entomological and immunological data, before and after the well-controlled use of ITNs (installation in Feb. 2006). Significant decrease of the percentage of immune responders and of anti-gSG6-P1 IgG Ab level was observed just after the ITNs use and was correlated with the decrease of malaria parasitemia, the current and referent criteria of ITNs efficacy. Interestingly, the decrease of specific IgG level was observed in all age groups (0-6; 7-14 and >14 years-old) and for the majority of ITNs-protected individuals, suggesting its potentiality as an individual biomarker. However, in concordance with the considerable loss of ITNs and lack of ITNs use, specific IgG response increased only four months after ITNs introduction in this studied population. It suggests that this salivary tool could be also an indicator to the time-dependent incorrect use of ITNs. This study shows that the assessment of IgG response to gSG6-P1 salivary peptide could be a pertinent tool to evaluate the ITNs efficacy, whatever age, and potentially a biomarker of efficacy at an individual level. This study represents a first approach to elaborate new tools of evaluation of malaria vector control and future studies are needed to confirm this hypothesis in other areas and using different vector control strategies.