



Bulletin 212 | 8 June 2009

Publications

OPEN ACCESS | Editorial: Good News in Malaria Control... Now What?

Richard W. Steketee

Am J Trop Med Hyg 2009;80 879-880

In this issue of the American Journal of Tropical Medicine and Hygiene, Immo Kleinschmidt and colleagues describe remarkable malaria control progress and benefits on the island of Bioko in Equatorial Guinea over the last 4 years. <http://tinyurl.com/nd9xba>

OPEN ACCESS | Images in Clinical Tropical Medicine: Severe Retinal Whitening in an Adult with Cerebral Malaria

Richard J. Maude, Mahtab Uddin Hassan, and Nicholas A. V. Beare

Am J Trop Med Hyg 2009;80 881

A composite digital photograph of the right retina of a 24-year-old Bangladeshi man with non-fatal cerebral malaria was taken on admission to hospital (Figure 1). He presented with 1 day of unconsciousness, pulmonary edema, and black-water fever. Peripheral blood parasitemia was 79 *Plasmodium falciparum* per 1,000 red cells and hemoglobin was 10.9 g/dL. He recovered consciousness within 48 hours of starting intra- venous artesunate and was discharged home after 6 days. Visual function and neurologic examination were normal on discharge. <http://tinyurl.com/mlpaqq>

OPEN ACCESS | Graph theoretical approach to study eQTL: a case study of Plasmodium falciparum

Yang Huang, Stefan Wuchty, Michael T. Ferdig and Teresa M. Przytycka

Bioinformatics, Vol. 25 ISMB 2009, pages i15–i20, doi:10.1093/bioinformatics/btp189

Analysis of expression quantitative trait loci (eQTL) significantly contributes to the determination of gene regulation programs. However, the discovery and analysis of associations of gene expression levels and their underlying sequence polymorphisms continue to pose many challenges. Methods are limited in their ability to illuminate the full structure of the eQTL data. Most rely on an exhaustive, genome scale search that considers all possible locus–gene pairs and tests the linkage between each locus and gene. <http://tinyurl.com/kur2b8>

OPEN ACCESS | Delay in diagnosis: malaria in a returning traveller

Andrea K. Boggild, Andrea V. Page, Jay S. Keystone, Andrew M. Morris, and W. Conrad Liles

CMAJ. 2009 May 26; 180(11): 1129–1131, doi: 10.1503/cmaj.090171.

Malaria is a potentially fatal, but readily treatable, condition. This case highlights the importance of obtaining a travel history for febrile patients and including malaria in the differential diagnosis for those who have recently travelled to regions where malaria is endemic. Fever is a common manifestation of travel-

acquired illness and occurs in about one-quarter of returning travellers who visit post-travel clinics. <http://tinyurl.com/mxe2hb>

OPEN ACCESS | Review: Adhesion of Plasmodium falciparum-infected erythrocytes to human cells: molecular mechanisms and therapeutic implications

Alexandra Rowe, Antoine Claessens, Ruth A. Corrigan and Mònica Arman

Expert Reviews in Molecular Medicine (2009), 11:e16

Severe malaria has a high mortality rate (15–20%) despite treatment with effective antimalarial drugs. Adjunctive therapies for severe malaria that target the underlying disease process are therefore urgently required. Further research is needed to realise the untapped potential of antiadhesion adjunctive therapies, which could revolutionise the treatment of severe malaria and reduce the high mortality rate of the disease.

OPEN ACCESS | Editorial commentary: Polymerase Chain Reaction Adjustment in Antimalarial Trials: Molecular Malarkey?

Jonathan J. Juliano, Steve M. Taylor, and Steven R. Meshnick

The Journal of Infectious Diseases 1 July 2009, Vol. 200, No. 1: 5-7

Malaria drug trials use both clinical and microbiologic end points to establish efficacy. The recurrence of parasitemia after treatment is an indicator of treatment failure. The study by Faucher et al. [1] from Benin in this issue of the Journal demonstrates both substantial in vivo resistance to sulfadoxine-pyrimethamine (SP) and good effectiveness of 2 new artemisinin combination therapies (ACTs): artemether-lumefantrine (AL) and artesunate-amodiaquine (ASAQ).

OPEN ACCESS | Comparison of Sulfadoxine-Pyrimethamine, Unsupervised Artemether-Lumefantrine, and Unsupervised Artesunate-Amodiaquine Fixed-Dose Formulation for Uncomplicated Plasmodium falciparum Malaria in Benin: A Randomized Effectiveness Noninferiority Trial

Jean-François Faucher et al.

The Journal of Infectious Diseases 1 July 2009, Vol. 200, No. 1: 57-65

We compared sulfadoxine-pyrimethamine (SP) with unsupervised artemether-lumefantrine (AL) and unsupervised amodiaquine-artesunate (ASAQ) fixed-dose formulation for the treatment of uncomplicated malaria in children in Benin. This was the first trial, to our knowledge, to compare unsupervised AL with unsupervised ASAQ fixed-dose formulation; both treatments provided high PCR-adjusted day 28 effectiveness rates. Efficacy rates for SP were surprisingly low.

OPEN ACCESS | Research: Impact of child malnutrition on the specific anti-Plasmodium falciparum antibody response

Florie Fillol, Jean Biram Sarr, Denis Boulanger, Badara Cisse, Cheikh Sokhna, Gilles Riveau, Kirsten Bork Simondon, Franck Remoue

Malaria Journal 2009, 8:116 (2 June 2009)

This study provides further evidence about the influence of malnutrition on the specific anti-malarial immune response and points to the importance of taking child malnutrition into account in malaria epidemiological studies and vaccine trials.

OPEN ACCESS | Methodology: Effective and cheap removal of leukocytes and platelets from Plasmodium vivax infected blood

Kanlaya Sriprawat et al.

Malaria Journal 2009, 8:115 (2 June 2009)

A concise study on alternate methods available for removing white blood cells and platelets from Plasmodium vivax infected blood. Validation of a cheap alternative

will be particularly helpful for disease endemic country scientists with limited access to expensive Plasmidopur filters.

OPEN ACCESS | Research: Utilization, retention and bio-efficacy studies of PermaNet(R) in selected villages in Buie and Fentalie districts of Ethiopia

Messay Fettene, Meshesha Balkew, Ciara Gimblet

Malaria Journal 2009, 8:114 (30 May 2009)

Malaria remains a major public health problem in Ethiopia. Pyrethroid-treated mosquito nets are one of the major tools available for the prevention and control of malaria transmission. PermaNet(R) is a long-lasting insecticide-treated net (LLIN) recommended by WHO for malaria control. The objective of the study was to assess utilization and retention of PermaNet(R) nets distributed for malaria control in Buie and Fentalie districts and monitor the bio-efficacy of the nets using the WHO cone bioassay test procedures.

OPEN ACCESS | Research: Co-ordinated stage-dependent enhancement of Plasmodium falciparum antioxidant enzymes and heat shock protein expression in parasites growing in oxidatively stressed or G6PD-deficient red blood cells

Oskar Bate Akide-Ndunge, Elisa Tambini, Giuliana Giribaldi, Paul J McMillan, Sylke Muller, Paolo Arese, Franco Turrini

Malaria Journal 2009, 8:113 (29 May 2009)

A study of the expression of antioxidant enzymes and heat shock proteins of infected red blood cells under normal and oxidative conditions. Exogenous oxidative stress or cultivation of parasites in G6PD-deficient RBCs resulted in enhanced transcription and expression of all genes tested. The outstanding finding of this investigation is that the expression of Hsps was redox-responsive.

OPEN ACCESS | A New Malaria Agent in African Hominids

Ollomo B, Durand P, Prugnolle F, Douzery E, Arnathau C, et al.

PLoS Pathog 5(5): e1000446. doi:10.1371/journal.ppat.1000446

Plasmodium falciparum is the major human malaria agent responsible for 200 to 300 million infections and one to three million deaths annually, mainly among African infants. The origin and evolution of this pathogen within the human lineage is still unresolved. A single species, P. reichenowi, which infects chimpanzees, is known to be a close sister lineage of P. falciparum. Here we report the discovery of a new Plasmodium species infecting Hominids.

Iodide-SAD, SIR and SIRAS phasing for structure solution of a nucleosome assembly protein

Acta Crystallographica Section D, Volume 65, Issue 6, Date: June 2009, Pages: 618-622, Doi 10.1107/S0907444909013171

The crystal structure of Plasmodium falciparum nucleosome assembly protein (PfNapL) was determined by iodide-SAD/SIRAS phasing methods using iodide-SAD data to 3.0 Å resolution and native data to 2.4 Å resolution. Halide-derivatized PfNapL crystals were obtained using the quick cryo-soaking method in which the native crystals were soaked in a cryosolution consisting of 500 mM NaI for a short period of 30–60 s and data were collected at an in-house X-ray source using Cu K α radiation. Despite a low anomalous signal-to-noise ratio of <1.2 in the >3.5 Å resolution bin, the data were sufficient to determine the structure by SAD/SIR/SIRAS methods using the soaked iodides. Previously, structure solution had failed with both molecular-replacement and selenomethionine-derivatization techniques owing to reasons that are detailed in this work. The phasing at low resolution with three iodides per monomer with high temperature factors was successful using any of the SAD, SIR or SIRAS methods.

Marked Increase in Child Survival after Four Years of Intensive Malaria Control

Immo Kleinschmidt, Christopher Schwabe, Luis Benavente, Miguel Torrez, Frances C. Ridl, Jose Luis Segura, Paul Ehmer, and Gloria Nseng Nchama

Am J Trop Med Hyg 2009;80 882-888

In malaria-endemic countries in Africa, a large proportion of child deaths are directly or indirectly attributable to infection with *Plasmodium falciparum*. Four years after high coverage, multiple malaria control interventions were introduced on Bioko Island, Equatorial Guinea, changes in infection with malarial parasites, anemia, and fever history in children were estimated and assessed in relation to changes in all-cause under-5 mortality.

The Participation of Secondary Clinical Episodes in the Epidemiology of Vivax Malaria during Pre- and Post-Implementation of Focal Control in the State of Oaxaca, Mexico

Mario H. Rodriguez, Angel F. Betanzos-Reyes, Juan E. Hernandez-Avila, Jorge F. Mendez-Galvan, Rogelio Danis-Lozano, and Armando Altamirano-Jimenez

Am J Trop Med Hyg 2009;80 889-895

The participation of vivax malaria secondary clinical was researched in a retrospective cohort of 33,414 confirmed cases occurring between 1994 and 2005 in the state of Oaxaca, Mexico. These findings highlight the need for new therapeutic schemes to radical cure of *P. vivax* infections and operational research aimed at parasite pool elimination.

Malaria and Intestinal Helminth Co-infection Among Pregnant Women in Ghana: Prevalence and Risk Factors

Nelly J. Yatich et al.

Am J Trop Med Hyg 2009;80 896-901

Both malaria and intestinal helminths are endemic in sub-Saharan Africa, and their co-infection occurs commonly. This cross-sectional study assessed the prevalence of malaria and intestinal helminth co-infection in a sample of > 700 pregnant women in Ghana and identified risk factors for co-infection. This study shows relatively high prevalence rates of malaria, intestinal helminths, and co-infection in pregnant women in Ghana.

Antimalarial Drug Susceptibility of Plasmodium vivax in the Republic of Korea

Kesinee Chotivanich et al.

Am J Trop Med Hyg 2009;80 902-904

The antimalarial susceptibility of ring stage (> 80%) *Plasmodium vivax* from the Republic of Korea, where long incubation-period strains are prevalent, was evaluated using the schizont maturation inhibition technique. Compared with *P. vivax* in Thailand, *P. vivax* in the Republic of Korea was more sensitive to quinine and mefloquine, but equally sensitive to chloroquine and artesunate.

Impact of Ministry of Health Interventions on Private Medicine Retailer Knowledge and Practices on Anti-Malarial Treatment in Kenya

Timothy Abuya, Greg Fegan, Yvone Rowa, Baya Karisa, Sam Ochola, Wilfred Mutemi, and Vicki Marsh

Am J Trop Med Hyg 2009;80 905-913

Small-scale interventions on training medicine retailers on malaria treatment improve over-the-counter medicine use, but there is little evidence on effectiveness when scaled up. This study evaluated the impact of Ministry of Health (MoH) training programs on the knowledge and practices of medicine retailers in three districts in Kenya. Large-scale retailer training programs within the national malaria control framework led to significant improvements in retailers' practices across three districts.

Efficacy of Artemisinin-Based Combination Therapy for Treatment of Persons with Uncomplicated Plasmodium falciparum Malaria in West

Sumba District, East Nusa Tenggara Province, Indonesia, and Genotypic Profiles of the Parasite

Puji B. S. Asih et al.

Am J Trop Med Hyg 2009;80 914-918

Reports on treatment failures associated with the use of first-and second-line antimalarial drugs chloroquine and sulfadoxine-pyrimethamine have recently increased in many parts of Indonesia. The present study evaluated artemisinin-based combination therapy for treatment of persons with uncomplicated *Plasmodium falciparum* malaria in West Sumba District, East Nusa Tenggara Province. Artesunate-amodiaquine proved efficacious therapy for treatment of persons with uncomplicated *P. falciparum* malaria at one site in eastern Indonesia but it may have tolerability problems that merit further investigation.

Effect of Malaria Rapid Diagnostic Tests on the Management of Uncomplicated Malaria with Artemether-Lumefantrine in Kenya: A Cluster Randomized Trial

Jacek Skarbinski et al.

Am J Trop Med Hyg 2009;80 919-926

Shortly after Kenya introduced artemether-lumefantrine (AL) for first-line treatment of uncomplicated malaria, we conducted a pre-post cluster randomized controlled trial to assess the effect of providing malaria rapid diagnostic tests (RDTs) on recommended treatment (patients with malaria prescribed AL) and overtreatment (patients without malaria prescribed AL) in outpatients 5 years old. RDTs could potentially improve malaria case management, but we urgently need to develop more effective strategies for implementing guidelines before large scale implementation.

Case Report: Monkey Malaria in Humans: A Diagnostic Dilemma with Conflicting Laboratory Data

Catherine W. M. Ong, Shir Ying Lee, Wee Hong Koh, Eng-Eong Ooi, and Paul A. Tambyah

Am J Trop Med Hyg 2009;80 927-928

Plasmodium knowlesi has recently been recognized as the fifth *Plasmodium* species causing malaria in humans. Diagnosis is difficult morphologically, and currently, available rapid tests have not been comprehensively evaluated with this pathogen. We report a case of *P. knowlesi* malaria that was confirmed after the initial clue of discordant microscopy and immunochromatographic results, highlighting the importance of molecular diagnostics in cases with the relevant clinical and epidemiologic history.

Morphology-sensitive Raman modes of the malaria pigment hemozoin

Torsten Frosch, Sasa Koncarevic, Katja Becker and Jürgen Popp

Analyst, 2009, 134, 1126 - 1132, DOI: 10.1039/b821705j

Resonance Raman spectroscopy was applied for investigating the malaria pigment hemozoin, which is an important target structure of antimalarial drugs.

Resonance Raman microscopy in combination with partial dark-field microscopy lights up a new path in malaria diagnostics

Bayden R. Wood et al.

Analyst, 2009, 134, 1119 - 1125, DOI: 10.1039/b822603b

Our goal is to produce a rapid and accurate diagnostic tool for malaria using resonance Raman spectroscopy to detect small inclusions of haemozoin in *Plasmodium falciparum* infected red blood cells. In pursuit of this aim we serendipitously discovered a partial dark-field effect generated by our experimental setup, which helps identify in thick blood films potential parasites that are normally difficult to see with conventional bright-field microscopy.

Generation and Evaluation of a Homology Model of PfGSK-3

Sebastian Kruggel, Thomas Lemck

Archiv der Pharmazie, Published Online: 27 May 2009

Plasmodial GSK-3 is a potential new target for malaria therapy. For a structure-based design project, the three-dimensional information of the designated target is needed. Unfortunately, experimental structure data for plasmodial GSK-3 is not yet available. Homology building can be used to generate such three-dimensional structure data using structure information of a homologous protein.

Cold War, Deadly Fevers. Malaria Eradication in Mexico 1955–1975 - by Cueto, Marcos

Natalia Priego

Bulletin of Latin American Research, Volume 28, Issue 3, Date: July 2009, Pages: 444-446, 10.1111/j.1470-9856.2009.00310_12.x

No abstract available

Discovery of Plasmepsin Inhibitors by Fragment-Based Docking and Consensus Scoring

Ran Friedman, Dr., Amedeo Caflisch

ChemMedChem, Published Online: 26 May 2009

Plasmepsins (PMs) are essential proteases of the plasmodia parasites and are therefore promising targets for developing drugs against malaria. We have discovered six inhibitors of PM II by high-throughput fragment-based docking of a diversity set of ~40 000 molecules, and consensus scoring with force field energy functions.

Vivax Malaria: A Major Cause of Morbidity in Early Infancy

Jeanne R. Poespoprodjo

Clinical Infectious Diseases. Volume 48, Issue 12, Page 1704–1712, Jun 2009, DOI: 10.1086/599041

In areas where malaria is endemic, infants aged <3 months appear to be relatively protected from symptomatic and severe *Plasmodium falciparum* malaria, but less is known about the effect of *Plasmodium vivax* infection in this age group. *P. vivax* malaria is a major cause of morbidity in early infancy. Preventive strategies, early diagnosis, and prompt treatment should be initiated in the perinatal period.

Correspondence: Risk of Enterically Transmitted Hepatitis A, Hepatitis E, and Plasmodium falciparum Malaria in Afghanistan

Thierry Carmoi, Safi Safiullah, and Elisabeth Nicand

Clinical Infectious Diseases. Volume 48, Issue 12, Page 1800, Jun 2009, DOI: 10.1086/599231

No abstract available

Plasmodium berghei ANKA: Selection of resistance to piperazine and lumefantrine in a mouse model

D.M. Kiboi, B.N. Irungu, B. Langat, S. Wittlin, R. Brun, J. Chollet, O. Abiodun, J.K. Nganga, V.C.S. Nyambati, G.M. Rukunga, A. Bell, A. Nzila

Experimental Parasitology, Volume 122, Issue 3, July 2009, Pages 196-202, doi: 10.1016/j.exppara.2009.03.010

We have selected piperazine (PQ) and lumefantrine (LM) resistant *Plasmodium berghei* ANKA parasite lines in mice by drug pressure. Cross-resistance studies showed that the PQ-resistant line was highly resistant to LM, while the LM-resistant line remained sensitive to PQ. Thus, if the mechanism of resistance is similar in *P. berghei* and *Plasmodium falciparum*, the use of LM (as part of Coartem®) should not select for PQ resistance.

Plasmodium yoelii: Adverse outcome of non-lethal P. yoelii malaria during co-infection with Schistosoma mansoni in BALB/c mouse model

Davison Sangweme, Clive Shiff, Nirbhay Kumar

Experimental Parasitology, Volume 122, Issue 3, July 2009, Pages 254-259, doi: 10.1016/j.exppara.2009.04.003

Plasmodium yoelii and *Schistosoma mansoni* co-infections were studied in female BALB/c mice aged 4–6 weeks to determine the effect of time and stage of concomitant infections on previous term malarianext term disease outcome. The results suggest a complex relationship between schistosome co-infection and previous term malarianext term disease outcome in which the timing of previous term malarianext term infection in relation to schistosome acquisition is critical to disease outcome and pathology.

Existing antimalarial agents and malaria-treatment strategies

Umberto D'Alessandro

Expert Opinion on Pharmacotherapy, June 2009, Vol. 10, No. 8, Pages 1291-1306, DOI 10.1517/14656560902942319

In the absence of prompt and efficacious treatment, malaria patients may progress within a few hours from having minor symptoms to severe disease and death. These last years have seen the development of several artemisinin-based combinations, new treatments for severe malaria patients, and new strategies such as intermittent preventive treatment or the home-based/near-home management of malaria. The health sector is now confronted with several treatment options and strategies, in contrast with the period when chloroquine monotherapy was the standard treatment. The major challenge remains the large-scale deployment, in the most efficient way, of the tools available today, including artemisinin-based combination treatments, within health systems that remain extremely weak in malaria endemic countries, particularly in sub-Saharan Africa.

The salivary transcriptome of *Anopheles gambiae* (Diptera: Culicidae) larvae: A microarray-based analysis

M. Neira Oviedo, J.M.C. Ribeiro, A. Heyland, L. VanEkeris, T. Moroz, P.J. Linsler
Insect Biochemistry and Molecular Biology, Volume 39, Issues 5-6, May-June 2009, Pages 382-394, doi:10.1016/j.ibmb.2009.03.001

In spite of the many recent developments in the field of vector sialomics, the salivary glands of larval mosquitoes have been largely unexplored. We used whole-transcriptome microarray analysis to create a gene-expression profile of the salivary gland tissue of fourth-instar *Anopheles gambiae* larvae, and compare it to the gene-expression profile of a matching group of whole larvae.

Anopheles gambiae* Croquemort SCRQB2, expression profile in the mosquito and its potential interaction with the malaria parasite *Plasmodium berghei

Mónica González-Lázaro et al.

Insect Biochemistry and Molecular Biology, Volume 39, Issues 5-6, May-June 2009, Pages 395-402, doi:10.1016/j.ibmb.2009.03.008

The scavenger receptor family comprises transmembrane proteins involved in the recognition of polyanionic ligands. Several studies have established that members of this family are involved both in immunity and in developmental processes. In *Drosophila melanogaster*, one of the best characterized scavenger receptors is Croquemort, which participates in the recognition of apoptotic cells in the embryo. Although comparative genomic studies have revealed the presence of four orthologs of this receptor in the malaria vector *Anopheles gambiae*, little is known about their function. We have investigated the expression pattern of the four Croquemort orthologs during the mosquito life cycle.

PfEMP1: An antigen that plays a key role in the pathogenicity and immune evasion of the malaria parasite *Plasmodium falciparum*

Noa D. Pasternak, Ron Dzikowski

The International Journal of Biochemistry & Cell Biology, Volume 41, Issue 7, July 2009, Pages 1463-1466, doi:10.1016/j.biocel.2008.12.012

P. falciparum virulence is attributed to its ability to evade the human immune system by modifying infected host red blood cells to adhere to the vascular endothelium and to undergo antigenic variation. The main antigenic ligands responsible for both cytoadherence and antigenic variation are members of the *P. falciparum* Erythrocyte Membrane Protein-1 (PfEMP1) family. These polymorphic proteins are encoded by a multi-copy gene family called var. Each individual parasite expresses a single var gene at a time, maintaining the remaining not, vert, similar60 var genes found in its genome in a transcriptionally silent state. As the antibody response against the single expressed PfEMP1 develops, small sub-populations of parasites switch expression to alternative forms of PfEMP1 and re-establish the infection. Therefore, PfEMP1 is considered a key player in the pathogenicity of *P. falciparum*.

MAPK-activated Protein Kinase 2 Differentially Regulates Plasmodium falciparum Glycosylphosphatidylinositol-induced Production of Tumor Necrosis Factor- α and Interleukin-12 in Macrophages

Jianzhong Zhu et al.

J. Biol. Chem. 2009;284 15750-15761

Proinflammatory responses induced by *Plasmodium falciparum* glycosylphosphatidylinositols (GPIs) are thought to be involved in malaria pathogenesis. In this study, we investigated the role of MAPK-activated protein kinase 2 (MK2) in the regulation of tumor necrosis factor- (TNF-) and interleukin (IL)-12, two of the major inflammatory cytokines produced by macrophages stimulated with GPIs. We show that MK2 differentially regulates the GPI-induced production of TNF- and IL-12.

Buffer Optimization of Thermal Melt Assays of Plasmodium Proteins for Detection of Small-Molecule Ligands

Gregory J. Crowther

Journal of Biomolecular Screening 2009, doi:10.1177/1087057109335749

In the past decade, thermal melt/thermal shift assays have become a common tool for identifying ligands and other factors that stabilize specific proteins. Increased stability is indicated by an increase in the protein's melting temperature (T_m). In optimizing the assays for subsequent screening of compound libraries, it is important to minimize the variability of T_m measurements so as to maximize the assay's ability to detect potential ligands. The authors present an investigation of T_m variability in recombinant proteins from *Plasmodium* parasites.

High Prevalence of Asymptomatic Plasmodium falciparum Infections in a Highland Area of Western Kenya: A Cohort Study

Frederick N. Baliraine, Yaw A. Afrane et al.

The Journal of Infectious Diseases 1 July 2009, Vol. 200, No. 1: 66-74

Transmission of malaria in an area of hypoendemicity in the highlands of western Kenya is not expected to lead to rapid acquisition of immunity to malaria. However, the subpopulation of individuals with asymptomatic *Plasmodium falciparum* infection may play a significant role as an infection reservoir and should be considered in malaria-control programs. Determination of the spatiotemporal dynamics of asymptomatic subpopulations provides an opportunity to estimate the epidemiological importance of this group to malaria transmission.

Toll-like receptors, a double-edged sword in immunity to malaria

Chen Jide, He Ying, Xu Wenyue, Huang Fusheng

Toll-like receptors (TLRs) are a central component of innate immune system and play a major role as the initiator of the innate immune responses to defend against bacteria, viruses, parasite and other pathogens. During malaria infection, TLRs signaling pathways are initiated with the recognition of Plasmodium glycosylphosphatidylinositols (GPI) and hemozoin as pathogen-associated molecular patterns (PAMPs). And then, activation of TLRs signaling induces specific biological responses against malaria parasites invasion. However, TLRs are also involved in malaria pathogenesis and enhancement of immune tolerance and evasion for malaria infection. Moreover, malaria parasites regulate selectively TLRs expression on immune cells. Thus, these evidences indicated that TLRs have contrary roles on malaria infection. Understanding the complicated roles of TLRs on malaria infection will contribute us to design more effective anti-malaria drugs or vaccines.

Antiplasmodial and Antidiabetic Activities of Ethanolic Leaf Extract of Heinsia crinata

Jude E. Okokon, Emem E. Umoh, Emmanuel I. Etim, Clement L. Jackson

Journal of Medicinal Food. February 2009, 12(1): 131-136, doi:10.1089/jmf.2008.0116.

The ethanolic leaf extract of Heinsia crinata, grown particularly for the leaf in Niger Delta region of Nigeria, was evaluated for antiplasmodial activity in Plasmodium berghei-infected mice as well as for hypoglycemic and antidiabetic activities in alloxan-induced diabetic rats. The results suggest that the leaf extract of H. crinata possesses significant ($P < .05$) antiplasmodial as well as hypoglycemic and antidiabetic effects that can be employed in health care.

Plasmodium falciparum malaria in pregnancy: Prevalence of peripheral parasitaemia, anaemia and malaria care-seeking behaviour among pregnant women attending two antenatal clinics in Edo State, Nigeria

E. F. O. Enato; P. F. Mens; A. O. Okhamafe; E. E. Okpere; E. Pogoson; H. D. F. H. Schallig

Journal of Obstetrics and Gynaecology, Volume 29, Issue 4 May 2009 , pages 301 – 306, DOI: 10.1080/01443610902883320

This study evaluated malaria care-seeking behaviour, as well as the prevalence of parasitaemia and anaemia among pregnant women attending antenatal clinics of two tertiary healthcare facilities in Edo State, Nigeria. Efforts to improve antimalaria healthcare must be intensified, targeting pregnant women, particularly the primigravidae and secundigravidae and the healthcare providers.

Prevalence, risk factors and effects of placental malaria in the UMTH, Maiduguri, North-eastern, Nigeria: A cross-sectional study

B. G. Bako; B. M. Audu; A. D. Geidam; A. A. Kullima; G. M. Ashiru; M. B. Malah; H. A. Ngadda; A. B. Musa

Journal of Obstetrics and Gynaecology, Volume 29, Issue 4 May 2009 , pages 307 – 310, DOI: 10.1080/01443610902878783

Most of the adverse effects of malaria in pregnancy on the fetus are usually as a consequence of placental malaria (PM). This study was conducted with the objective of determining the prevalence, risk factors and pregnancy outcome of PM.

Autofluorescence of Condensed Heme Aggregates in Malaria Pigment and Its Synthetic Equivalent Hematin Anhydride (β -Hematin)

Marie-Jose Bellemare et al.

J. Phys. Chem. B, Article ASAP, DOI: 10.1021/jp8104375

The condensed crystalline phase of iron(III) protoporphyrin IX either isolated from parasite culture as malaria pigment (hemozoin) or synthetic equivalent hematin anhydride exhibits a solid-state autofluorescence characterized by an excitation maximum of 555 nm and an emission maximum of 577 nm. The autofluorescence can be used for in vivo tracking of hemozoin, for determination of parasitemia levels, and for infection monitoring and possibly for drug screening studies.

Liquid Chromatography: Quantitation of SAR97276 in mouse tissues by rapid resolution liquid chromatography-mass spectrometry

Delphine Margout, Sharon Wein, Hermine Gandon, Florence Gattacceca, Henri J. Vial, Françoise M. M. Bressolle

Journal of Separation Science, Volume 32, Issue 11, Date: June 2009, Pages: 1808-1815, doi 10.1002/jssc.200900059

1,12-Bis[5-(2-hydroxyethyl)-4-methyl-1,3-thiazol-3-ium]dodecane dibromide (SAR97276, T3) is a new antimalarial drug, which is currently being evaluated in clinical trials for severe malaria. Drug accumulation inside the parasite and a dual mechanism of action are a major strength of this compound, as it could help delay the development of resistance. The purpose of this article was to develop a rapid resolution LC-MS method for quantifying SAR97276 in mouse tissues.

News In Brief: Malaria vaccine enters phase III clinical trials

Nature 459, 627-627 (3 June 2009), doi:10.1038/459627c

GlaxoSmithKline's RTS,S malaria vaccine entered its final phase of pre-approval testing last week in Bagamoyo, Tanzania. In the coming months, the study will become the largest ever trial of a malaria vaccine candidate, involving 16,000 children under the age of two at eleven sites.

Genome-wide and fine-resolution association analysis of malaria in West Africa

Muminatou Jallow et al.

Nature Genetics 41, 657 - 665 (2009), doi:10.1038/ng.388

Dominic Kwiatkowski and colleagues of the MalariaGEN and the WTCCC consortiums report a genome-wide analysis of severe malaria in The Gambia. They provide guidance for design of GWAS in African populations, and demonstrate the usefulness of multipoint imputation based on population-specific sequencing data.

Research highlight: Antimalarial drugs: Double whammy

Nature Reviews Drug Discovery 8, 451 (June 2009) | doi:10.1038/nrd2902

No abstract available

Feature: The anti-Methuselah bug: A plague on plagues

Rachel Nowak

The New Scientist, Volume 202, Issue 2710, 27 May 2009, Pages 38-41, doi: 10.1016/S0262-4079(09)61452-4

A cunning new strategy promises to eliminate killers like dengue and malaria, but it's not without risk.

Antiplasmodial and other constituents from four Indonesian Garcinia spp.

Elfita Elfita et al.

Phytochemistry, In Press, Corrected Proof, Available online 27 May 2009

Phytochemical investigations of four Garcinia spp. from Indonesia, i.e. *Garcinia griffithii* T. Anderson, *Garcinia celebica* L., *Garcinia cornea* L. and *Garcinia cymosa* K. Schum (Clusiaceae), have resulted in the isolation of a xanthone, 1,5-dihydroxy-3,6-dimethoxy-2,7-diprenylxanthone, 1,7-dihydroxyxanthone, isoxanthochymol, β -sitosterol-3-O- β -d-glucoside and stigmasterol-3-O- β -d-

glucoside from the stem bark of *G. griffithii*; friedelin and 3 β -hydroxy-23-oxo-9,16-lanostadien-26-oic acid or garcihombronane D from leaves of *G. celebica*; 23-hydroxy-3-oxo-cycloart-24-en-26-oic acid and epicatechin from stem bark of *G. cornea*; (\pm)-morelloflavone, morelloflavone-7-O- β -d-glucoside or fukugiside, the triterpene 3 β -hydroxy-5-glutinen-28-oic acid and canophyllol from stem bark of *G. cymosa*. The xanthone and garcihombronane D displayed a selective activity against *Plasmodium falciparum*; isoxanthochymol and the triterpene β -hydroxy-5-glutinen-28-oic acid a broad but non-selective antiprotozoal activity.

Phytotherapy used in orissa state, india for treating malaria Venkata Siva Satyanarayana Kantamreddi, Sagarika Parida, Suryanarayana Murty Kommula, Colin W. Wright

Phytotherapy Research, Early View

This paper reports 35 medicinal plants belonging to 25 families used in the treatment of malaria by the people inhabiting the forests located near to Bhubaneswar, the capital city of Orissa, a south-eastern state in India. The methods adopted for the preparation of plant parts are discussed along with their family and local name(s).

Letter: On the location of the aminopeptidase N homolog PfA-M1 in Plasmodium falciparum

Michael Klemba

PNAS 2009 106:E55; published online before print May 22, 2009, doi:10.1073/pnas.0903493106

The malaria parasite *Plasmodium falciparum* contains a single aminopeptidase N homolog (termed PfA-M1; ref. 1 1) that has been proposed to play an important role in the parasite's catabolism of host red blood cell hemoglobin in its food vacuole (1 2).

Letter: Reply to Klemba: Intracellular processing of the membrane-bound PfA-M1 neutral aminopeptidase, a target for new antimalarials

James C. Whisstock, Sheena McGowan, Katharine R. Trenholme, Donald L. Gardiner, and John P. Dalton

PNAS 2009 106:E56; published online before print May 22, 2009, doi:10.1073/pnas.0903872106

In reply to Michael Klemba's letter (1 1), we investigated the cellular location of the PfA-M1 aminopeptidase by transfecting *Plasmodium falciparum* malaria with a GFP-PfA-M1 conjugate and by probing parasite-infected erythrocytes with antibodies prepared against the recombinant protein; these antibodies should bind to native full-length protease (1 2).

Competitive facilitation of drug-resistant Plasmodium falciparum malaria parasites in pregnant women who receive preventive treatment

W. E. Harrington, T. K. Mutabingwa, A. Muehlenbachs, B. Sorensen, M. C. Bolla, M. Fried, and P. E. Duffy

PNAS 2009 106:9027-9032; published online before print May 18, 2009, doi: 10.1073/pnas.0901415106

Intermittent preventive treatment in pregnancy (IPTp) is used to prevent *Plasmodium falciparum* malaria. However, parasites resistant to the IPTp drug sulfadoxine-pyrimethamine (SP) have emerged worldwide, and infections with mixed resistant and susceptible parasites are exacerbated by pyrimethamine in mice. In a prospective delivery cohort in Muheza, Tanzania, we examined the effects of SP IPTp on parasite resistance alleles, parasite diversity, level of parasitemia, and inflammation in the placenta.

Short communication: Impact assessment of the use of insecticide-treated bed nets on parasitaemia and anaemia for malaria control in children, Ogun State, Nigeria

P.O. Adah, C.F. Mafiana, S.O. Sam-Wobo

Public Health, Volume 123, Issue 5, May 2009, Pages 390-392, doi:10.1016/j.puhe.2008.10.017

No abstract available

Estimation of parasite load using Rapid diagnostic test ICT [®]Now Malaria P.f/P.v in Plasmodium falciparum malaria

Najia K. Ghanchi, Mohammad A. Beg, Rabia Hussain

Scandinavian Journal of Infectious Diseases, DOI: 10.1080/00365540903022832

Rapid tests such as ICT Malaria are an effective field tool in determining the presence of malarial parasites but do not provide an estimate of parasite load. We have evaluated the utility of ICT for providing semi-quantitative estimates of parasite load. Rapid semi-quantitative assessment of parasite load in conjunction with the Plasmodium speciation may provide a useful bedside and field aid in the diagnosis of malaria.

Research Focus: Purine uptake in Plasmodium: transport versus metabolism

Kiaran Kirk, Susan M. Howitt, Stefan Bröer, Kevin J. Saliba, Megan J. Downie

Trends in Parasitology, Volume 25, Issue 6, June 2009, Pages 246-249, doi: 10.1016/j.pt.2009.03.006

In a recent paper, Quashie et al. have proposed that purine uptake into the intraerythrocytic malaria parasite involves four different plasma membrane transporters – two high affinity and two low affinity. They equate one of the two high-affinity transporters with PfNT1, a transporter reported previously to be a low-affinity system. Here, we offer an alternative interpretation of their data, suggesting that the conclusions drawn by Quashie et al. take insufficient account of metabolism.

Review: The role of the Maurer's clefts in protein transport in Plasmodium falciparum

Tobili Y. Sam-Yellowe

Trends in Parasitology, Volume 25, Issue 6, June 2009, Pages 277-284, doi: 10.1016/j.pt.2009.03.009

Maurer's clefts (MCs) are membranous structures that are formed by *Plasmodium falciparum* and used by the parasite for protein sorting and protein export. Virulence proteins, as well as other proteins used to remodel the erythrocyte, are exported. Discontinuity between major membrane compartments within the infected erythrocyte cytoplasm suggests multiple traffic routes for exported proteins. The sequences of the conserved *Plasmodium* export element seem insufficient for export of all parasite proteins. The parasite displays remarkable versatility in the types of proteins exported to the MCs and in the functions of the proteins within the MCs. In this Review, protein export to the MCs and the role of the MCs in the transport of proteins to the erythrocyte membrane are summarized.

Jobs



Group leader in Molecular Parasitology

Deadline for application: 30 June 2009

The Swiss Tropical Institute (STI) in Basel, Switzerland, seeks applications for the position of a tenure track group leader in

Molecular Parasitology.

The candidate is expected to develop an independent research program to complement ongoing programs on vaccine and drug development, molecular epidemiology, and cell biology of malaria. Emphasis should be placed on proteomic studies, in particular to understand nuclear function and gene regulation. The candidate is expected to participate in graduate and post-graduate teaching of the University of Basel.

The Swiss Tropical Institute is a multi-disciplinary health research institution affiliated to the University of Basel, and offers a young and dynamic research environment. Description of our activities can be found **at <http://www.sti.ch>** and following the link to the biennial report.

Submit a current C.V. and an outline of a research plan, as well as names, telephone numbers, e-mail addresses of three references until 30th June 2009 to: Swiss Tropical Institute, Human Resources, Socinstrasse 57, Postfach, CH 4002 Basel, Switzerland.

News

Africa

7 June 2009, New Vision

Uganda: Malaria Cases Increase in Kibaale

Kagadi Hospital in Kibaale district has been overwhelmed by malaria patients.

2 June 2009, SciDev.Net

Tanzania: Malaria Vaccine Enters Final Tests

Hopes that a malaria vaccine could be widely available by 2012 have risen with the start last week (26 May) of phase III trials of the world's most advanced candidate.

2 June 2009, Vanguard

Nigeria: Nafdac Seizes N32 Million Fake Anti-Malarial Drugs The National Agency for Food and Drug Administration and Control (NAFDAC), has foiled an attempt to import into the country a consignment of fake and adulterated antimalarial drugs Maloxine and Amalar tablets with an estimated street value of N32.1 million.

1 June 2009, This Day

Nigeria: Eliminating Mosquitoes - Battle Without End? [analysis]

If other parts of the world, especially the developed countries have completely eradicated malaria, Africa, especially Nigeria should do something drastic to tackle the problem that is killing their productive population and eating deep into their economy. Agha Ibiam writes

28 May 2009, Africa Science News Service

Kenya: Tanzania introduces new testing kit for malaria

Dr Sixbert Mkude, an official from the National Malaria Control Programme (NMCP) said in the initial stage, RDT machines had been placed in all government hospitals in Dar es Salaam Region, adding that they were expected to be launched in Iringa Region next month and eventually placed in all health centres in the country.

Asia

3 June 2009, Merinews

India: Multi drug resistant malaria: A review

Malaria is reemerging world wide. Plasmodium falciparum malaria has been recognised for its multi drug resistance factor. World Health Organisation has recommended Halofantrine drug to treat multi drug resistance malaria.

3 June 2009, Times of India

India: Steps on to curb malaria in Margao

In a bid to keep a check on malaria this monsoon, the urban health centre, Margao has begun a major drive to issue health cards to migrant labourers at various construction sites situated in the jurisdiction of Margao and Fatorda.

2 June 2009, Orissadiary.com

India: Vedanta starts Anti-malaria Drive in Lanjigarh of Orissa

Lanjigarh: Vedanta Aluminium, Lanjigarh organized a two-day workshop on eradication of malaria on June 01 and 02, 2009 to launch its 'Roll Back Malaria' program in collaboration with District Head Quarter Hospital, Kalahandi and National Vector Borne Disease Control Program, Bhubaneswar.

1 June 2009, KanglaOnline

India: Joint effort urged to eradicate malaria

There is still need for a joint effort by all sections of the public in order to eradicate malaria from the state, said state health and family welfare minister, Ph Parijat while inaugurating a month-long 'Anti Malaria Month' at the Kangla hall in Imphal this morning. The function was organised by the Manipur State Vector Borne Disease Control Society under the theme 'Malaria control: everyone's concern.'

30 May 2009, Daily News & Analysis

India: Malaria has got 'deadlier'

Mumbai: Malaria is likely to become more virulent, fear international experts after they found the parasite becoming resistant to the most effective drug used worldwide to treat it. If not controlled in time, it could kill millions, they warn.

Americas

2 June 2009, NgEX

USA: Federal government plans to eradicate malaria in Nigeria by 2013

The News Agency of Nigeria reported that the federal government plans to eradicate malaria in Nigeria by 2013. The govts says by 2013 malaria will no longer be a major public health problem and families will have universal access to prevention and treatment.

29 May 2009, Science Daily (press release)

USA: New Malaria Agent Found In Chimpanzees Close To That Commonly Observed In Humans

Researchers based in Gabon and France report the discovery of a new malaria agent infecting chimpanzees in Central Africa. This new species, named Plasmodium gaboni, is a close relative of the most virulent human agent P. falciparum.

29 May 2009, DigitalJournal.com

Canada: Malaria resistance to most effective drugs proven in Cambodia

About half the world's population is exposed to endemic malaria. The ancient disease, which was the plague of early civilizations, kills a million people a year, even today. Now, it's showing resistance to the artemisinin class of drugs in Cambodia.

28 May 2009, Online Journal

USA: Defeating malaria one mosquito net at a time

In the last decade, by providing insecticide treated mosquito nets to its people, and more importantly, making sure that every net is retreated every three months, Eritrea, in the impoverished, war torn Horn of Africa, has reduced malaria mortality by an astonishing 85 percent.

28 May 2009, Reuters

USA: Climate health costs: bug-borne ills, killer heat

Tree-munching beetles, malaria-carrying mosquitoes and deer ticks that spread Lyme disease are three living signs that climate change is likely to exact a heavy toll on human health.

28 May 2009, EurekAlert (press release)

USA: New malaria agent found in chimpanzees close to that commonly observed in humans

Researchers based in Gabon and France report the discovery of a new malaria agent infecting chimpanzees in Central Africa. This new species, named *Plasmodium gaboni*, is a close relative of the most virulent human agent *P. falciparum*; it is described in an article published May 29 in the open-access journal PLoS Pathogens.

27 May 2009, Examiner.com

USA: Islamic Relief's fight against malaria: a deadly, but preventable, disease

In his article published today, the National Islamic Examiner Yusuf Khan discusses Islamic Relief's campaign Bite the Bug to eradicate malaria. This article discusses this deadly disease and why Islamic Relief's effort is so important.

Europe

2 June 2009, Telegraph.co.uk

United Kingdom: Galapagos giant tortoise 'at risk from malaria brought in by tourists'

The Galapagos giant tortoise and other unique wildlife on the island are facing a new threat from diseases brought in by tourists, claim scientists.

29 May 2009, BBC News

UK: New fears over anti-malaria drugs

Scientists working with the World Health Organisation say they have found the first evidence of resistance to the world's most effective anti-malaria drugs.

29 May 2009, ReliefWeb (press release)

Switzerland: UK-backed anti-malaria initiative could cost lives

Promotion of medicine distribution through private shops instead of expanding public health care risks accelerating the spread of drug-resistant strains of malaria in developing countries, Oxfam warned today.

28 May 2009, TropIKA

Switzerland: Redesign your house to stop malaria

Insecticide-treated bednets (ITNs) now play a big part in malaria control programmes. They have been shown to be effective in protecting those who sleep under them from mosquito bites and to reduce the incidence of malaria. But during the hours that mosquitoes are out and about adults, in particular, do not spend all their time in bed. Researchers in Kenya, working in a rural area in the west of the country, have been looking at ways of reducing the number of mosquitoes entering the house itself.

MalariaWorld - Knowledge for Empowerment & Solutions

K&S Consulting is an independent consultancy firm concerned with medical information provision, training activities, and infectious diseases consultations.

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