



Bulletin 173 | 25 August 2008

## From K&S

This is the first issue after the summer break. We are making an effort to capture the publications published in the past three weeks. Therefore for the coming two weeks MalariaWorld will mainly include publications. In September we will continue with news and other announcements as well.

## Announcement

### Open access of MSF articles in Field Research database

Médecins Sans Frontières is making its database of research accessible to health workers in developing countries through a new open-access website known as the MSF Field Research database. At its launch, the field research site included over 400 archived articles on issues including HIV care, malaria, tuberculosis, leishmaniasis, refugees and health politics. It also features conference abstracts and a section called 'Programme Descriptions' that describes lessons learnt from MSF's field experience.

The hope is that making these reports freely available, as opposed to hidden away in subscription based journals, will enable the sharing of experience and benefit those in developing countries that might not have been able to afford the subscriptions to the journals.

The journals who have agreed to this system include The Lancet, BMJ, New England Journal of Medicine, PLoS Medicine and Transactions of the Royal Society of Tropical Medicine and Hygiene, and perhaps demonstrates a change in their business model to a more open access approach.

## Publications

### Open access | **From strategy development to routine implementation: the cost of Intermittent Preventive Treatment in Infants for malaria control**

Fatuma Manzi, Guy Hutton, Joanna Schellenberg, Marcel Tanner, Pedro Alonso, Hassan Mshinda and David Schellenberg

BMC Health Services Research 2008, 8:165

The costs presented here show the order of magnitude of expenditures needed to initiate and to implement IPTi at national scale in settings with high Expanded Programme on Immunization (EPI) coverage. The IPTi intervention appears to be affordable even within the budget constraints of Ministries of Health of most sub-Saharan African countries.

### Open access | **Molecular epidemiology of drug-resistant malaria in western Kenya highlands**

Zhong D, Afrane Y, Githeko A, Cui L, Menge D, Yan G

BMC Infectious Diseases, 2008 8:105 (31 July 2008)

Since the late 1980s a series of malaria epidemics has occurred in western Kenya highlands. Among the possible factors that may contribute to the highland malaria epidemics, parasite resistance to antimalarials has not been well investigated.



These findings suggest that drug resistance of malaria parasites in the highlands could be contributed by the mutations and their high frequencies as found in the lowland. The results are discussed in terms of the role of drug resistance as a driving force for malaria outbreaks in the highlands.

**Open access | Phagocytosis of haemozoin (malarial pigment) enhances metalloproteinase-9 activity in human adherent monocytes: Role of IL-1beta and 15-HETE**

Mauro Prato, Valentina Gallo, Giuliana Giribaldi, Paolo Arese

Malaria Journal 2008, 7:157 (18 August 2008)

Haemozoin-containing trophozoites alters the functionality of human monocytes and macrophages, including an increase in TNF produced. This paper suggests a potential role for matrix metalloproteinases in this pathway.

**Open access | Dry season ecology of Anopheles gambiae complex mosquitoes in The Gambia**

Musa Jawara, Margaret Pinder, Chris J Drakeley, Davis C Nwakanma, Ebrima Jallow, Claus Bogh, Steve W Lindsay, David J Conway

Malaria Journal 2008, 7:156 (18 August 2008)

Results of a longitudinal follow up of mosquito population dynamics at the end of the dry season in four villages in The Gambia, with emphasis on mosquitoes from the Anopheles gambiae complex. Important contribution to a neglected aspect of mosquito ecology.

**Open access | Acquisition of naturally occurring antibody responses to recombinant protein domains of Plasmodium falciparum erythrocyte membrane protein 1**

Claire L Mackintosh, Zoe Christodoulou, Tabitha W Mwangi, Moses Kortok, Robert Pinches, Thomas N Williams, Kevin Marsh, Christopher I Newbold

Malaria Journal 2008, 7:155 (16 August 2008)

Using antigens of an expressed PfEMP1 variant, the study assesses the natural acquired immunity to these proteins as well as to the parasites expressing this antigen.

**Open access | Different methodological approaches to the assessment of in vivo efficacy of three artemisinin-based combination antimalarial treatments for the treatment of uncomplicated falciparum malaria in African children**

Elizabeth A Ashley et al.

Malaria Journal 2008, 7:154 (9 August 2008)

Data from different in vivo studies of ACT treatment of uncomplicated falciparum malaria were combined in a single database. Efficacy at day 28 corrected by PCR genotyping was estimated using four methods.

**Open access | Gains in awareness, ownership and use of insecticide-treated nets in Nigeria, Senegal, Uganda and Zambia**

Carol A Baume, Celeste Marin

Malaria Journal 2008, 7:153 (7 August 2008)

A mix of demand creation, a strengthened commercial sector, reduced taxes and tariffs, and programmes making ITNs available at reduced prices resulted in impressive gains in awareness, ownership, and use of nets and ITNs in Nigeria, Senegal, Zambia, and Uganda between 2000 and 2004-2006. None of the countries reached the ambitious Abuja targets for ITN use, but they made substantial progress towards them.

**Open access | Ethnobotanical study of some of mosquito repellent plants in north-eastern Tanzania**

Eliningaya J Kweka et al.



Malaria Journal 2008, 7:152 (7 August 2008)

The use of whole plants and their products as insect repellents is common among village communities of north-eastern Tanzania and the results indicate that the use of *O. suave* and *O. kilimandscharicum* as a repellent would be beneficial in reducing vector biting. The widespread use of this approach has a potential to complement other control measures.

**Open access | Impact of urban agriculture on malaria vectors in Accra, Ghana**

Eveline Klinkenberg, PJ McCall, Michael D Wilson, Felix P Amerasinghe, Martin J Donnelly  
Malaria Journal 2008, 7:151 (4 August 2008)

To investigate the impact of urban agriculture on malaria transmission risk in urban Accra larval and adult stage mosquito surveys, were performed. Local transmission was implicated as *Anopheles* spp. were found breeding and infected *Anopheles* mosquitoes were found resting in houses in the study sites. The predominant *Anopheles* species was *Anopheles gambiae* s.s..

**Open access | Consanguineous marriages and endemic malaria: can inbreeding increase population fitness?**

Srdjan Denic, Nico Nagelkerke, Mukesh M Agarwal

Malaria Journal 2008, 7:150 (2 August 2008)

The practice of consanguineous marriages is widespread in countries with endemic malaria. In these regions, consanguinity increases the prevalence of alpha+-thalassemia, which is protective against malaria. However, it also causes an excessive mortality amongst the offspring due to an increase in homozygosis of recessive lethal alleles. The aim of this study was to explore the overall effects of inbreeding on the fitness of a population infested with malaria. Consanguineous marriages may increase the overall fitness of populations with endemic malaria.

**Open access | The relationship between the haemoglobin concentration and the haematocrit in Plasmodium falciparum malaria**

Sue J Lee et al.

Malaria Journal 2008, 7:149 (2 August 2008)

Malaria is a very important cause of anaemia in tropical countries. Anaemia is assessed either by measurement of the haematocrit or the haemoglobin concentration. For comparisons across studies, it is often necessary to derive one measure from the other. Based on this large data set, an accurate and robust conversion factor both in acute malaria and in convalescence was obtained. The commonly used threefold conversion is also valid.

**Open access | Malaria morbidity in Papua Indonesia, an area with multidrug resistant Plasmodium vivax and Plasmodium falciparum**

Muhammed Karyana et al.

Malaria Journal 2008, 7:148 (2 August 2008)

In this region of multidrug-resistant *P. vivax* and *P. falciparum*, both species are associated with substantial morbidity, but with significant differences in the age-related risk of infection.

**Open access | A quantitative risk assessment approach for mosquito-borne diseases: malaria re-emergence in southern France**

Nicolas Poncon, Annelise Tran, Celine Toty, Adrian JF Luty, Didier Fontenille

Malaria Journal 2008, 7:147 (1 August 2008)

The Camargue region is a former malaria endemic area, where potential *Anopheles* vectors are still abundant. Considering the importation of *Plasmodium* due to the high number of imported malaria cases in France, the aim of this article was to make some



predictions regarding the risk of malaria re-emergence in the Camargue. The current risk of malaria re-emergence seems negligible due to the very low number of imported Plasmodium. This model demonstrated its efficiency for mosquito-borne diseases risk assessment.

**Open access | Malaria vector control practices in an irrigated rice agro-ecosystem in central Kenya and implications for malaria control**

Peter N Ng'ang'a, Josephat Shililu, Gayathri Jayasinghe, Violet Kimani, Charity Kabutha, Lucy Kabuage, Ephantus Kabiru, John Githure, Clifford Mutero

Malaria Journal 2008, 7:146 (31 July 2008)

Malaria transmission in most agricultural ecosystems is complex and hence the need for developing a holistic malaria control strategy with adequate consideration of socio-economic factors driving transmission at community level. The study provides relevant information necessary for the management, prevention and control of malaria in irrigated agro-ecosystems, where vectors of malaria are abundant and disease transmission is stable.

**Open access | Utilization of insecticide-treated nets by under-five children in Nigeria: Assessing progress towards the Abuja targets**

Olusola B Oresanya, Moshe Hoshen, Olayemi T Sofola

Malaria Journal 2008, 7:145 (30 July 2008)

The Abuja target of increasing the proportion of people sleeping under insecticide-treated nets (ITNs) to 60% by the year 2005, as one of the measures for malaria control in Africa, has generated an influx of resources for malaria control in several countries in the region. A national household survey conducted in 2005 by the Malaria Control Programme in Nigeria assessed the progress made with respect to ITN ownership and use among pregnant women and children under five years of age since 2000. This study demonstrated that the substantial increase in ITN utilization among children under five years of age in Nigeria is still far from the Abuja targets.

**Open access | Evaluation of the genetic polymorphism of Plasmodium falciparum P126 protein (SERA or SERP) and its influence on naturally acquired specific antibody responses in malaria-infected individuals living in the Brazilian Amazon**

Lilian Rose Pratt-Riccio et al.

Malaria Journal 2008, 7:144 (30 July 2008)

The aim of the present study was to investigate the polymorphism of P126 N-terminal region OR domain in *P. falciparum* isolates from two Brazilian malaria endemic areas and its impact on anti-OR naturally acquired antibodies.

**Open access | Early home treatment of childhood fevers with ineffective antimalarials is deleterious in the outcome of severe malaria**

Adebola E Orimadegun, Olukemi K Amodu, Peter E Olumese, Olayemi O Omotade

Malaria Journal 2008, 7:143 (29 July 2008)

This study showed that, home treatment with chloroquine significantly impacts on the outcome of severe malaria. This finding underscores the need for wide-scale monitoring to withdraw chloroquine from circulation in Nigeria and efforts intensified at promoting prompt treatment with effective medicines in the community.

**Open access | Cohort study of the association of antibody levels to AMA1, MSP119, MSP3 and GLURP with protection from clinical malaria in Ghanaian children**

Daniel Doodoo et al.

Malaria Journal 2008, 7:142 (29 July 2008)



This study was aimed at assessing in a standardized manner the relationship between the antibody responses to four malaria vaccine candidate antigens and protection from clinical malaria, in a cohort of Ghanaian children. Using standardized procedures, the study has confirmed the importance of antibodies to MSP119 in reducing the risk of clinical malaria in Ghanaian children, thus substantiating its potential as a malaria vaccine candidate.

**Open access | Short communication: Concurrent gastro-intestinal nematode infection does not alter the development of experimental cerebral malaria**

Brian de Souza, Helena Helmby

*Microbes and Infection*, Volume 10, Issue 8, July 2008, Pages 916-921

Concurrent helminth infections have been suggested to be associated with protection against cerebral malaria in humans, a condition characterised by systemic inflammation. Here we show that a concurrent chronic gastro-intestinal nematode infection does not alter the course of murine cerebral malaria.

**Open access | Malaria Prevention in Short-Term Travelers**

D.O. Freedman

*NEJM*, Volume 359:603-612 August 7, 2008 Number 6

A family of three persons is planning a safari to southern Africa. The itinerary includes 3 days in Cape Town, South Africa, 3 days in Kruger National Park, South Africa, and 3 days in Victoria Falls, Zambia. The 31-year-old husband takes no medications currently, but he recently discontinued fluoxetine, which he had taken for depression. His 29-year-old wife, who won the trip in a corporate sales competition, is healthy and 15 weeks pregnant. Their 7-year-old child is in good health. How should the risk and prevention of malaria be managed in this family?

**Open access | Assessing Antimalarial Efficacy in a Time of Change to Artemisinin-Based Combination Therapies: The Role of Médecins Sans Frontières**

Guthmann JP, Checchi F, van den Broek I, Balkan S, van Herp M, et al.

*PLoS Med* 5(8): e169

Jean-Paul Guthmann and colleagues describe the output of MSF's work in antimalarial efficacy assessment during the last decade.

**Open access | Divergent Goals and Commitments in Global Malaria Intervention**

Kiszewski AE

*PLoS Med* 5(7): e159

International Funding for Malaria Control in Relation to Populations at Risk of Stable *Plasmodium falciparum* Transmission.

**Open access | International Funding for Malaria Control in Relation to Populations at Risk of Stable Plasmodium falciparum Transmission**

Snow RW, Guerra CA, Mutheu JJ, Hay SI

*PLoS Med* 5(7): e142

Without further increases in funding and appropriate targeting of global malaria control investment it is unlikely that international goals to halve disease burdens by 2015 will be achieved. Moreover, the additional financing requirements to move from malaria control to malaria elimination have not yet been considered by the scientific or international community.

**Open access | Phase 1 Trial of AMA1-C1/Alhydrogel plus CPG 7909: An Asexual Blood-Stage Vaccine for Plasmodium falciparum Malaria**

Mullen GED, Ellis RD, Miura K, Malkin E, Nolan C, et al.

*PLoS ONE* 3(8): e2940



Apical Membrane Antigen 1 (AMA1), a polymorphic merozoite surface protein, is a leading blood-stage malaria vaccine candidate. This is the first reported use in humans of an investigational vaccine, AMA1-C1/Alhydrogel, with the novel adjuvant CPG 7909. The safety profile of the AMA1-C1/Alhydrogel+CPG 7909 malaria vaccine is acceptable, given the significant increase in immunogenicity observed. Further clinical development is ongoing.

**Open access | A Randomised Trial of an Eight-Week, Once Weekly Primaquine Regimen to Prevent Relapse of Plasmodium vivax in Northwest Frontier Province, Pakistan**

Leslie T, Mayan I, Mohammed N, Erasmus P, Kolaczinski J, et al.

PLoS ONE 3(8): e2861

A practical radical treatment for vivax malaria is essential for control and elimination of the disease. The 8-week PQ course is more effective at preventing relapse than current treatment with chloroquine alone. Widespread use of the 8-week regimen could make an important contribution to reservoir reduction or regional elimination where G6PD testing is not available.

**Open access | Effect of Transmission Setting and Mixed Species Infections on Clinical Measures of Malaria in Malawi**

Bruce MC, Macheso A, Kelly-Hope LA, Nkhoma S, McConnachie A, et al.

PLoS ONE 3(7): e2775

Our study suggests that the interaction of Plasmodium co-infecting species can have protective effects against some clinical outcomes of malaria but that this is dependent on the seasonality and intensity of malaria transmission.

**Open access | An Erythrocyte Vesicle Protein Exported by the Malaria Parasite Promotes Tubovesicular Lipid Import from the Host Cell Surface**

Tamez PA, Bhattacharjee S, van Ooij C, Hiller NL, Llinás M, et al.

PLoS Pathog 4(8): e1000118

In this study, we designed a strategy to characterize 'hypothetical' proteins and use one as an example to illustrate the principle. We show that this protein resides within a novel compartment within the red cell and changes lipid transport at the host surface to stabilize a major nutrient pathway formed within the human cell. In principle, this strategy is applicable in determining the functions of other parasite genes involved in pathogen-host interactions.

**Open access | Temperature Shift and Host Cell Contact Up-Regulate Sporozoite Expression of Plasmodium falciparum Genes Involved in Hepatocyte Infection**

Siau A, Silvie O, Franetich J-F, Yalaoui S, Marinach C, et al.

PLoS Pathog 4(8): e1000121

We studied the changes in gene expression in sporozoites, from the parasite species *P. falciparum* that infects humans, in an in vitro system where they were co-cultured with their natural host cells, primary human hepatocytes. Functional studies on four of the up-regulated genes we identified validated our approach as one means to determine the repertoire of proteins implicated during the early events in the infection by *P. falciparum*, the species responsible for the severest forms of malaria.

**Pre-departure and Post-arrival Management of *P. falciparum* Malaria in Refugees Relocating from Sub-Saharan Africa to the United States**

William M. Stauffer, Michelle Weinberg, Robert D. Newman, Louise M. Causer, Mary J. Hamel, Laurence Slutsker, and Martin S. Cetron

Am J Trop Med Hyg 2008;79 141-146



In response to increasing numbers of refugees originating in sub-Saharan Africa guidelines for the management of malaria in refugees migrating to the United States have been broadened and updated. The guidelines are based on available evidence-based literature and recent public health experience. These guidelines were critically reviewed, assessed, and approved by multiple National and State entities as well as outside experts.

### **Microscopy Underestimates the Frequency of Plasmodium Falciparum Infection in Symptomatic Individuals in a Low Transmission Highland Area**

David M. Menge, Kacey C. Ernst, John M. Vulule, Peter A. Zimmerman, Hongfei Guo, and Chandy C. John

*Am J Trop Med Hyg* 2008;79 173-177

In this highland area, *P. falciparum* infection in symptomatic individuals is detected more frequently by PCR than microscopy, and most frequently by LDR-FMA. *P. falciparum* infection appears to resolve without treatment in most LDR-FMA-positive, microscopy-negative individuals, but is persistent in a subset of these individuals and requires treatment.

### **Effects of Plasmodium falciparum Mixed Infections on In Vitro Antimalarial Drug Tests and Genotyping**

Shengfa Liu, Jianbing Mu, Hongying Jiang, and Xin-zhuan Su

*Am J Trop Med Hyg* 2008;79 178-184

We studied the effects of mixed parasite populations containing various ratios of parasites resistant and sensitive to chloroquine on outcomes of drug tests and how ratios of parasite mixtures correlated with genotypes using polymerase chain reaction-based methods. Our results show that a mixture with a resistant population as low as 10% could greatly impact a drug test outcome.

### **Relationship Between Exposure, Clinical Malaria, and Age in an Area of Changing Transmission Intensity**

Wendy P. O'Meara, Tabitha W. Mwangi, Thomas N. Williams, F. Ellis McKenzie, Robert W. Snow, and Kevin Marsh

*Am J Trop Med Hyg* 2008;79 185-191

The relationship between malaria transmission intensity and clinical disease is important for predicting the outcome of control measures that reduce transmission. Comparisons of hospital data between areas of differing transmission intensity suggest that the mean age of hospitalized clinical malaria is higher under relatively lower transmission, but the total number of episodes is similar until transmission drops below a threshold, where the risks of hospitalized malaria decline. These observations have rarely been examined longitudinally in a single community where transmission declines over time.

### **NADPH-cytochrome P450 oxidoreductase from the mosquito Anopheles minimus: Kinetic studies and the influence of Leu86 and Leu219 on cofactor binding and protein stability**

Songklod Saraputit, Chuanwu Xia, Ila Misra, Pornpimol Rongnoparut, Jung-Ja P. Kim

*Archives of Biochemistry and Biophysics*, Volume 477, Issue 1, 1 September 2008, Pages 53-59

NADPH-cytochrome c oxidoreductase from the mosquito *Anopheles minimus* lacking the first 55 amino acid residues was expressed in *Escherichia coli*. The purified enzyme loses FMN, leading to an unstable protein and subsequent aggregation. To understand the basis for the instability, we constructed single and triple mutants of L86F, L219F, and P456A, with the first two residues in the FMN domain and the third in the FAD domain. The triple mutant was purified in high yield with stoichiometries of 0.97 FMN and 0.55 FAD. Deficiency in FAD content was overcome by addition of exogenous FAD to the



enzyme. Both wild-type and the triple mutant follow a two-site Ping-Pong mechanism with similar kinetic constants arguing against any global structural changes. Analysis of the single mutants indicates that the proline to alanine substitution has no impact, but that both leucine to phenylalanine substitutions are essential for FMN binding and maximum stability of the enzyme.

### **Heme activates artemisinin more efficiently than hemin, inorganic iron, or hemoglobin**

Shiming Zhang, Glenn S. Gerhard

Bioorganic & Medicinal Chemistry, Volume 16, Issue 16, 15 August 2008, Pages 7853-7861

Artemisinin derivatives appear to mediate their anti-malarial through an initial redox-mediated reaction. Heme, inorganic iron, and hemoglobin have all been implicated as the key molecules that activate artemisinins. The reactions of artemisinin with different redox forms of heme, ferrous iron, and deoxygenated and oxygenated hemoglobin were analyzed under similar in vitro conditions. Heme reacted with artemisinin much more efficiently than the other iron-containing molecules, supporting the role of redox active heme as the primary activator of artemisinin.

### **Design, synthesis, and biological activities of conformationally restricted analogs of primaquine with a 1,10-phenanthroline framework**

Cheikh Sall, Ange-Désiré Yapi, Nicolas Desbois, Séverine Chevalley, Jean-Michel Chezal, Kimny Tan, Jean-Claude Teulade, Alexis Valentin, Yves Blache

Bioorganic & Medicinal Chemistry Letters, Volume 18, Issue 16, 15 August 2008, Pages 4666-4669

A series of primaquine analogs was prepared, according to a conformationally restricted conformation of primaquine. In vitro antiplasmodial activities were evaluated and showed that all compounds were active on different strains of Plasmodium falciparum. In particular compounds 5 and 15 possessing a methoxy group were more active than was primaquine. Furthermore, analog 5 displayed good in vitro gametocytocidal activity. In addition selectivity indexes were calculated in respect with cytotoxic activities on Vero cell lines.

### **Potent and selective antiplasmodial activity of the cyanobacterial alkaloid nostocarboline and its dimers**

Damien Barbaras, Marcel Kaiser, Reto Brun, Karl Gademann

Bioorganic & Medicinal Chemistry Letters, Volume 18, Issue 15, 1 August 2008, Pages 4413-4415

The quaternary  $\beta$ -carbolinium alkaloid nostocarboline from the cyanobacterium Nostoc 78-12A and 10 bis-cationic dimeric derivatives were evaluated against four protozoan parasites and low micromolar values against Trypanosoma brucei, submicromolar values against Leishmania donovani and low nanomolar values against Plasmodium falciparum K1 were determined. Selectivity against rat myoblasts (L6 cells) was found to be up to >2500-fold.

### **Letter: Imported malaria is falling in Netherlands and Europe**

Perry J van Genderen, Dennis A Hesselink, and Jacob M Bezemer

BMJ. 2008; 337(jul28\_2): p. a1026

The increase in falciparum malaria in the UK reported by Smith et al<sup>1</sup> does not correspond with our own observations on imported malaria in the Netherlands during recent years.

### **Travel industry should highlight malaria prophylaxis**

Edward Green, Rohit Bazaz, and Steve T Green



BMJ. 2008; 337(jul31\_3): p. a1027

Smith et al reported an increase in cases of imported malaria in the UK.<sup>1</sup> We recently reviewed travel brochures from 27 British tour operators which featured holidays to malarious African countries.<sup>2</sup> Such literature would be an ideal place to target advice to travellers, and our results show that this opportunity is being missed.

### **High frequency of Plasmodium falciparum CICNI/SGEAA and CVIET haplotypes without association with resistance to sulfadoxine/pyrimethamine and chloroquine combination in the Daraweesh area, in Sudan**

I. E. A-Elbasit, I. F. Khalil, M. I. Elbashir, E. M. Masuadi, I. C. Bygbjerg, M. Alifrangis, H. A. Giha

European Journal of Clinical Microbiology & Infectious Diseases, Volume 27, Number 8 / August, 2008 : 725-732

Estimation of the prevalence of the molecular markers of sulfadoxine/pyrimethamine (SP) and chloroquine (CQ) resistance and validation of the association of mutations with resistance in different settings is needed for local policy guidance and for contributing to a global map for anti-malarial drug resistance. Finally, these data represent a baseline for SP resistance molecular markers needed before the deployment of SP/artesunate combination therapy in the Sudan.

### **Molecular Characterization, Heterologous Expression and Kinetic Analysis of Recombinant Plasmodium falciparum Thymidylate Kinase**

Mahmoud Kandeel and Yukio Kitade

J Biochem 2008 144: 245-250

The gene encoding for thymidylate kinase from Plasmodium falciparum was obtained by PCR and expressed in Escherichia coli and the enzyme was investigated as a possible new drug target. From the present study, we suggest that the design of appropriate inhibitors especially purine based compounds could have a selective inhibitory effect on the parasite enzyme.

### **Variants in the Toll-Like Receptor Signaling Pathway and Clinical Outcomes of Malaria**

Fabiana M. S. Leoratti, Lilian Farias, Fabiana P. Alves, Martha C. Suarez-Mútiis, José R. Coura, Jorge Kalil, Erney P. Camargo, Sandra L Moraes, and Rajendranath Ramasawmy

The Journal of Infectious Diseases 1 September 2008, Vol. 198, No. 5: 772-780

Our findings indicate that the TLR-1 and TLR-6 variants are significantly associated with mild malaria, whereas the TLR-9-1486C/T variants are associated with high parasitemia. These discoveries may bring additional understanding to the pathogenesis of malaria.

### **Potent, Plasmodium-Selective Farnesyltransferase Inhibitors That Arrest the Growth of Malaria Parasites: Structure–Activity Relationships of Ethylenediamine-Analogue Scaffolds and Homology Model Validation**

Steven Fletcher et al.

J. Med. Chem., ASAP Article

New chemotherapeutics are urgently needed to combat malaria. We previously reported on a novel series of antimalarial, ethylenediamine-based inhibitors of protein farnesyltransferase (PFT). In the current study, we designed and synthesized a series of second generation inhibitors, wherein the core ethylenediamine scaffold was varied in order to examine both the homology model of Plasmodium falciparum PFT (PfPFT) and our predicted inhibitor binding mode.

### **Perspective: Brian Greenwood: making milestones in malaria research**

Priya Shetty

The Lancet, Volume 372, Issue 9636, 2 August 2008-8 August 2008, Page 365



No abstract available

**Review: Mosquito-based transmission blocking vaccines for interrupting Plasmodium development**

Catherine Lavazec, Catherine Bourgouin

*Microbes and Infection*, Volume 10, Issue 8, July 2008, Pages 845-849

Reduction of transmission is critical for effective malaria control. Transmission blocking vaccines, which are intended to prevent the parasites from infecting the mosquito vectors, could target mosquito antigens that are required for the successful development of the parasite in its vector. Here we review recent advances in the identification of promising candidate antigens for a mosquito-based transmission blocking vaccine.

**Plasmodium falciparum glycosylphosphatidylinositol toxin interacts with the membrane of non-parasitized red blood cells: a putative mechanism contributing to malaria anemia**

Norbert W. Brattig, Katharina Kowalsky, Xinyu Liu, Gerd D. Burchard, Faustin Kamena, Peter H. Seeberger

*Microbes and Infection*, Volume 10, Issue 8, July 2008, Pages 885-891

Following exposure to synthetic *Plasmodium falciparum* glycosylphosphatidylinositol (P.f.-GPI), red blood cells (RBCs) reacted with antibodies in the serum of a patient with severe acute *P. falciparum* malaria. These results strongly support the notion that released P.f.-GPI can insert into non-parasitized RBC membranes and results in recognition by circulating anti-GPI antibodies and possibly subsequent elimination. This process may contribute to malaria-associated anemia.

**Short communication: Investigation of host factors possibly enhancing the emergence of the chondroitin sulfate A-binding phenotype in Plasmodium falciparum**

Marta C. Nunes, Yvon Sterkers, Benoit Gamain, Artur Scherf

*Microbes and Infection*, Volume 10, Issue 8, July 2008, Pages 928-932

Malaria during pregnancy is associated with a massive sequestration of infected erythrocytes in the placenta and the emergence of a unique parasite-derived adhesive molecule (encoded by var2CSA) that binds to chondroitin sulfate A (CSA). How *P. falciparum* achieves the timely expression of the CSA ligand in pregnant women remains puzzling. We investigated whether host serum-specific factors present only during pregnancy may induce var2CSA expression. Our panel of experiments did not reveal significant changes in var2CSA levels and CSA-binding capacity.

**Obituary - Professor Chris Curtis**

Lines, Jo

*Outlooks on Pest Management*, Volume 19, Number 4, August 2008 , pp. 159-159(1)

No abstract available

**Insecticide Treated Bed Nets: A Significant Contribution Towards Malaria Control**

Invest, John

*Outlooks on Pest Management*, Volume 19, Number 4, August 2008 , pp. 160-163(4)

No abstract available

**Ribozyme cleavage of Plasmodium falciparum gyrase A gene transcript affects the parasite growth**

Anwar Ahmed and Yagya D. Sharma

*Parasitology Research*, Volume 103, Number 4 / September, 2008 : 751-763



Deoxyribonucleic acid (DNA) gyrase is an important enzyme that facilitates the movement of replication and transcription complexes through DNA by creating negative supercoils ahead of the complex. Its presence in *Plasmodium falciparum* is now established and considered a good drug target since it is absent in the human host. The sequence of *P. falciparum* gyrase A subunit was analyzed for its messenger ribonucleic acid (mRNA) folding as well as target accessibility for ribozymes.

### **Letter to the Editors: Thrombotic microangiopathy associated with *Plasmodium vivax* malaria**

Sunil Saharan, Utkarsh Kohli, Rakesh Lodha, Alok Sharma, and Arvind Bagga

Pediatric Nephrology, Online First

While severe malaria is usually associated with infection due to *Plasmodium falciparum*, there have been recent reports of life-threatening manifestations in patients with *P. vivax* infection. Acute renal failure (ARF) is reported to occur in 1–30% patients with *falciparum* malaria but rarely with *vivax* malaria [1–3]. We recently reported a case of *P. vivax* malaria with acute renal failure [3]. We now describe a boy with *vivax* malaria complicated by anemia, thrombocytopenia, ARF secondary to thrombotic microangiopathy, and acute respiratory distress syndrome.

### **Development of pilot scale production process and characterization of a recombinant multi-epitope malarial vaccine candidate FALVAC-1A expressed in *Escherichia coli***

G. Ravi, Krishna Ella, M. Lakshmi Narasu

Protein Expression and Purification, Volume 61, Issue 1, September 2008, Pages 57-64

A highly immunogenic, synthetic protein consisting of 21 epitopes from pre-erythrocytic and blood stages of *P. falciparum* (FALVAC-1A) was constructed and expressed in *Escherichia coli*. This vaccine candidate was highly immunogenic and induced protective antibodies in rabbits when produced through lab-scale processes in milligram quantities. In order to take this vaccine candidate for further clinical trial, we optimized the process for industrial scale production and purification. Here we describe various methods used in pilot scale production and characterization of FALVAC-1A. This study confirms that industrial scale clinical grade FALVAC-1A can be produced in a cost-effective manner for clinical trials.

## **MalariaWorld - Knowledge for Solutions**

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