



Bulletin 225 | 28 September 2009

## From K&S

We shall soon be back with our News section. For the time being, visit the Newsflash at our website [www.malariaworld.org](http://www.malariaworld.org) for the latest news.

More publications later this week.

Kind regards,  
Inga & Bart

## Publications

### Open access

#### **Revisiting the Plasmodium falciparum RIFIN family: from comparative genomics to 3D-model prediction**

Bultrini E, Brick K, Mukherjee S, Zhang Y, Silvestrini F, Alano P, Pizzi E  
BMC Genomics 2009, 10:445 (21 September 2009)

Subtelomeric RIFIN genes constitute the most abundant multigene family in Plasmodium falciparum. RIFIN products are targets for the human immune response and contribute to the antigenic variability of the parasite. They are transmembrane proteins grouped into two sub-families (RIF\_A and RIF\_B). Although recent data show that RIF\_A and RIF\_B have different sub-cellular localisations and possibly different functions, the same structural organisation has been proposed for members of the two sub-families. Despite recent advances, our knowledge of the regulation of RIFIN gene expression is still poor and the biological role of the protein products remain obscure. <http://tinyurl.com/ya4zzfu>

### Open access

#### **House screening for malaria control**

John E Gimnig, Laurence Slutsker

The Lancet, Volume 374, Issue 9694, 19 September 2009-25 September 2009, Pages 954-955, doi:10.1016/S0140-6736(09)61078-3

Refers to: Effect of two different house screening interventions on exposure to malaria vectors and on anaemia in children in The Gambia: a randomised controlled trial

The Lancet, Volume 374, Issue 9694, 19 September 2009-25 September 2009, Pages 998-1009,

Matthew J Kirby et al. <http://tinyurl.com/y99luwq>



Open access

**Effect of two different house screening interventions on exposure to malaria vectors and on anaemia in children in The Gambia: a randomised controlled trial**

Matthew J Kirby et al.

The Lancet, Volume 374, Issue 9694, 19 September 2009-25 September 2009, Pages 998-1009, doi:10.1016/S0140-6736(09)60871-0

House screening should protect people against malaria. We assessed whether two types of house screening—full screening of windows, doors, and closing eaves, or installation of screened ceilings—could reduce house entry of malaria vectors and frequency of anaemia in children in an area of seasonal malaria transmission.

House screening substantially reduced the number of mosquitoes inside houses and could contribute to prevention of anaemia in children. <http://tinyurl.com/yc88frp>

Open access

**Reliable enumeration of malaria parasites in thick blood films using digital image analysis**

John A Freaan

Malaria Journal 2009, 8:218 (23 September 2009)

This paper describes the definition and evaluation of a computer-based imaging algorithm for enumeration of malaria parasites in thick films. While still a long way to go from routine use, the accuracy afforded by the technique may be relevant for clinical studies of vaccines or drugs. <http://tinyurl.com/y89d6sv>

Open access

**Geographic information system (GIS) maps and malaria control monitoring: intervention coverage and health outcome in distal villages of Khammouane province, Laos**

Yoshihisa Shirayama, Samlane Phompida, Kenji Shibuya

Malaria Journal 2009, 8:217 (22 September 2009)

Interesting results from poorly known communities of Laos. <http://tinyurl.com/y9ukdvo>

Open access

**An heteroskedastic error covariance matrix estimator using a first-order conditional autoregressive Markov simulation for deriving asymptotical efficient estimates from ecological sampled *Anopheles arabiensis* aquatic habitat covariates**

Benjamin G Jacob, Daniel A Griffith, Ephantus J Muturi, Erick X Caamano, John I Githure, Robert J Novak



Malaria Journal 2009, 8:216 (21 September 2009)

Various different analytical methods are applied to field data on mosquito larvae from rice fields at a well-characterized study site in the Mwea Irrigation scheme of Kenya. <http://tinyurl.com/yeltlvb>

Open access

### **Inversion 2La is associated with enhanced desiccation resistance in *Anopheles gambiae***

Emilie M Gray, Kyle AC Rocca, Carlo Costantini, Nora J Besansky

Malaria Journal 2009, 8:215 (21 September 2009)

This paper presents a very focused analysis of adult mosquito characteristics relevant to desiccation resistance. The major finding is that phenotypic characteristics of the adult female mosquitoes show an inversion-correlated resistance to desiccation phenotype shortly after emergence. <http://tinyurl.com/y9qj9r5>

Open access

### **Competitive endothelial adhesion between *Plasmodium falciparum* isolates under physiological flow conditions**

Happy Phiri, Jacqui Montgomery, Malcolm Molyneux, Alister Craig

Malaria Journal 2009, 8:214 (21 September 2009)

Sequestration of parasitized red blood cells in the microvasculature of major organs involves a sequence of events that is believed to contribute to the pathogenesis of severe falciparum malaria. *Plasmodium falciparum* infections are commonly composed of multiple subpopulations of parasites with varied adhesive properties. A key question is: do these subpopulations compete for adhesion to endothelium? This study investigated whether, in a laboratory model of cytoadherence, there is competition in binding to endothelium between pRBC infected with *P. falciparum* of variant adhesive phenotypes, particularly under flow conditions. <http://tinyurl.com/yatzweo>

Open access

### **Use of the slide positivity rate to estimate changes in malaria incidence in a cohort of Ugandan children**

Trevor P Jensen, Hasifa Bukirwa, Denise Njama-Meya, Damon Francis, Moses R Kanya, Philip J Rosenthal, Grant Dorsey

Malaria Journal 2009, 8:213 (15 September 2009)

As malaria control efforts intensify, it is critical to monitor trends in disease burden and measure the impact of interventions. A key surveillance indicator is the incidence of malaria. Yet measurement of incidence is challenging. The slide positivity rate (SPR) has been used as a surrogate measure of malaria incidence, but limited data exist on the relationship between SPR and the incidence of malaria. <http://tinyurl.com/ya2pw6k>



Open access

### **The role of simple mathematical models in malaria elimination strategy design**

Lisa J White et al.

Malaria Journal 2009, 8:212 (14 September 2009)

Mathematical models of various levels of complexity have been produced to consider the control and elimination of malaria infection. If available, detailed data on malaria transmission (such as the vector life cycle and behaviour, human population behaviour, the acquisition and decay of immunity, heterogeneities in transmission intensity, age profiles of clinical and subclinical infection) can be used to populate complex transmission models that can then be used to design control strategy. However, in many malaria countries reliable data are not available and policy must be formed based on information like an estimate of the average parasite prevalence. <http://tinyurl.com/yarlk6b>

Open access

### **Altered Immune Responses in Rhesus Macaques Co-Infected with SIV and Plasmodium cynomolgi: An Animal Model for Coincident AIDS and Relapsing Malaria**

Koehler JW, Bolton M, Rollins A, Snook K, deHaro E, et al.

PLoS ONE 4(9): e7139. doi:10.1371/journal.pone.0007139

Dual epidemics of the malaria parasite Plasmodium and HIV-1 in sub-Saharan Africa and Asia present a significant risk for co-infection in these overlapping endemic regions. Recent studies of HIV/Plasmodium falciparum co-infection have reported significant interactions of these pathogens, including more rapid CD4+ T cell loss, increased viral load, increased immunosuppression, and increased episodes of clinical malaria. Here, we describe a novel rhesus macaque model for co-infection that supports and expands upon findings in human co-infection studies and can be used to identify interactions between these two pathogens. <http://tinyurl.com/yb7ldxb>

Open access

### **Differential, Positional-Dependent Transcriptional Response of Antigenic Variation (var) Genes to Biological Stress in Plasmodium falciparum**

Rosenberg E, Ben-Shmuel A, Shalev O, Sinay R, Cowman A, et al.

PLoS ONE 4(9): e6991. doi:10.1371/journal.pone.0006991

1% of the genes of the human malaria causing agent Plasmodium falciparum belong to the heterogeneous var gene family which encodes P. falciparum erythrocyte membrane protein 1 (PFEMP1). This protein mediates part of the pathogenesis of the disease by causing adherence of infected erythrocytes (IE) to the host endothelium. At any given time, only one copy of the family is expressed on the IE surface. The cues which regulate the allelic exclusion of these genes are not known. We show the existence of a differential expression pattern of these genes upon exposure to biological stress in relation to their



positional placement on the chromosome – expression of centrally located var genes is induced while sub-telomeric copies of the family are repressed - this phenomenon orchestrated by the histone deacetylase pfsir2. <http://tinyurl.com/kmtqdy>

Open access

**Fine Pathogen Discrimination within the APL1 Gene Family Protects Anopheles gambiae against Human and Rodent Malaria Species.**

Mitri C, Jacques J-C, Thiery I, Riehle MM, Xu J, et al.

PLoS Pathog 5(9): e1000576. doi:10.1371/journal.ppat.1000576

Genetically controlled resistance of *Anopheles gambiae* mosquitoes to *Plasmodium falciparum* is a common trait in the natural population, and a cluster of natural resistance loci were mapped to the Plasmodium-Resistance Island (PRI) of the *A. gambiae* genome. The APL1 family of leucine-rich repeat (LRR) proteins was highlighted by candidate gene studies in the PRI, and is comprised of paralogs APL1A, APL1B and APL1C that share  $\geq 50\%$  amino acid identity. Here, we present a functional analysis of the joint response of APL1 family members during mosquito infection with human and rodent *Plasmodium* species. <http://tinyurl.com/yc5xfuy>

Open access

**From the Cover: Heme oxygenase-1 affords protection against noncerebral forms of severe malaria**

Elsa Seixas et al.

PNAS September 15, 2009 vol. 106 no. 37 15837-15842

Infection by *Plasmodium*, the causative agent of malaria, is associated with hemolysis and therefore with release of hemoglobin from RBC. Under inflammatory conditions, cell-free hemoglobin can be oxidized, releasing its heme prosthetic groups and producing deleterious free heme. Here we demonstrate that survival of a *Plasmodium*-infected host relies strictly on its ability to prevent the cytotoxic effects of free heme via the expression of the heme-catabolizing enzyme heme oxygenase-1 (HO-1; encoded by the Hmox1 gene). <http://tinyurl.com/yd774ze>

Open access

**Evolution: From the Cover: The origin of malignant malaria**

Stephen M. Rich et al.

PNAS September 1, 2009 vol. 106 no. 35 14902-14907

The closest known relative of *P. falciparum* is a chimpanzee parasite, *Plasmodium reichenowi*, of which one single isolate was previously known. The co-speciation hypothesis suggests that both parasites evolved separately from a common ancestor over the last 5–7 million years, in parallel with the divergence of their hosts, the hominin and chimpanzee lineages. Genetic analysis of eight new isolates of *P. reichenowi*, from wild and wild-born captive



chimpanzees in Cameroon and Côte d'Ivoire, shows that *P. reichenowi* is a geographically widespread and genetically diverse chimpanzee parasite. <http://tinyurl.com/yb7erkg>

Open access

### **Ecology: From the Cover: Understanding the link between malaria risk and climate**

Krijn P. Paaijmans, Andrew F. Read, and Matthew B. Thomas

PNAS August 18, 2009 vol. 106 no. 33 13844-13849

Here we use a thermodynamic malaria development model to demonstrate that temperature fluctuation can substantially alter the incubation period of the parasite, and hence malaria transmission rates. We find that, in general, temperature fluctuation reduces the impact of increases in mean temperature. <http://tinyurl.com/mceflb>

### **Health research ethics in public health: Trials and implementation of malaria mosquito control strategies**

Wen L. Kilama

Acta Tropica, Volume 112, Supplement 1, November 2009, Pages S37-S47, doi:10.1016/j.actatropica.2009.08.003

Health research ethics has its roots in protecting individuals participating in clinical trials. There is, however, nascent interest in ethics in public health, although it does not yet cover ethics in the development of public health products. The paper reviews the history of the development of malaria vector interventions, which initially aimed at promoting colonial interests. <http://tinyurl.com/y9396em>

### **Variations in the mitochondrial DNA markers in the Anopheles (Cellia) sundaicus population from the Andaman and Nicobar Islands, India**

Hema Bora, Manoj K. Das, Anwar Ahmed, Yagya D. Sharma

Acta Tropica, Volume 112, Issue 2, November 2009, Pages 120-124

Four sibling species in the *Anopheles sundaicus* complex have earlier been reported, including species D from the Andaman and Nicobar Islands of India where it constitutes 58% of all *Anopheles* population and is a major malaria vector. Earlier, we have reported the identical sequences for ribosomal DNA markers among the specimens of *A. sundaicus* from Andaman and Nicobar islands irrespective of their habitat. These ITS2 sequences were also identical to the reported sequence of variant III of Southeast Asian *A. sundaicus*. In the present study, we describe variations in three mitochondrial DNA markers among these specimens from Andaman and Nicobar islands. <http://tinyurl.com/y8z523r>



### **Knowledge, attitude and practice on malaria: A study in a tribal belt of Orissa state, India with reference to use of long lasting treated mosquito nets**

K.N. Vijayakumar, K. Gunasekaran, S.S. Sahu, P. Jambulingam

Acta Tropica, Volume 112, Issue 2, November 2009, Pages 137-142, doi: 10.1016/j.actatropica.2009.07.011

Local knowledge and practice related to malaria is important for the implementation of culturally appropriate, sustainable and effective interventions. In this context, to know people's knowledge, attitude and practice on malaria and its prevention, a study was carried out in two districts viz., Malkangiri and Koraput of Orissa state in India, the former with ongoing insecticide treated mosquito nets (ITNs) programme and the latter without such programme (non-ITNs). <http://tinyurl.com/ydbw6cl>

### **Acceptability, willing to purchase and use long lasting insecticide treated mosquito nets in Orissa State, India**

K. Gunasekaran, S.S. Sahu, K.N. Vijayakumar, P. Jambulingam

Acta Tropica, Volume 112, Issue 2, November 2009, Pages 149-155, doi: 10.1016/j.actatropica.2009.07.013

Long lasting insecticide treated nets (LLINs) that require no re-treatment have been advocated as an effective tool against malaria transmission. However, success of this community based intervention measure largely depends on its acceptability and proper usage by the target population, besides assuring access to bed nets. To determine the acceptability of LLIN, its usage and people's willingness to buy the net, a study was conducted in two tribal districts viz., Malkangiri (with ongoing ITN programme) and Koraput (no ITN programme) of Orissa State, India. <http://tinyurl.com/yc3j9jy>

### **Efficacy of permethrin treated long-lasting insecticidal nets on malaria transmission and observations on the perceived side effects, collateral benefits and human safety in a hyperendemic tribal area of Orissa, India**

Surya K. Sharma et al.

Acta Tropica, Volume 112, Issue 2, November 2009, Pages 181-187, doi: 10.1016/j.actatropica.2009.07.022

Studies were conducted on the efficacy of Olyset nets—a long-lasting insecticidal net (LLIN) factory treated with 2% (w/w) permethrin on malaria transmission in an area under the influence of pyrethroid susceptible vector species *Anopheles culicifacies* and *A. fluviatilis* in Sundargarh District, Orissa, India. The study showed that Olyset nets are effective personal protection tool that can be used in a community based intervention programme. <http://tinyurl.com/ycz8fbv>



### **Prevention of Plasmodium vivax malaria recurrence: Efficacy of the standard total dose of primaquine administered over 3 days**

Jaime Carmona-Fonseca, Amanda Maestre

Acta Tropica, Volume 112, Issue 2, November 2009, Pages 188-192, doi: 10.1016/j.actatropica.2009.07.024

The standard total dose (STD) of primaquine to prevent Plasmodium vivax recurrence is 0.25 mg/kg day administered over 14 days (STD-14). We evaluated, in an endemic zone of Colombia, the anti-recurrence efficacy of the STD dose administered over 3 and 14 days, and of sub-STD dose administered over 3 days (71%STD-3, 50%STD-3). <http://tinyurl.com/yad9u8p>

### **Management of malaria threat following tsunami in Andaman & Nicobar Islands, India and impact of altered environment created by tsunami on malaria situation of the islands**

Roop Kumari, P.L. Joshi, Shiv Lal, W. Shah

Acta Tropica, Volume 112, Issue 2, November 2009, Pages 204-211, doi: 10.1016/j.actatropica.2009.07.028

In this paper, effect of tsunami on malaria profile in these islands has been discussed along with action taken for its control. <http://tinyurl.com/ya4yf3u>

### **Short communication: Pro-apoptotic effects of antimalarial drugs do not affect mature human erythrocytes**

Paulo Renato Rivas Totino, Cláudio Tadeu Daniel-Ribeiro, Maria de Fátima Ferreira-da-Cruz

Acta Tropica, Volume 112, Issue 2, November 2009, Pages 236-238, doi: 10.1016/j.actatropica.2009.08.002

Many of the drugs used for malaria treatment have the ability to induce apoptosis in different cell types. In addition, apoptosis has also been identified in enucleated cells. The present work is aimed, therefore, to evaluate the pro-apoptotic aptness of chloroquine, quinine, artemisinin and mefloquine on mature erythrocytes by flow cytometry through the detection of cell shrinkage and phosphatidylserine exposure at the cell surface—hallmarks of apoptosis. <http://tinyurl.com/ybd9knj>

### **Stability of Interferon-Gamma and Interleukin-10 Responses to Plasmodium falciparum Liver Stage Antigen 1 and Thrombospondin-Related Adhesive Protein Immunodominant Epitopes in a Highland Population from Western Kenya**

Ann M. Moormann, Peter Odada Sumba, Daniel J. Tisch, Paula Embury, Charles H. King, James W. Kazura, and Chandy C. John

Am J Trop Med Hyg 2009;81 489-495

Long-term planning to prevent malaria epidemics requires in-depth understanding of immunity to Plasmodium falciparum in areas of unstable transmission. Cytokine responses to immunodominant epitope peptides from



liver stage antigen 1 (LSA-1) and thrombospondin-related adhesive protein (TRAP) were evaluated over a nine-month interval in adults and children in Kenya from a malaria epidemic-prone highland area after several years of low transmission. These results suggest that T cell memory to pre-erythrocytic stage malaria antigens is maintained but may be unavailable for consistent detection in peripheral blood, and that these antigens induce both pro-inflammatory and anti-inflammatory cytokine responses in this population. <http://tinyurl.com/md7j6c>

### **Cost-Effectiveness of Adding Bed Net Distribution for Malaria Prevention to Antenatal Services in Kinshasa, Democratic Republic of the Congo**

Sylvia I. Becker-Dreps, Andrea K. Biddle, Audrey Pettifor, Gertrude Musuamba, David Nku Imbie, Steven Meshnick, and Frieda Behets

*Am J Trop Med Hyg* 2009;81 496-502

We evaluated the cost-effectiveness of distributing insecticide-treated bed nets (ITNs) for malaria prevention at antenatal clinics in Kinshasa, Democratic Republic of the Congo. If resources were constrained, the greatest benefit would be among women in their first through fourth pregnancies. Thus, ITN distribution is a cost-effective addition to antenatal services. <http://tinyurl.com/nqgsuk>

### **Spatio-Temporal Distribution of Malaria in Yunnan Province, China**

Feng-Ming Hui et al.

*Am J Trop Med Hyg* 2009;81 503-509

The spatio-temporal distribution pattern of malaria in Yunnan Province, China was studied using a geographic information system technique. Both descriptive and temporal scan statistics revealed seasonal fluctuation in malaria incidences in Yunnan Province with only one peak during 1995–2000, and two apparent peaks from 2001 to 2005. <http://tinyurl.com/n76ywa>

### **A New Species Concealed by *Anopheles funestus* Giles, a Major Malaria Vector in Africa**

Belinda L. Spillings, Basil D. Brooke, Lizette L. Koekemoer, John Chipwanya, Maureen Coetzee, and Richard H. Hunt

*Am J Trop Med Hyg* 2009;81 510-515

The major malaria vector *Anopheles funestus* belongs to a group of morphologically similar species that are commonly distinguished from one another through the use of chromosomal and molecular techniques. Indoor resting collections of mosquitoes from Malawi were initially identified as *An. funestus* by morphology, but failed to have this confirmed by the species-specific polymerase chain reaction assay. These molecular and cytogenetic observations support the conclusion that this Malawi population is a new



species and it has provisionally been named *An. funestus*-like. <http://tinyurl.com/mzwmvz>

### **Short report: Detection of *Plasmodium knowlesi* by Real-Time Polymerase Chain Reaction**

N. Esther Babady, Lynne M. Sloan, Jon E. Rosenblatt, and Bobbi S. Pritt  
*Am J Trop Med Hyg* 2009;81 516-518

We previously developed a real-time polymerase chain reaction (PCR) assay for detection of the four *Plasmodium* species that infect humans. Recent studies have shown that natural transmission of the simian parasite *Plasmodium knowlesi* to humans occurs frequently in Southeast Asia. We have expanded our PCR assay to include detection of *P. knowlesi*. <http://tinyurl.com/nzzvj2>

### **Combining Indoor Residual Spraying and Insecticide-Treated Net Interventions**

Immo Kleinschmidt et al.  
*Am J Trop Med Hyg* 2009;81 519-524

Does scaling up of malaria control by combining indoor residual spraying (IRS) and long-lasting insecticidal nets (LLIN) enhance protection to populations? Results from a literature search and from recent household surveys in Bioko, Equatorial Guinea, and Zambezia, Mozambique are presented. <http://tinyurl.com/l4aj6j>

### **Short report: Prevalence of Antimalarial Drug Resistance Mutations in *Plasmodium vivax* and *P. falciparum* from a Malaria-Endemic Area of Pakistan**

Lubna Khatoon, Frederick N. Baliraine, Mariangela Bonizzoni, Salman A. Malik, and Guiyun Yan  
*Am J Trop Med Hyg* 2009;81 525-528

To study drug resistance in Bannu district, a malaria-endemic area in Pakistan, molecular-based analyses were undertaken. These results indicate an emerging multi-drug resistance problem in *P. vivax* and *P. falciparum* malaria parasites in Pakistan. <http://tinyurl.com/kv2t2r>

### **Infection of Mosquitoes with *Plasmodium falciparum* by Feeding on Humans and on Aotus Monkeys**

William E. Collins et al.  
*Am J Trop Med Hyg* 2009;81 529-533

Of 1,004 positive lots of mosquitoes fed on 229 humans infected with *Plasmodium falciparum*, 46.2% had 1–10 oocysts/(+)gut, 21.2% had 10–30 oocysts/(+)gut, 22.2% had 30–100 oocysts/(+)gut, and 10.4% had > 100 oocysts/(+) gut. The pattern of infection for mosquitoes fed on splenectomized Aotus monkeys was similar to that obtained by feeding on humans, but the intensity, based on oocyst/(+)gut, was much lower. <http://tinyurl.com/lfbpat>



### **Experimental Therapeutics: The Proteasome Inhibitor Epoxomicin Has Potent Plasmodium falciparum Gametocytocidal Activity**

Beata Czesny, Samrawit Goshu, James L. Cook, and Kim C. Williamson

Antimicrob. Agents Chemother. 2009 53: 4080-4085, doi:10.1128/AAC.00088-09

The work reported here demonstrates that nanomolar concentrations of the proteasome inhibitor epoxomicin effectively kill all stages of intraerythrocytic parasites but do not affect the viability of human or mouse cell lines. These findings provide strong support for the further development of proteasome inhibitors as antimalaria agents that are effective against asexual, sexual, and mosquito midgut stages of *P. falciparum*. <http://tinyurl.com/yeejykr>

### **Mechanisms of Action: Novel Antimalarial Aminoquinolines: Heme Binding and Effects on Normal or Plasmodium falciparum-Parasitized Human Erythrocytes**

Fausta Omodeo-Salè, Lucia Cortelezzi, Nicoletta Basilico, Manolo Casagrande, Anna Sparatore, and Donatella Taramelli

Antimicrob. Agents Chemother. 2009 53: 4339-4344, doi:10.1128/AAC.00536-09

Two new quinolizidinyl-alkyl derivatives of 7-chloro-4-aminoquinoline, named AM-1 and AP4b, which are highly effective in vitro against both the D10 (chloroquine [CQ] susceptible) and W2 (CQ resistant) strains of *Plasmodium falciparum* and in vivo in the rodent malaria model, have been studied for their ability to bind to and be internalized by normal or parasitized human red blood cells (RBC) and for their effects on RBC membrane stability. Taken together, these results suggest that the antimalarial activity of AM1 or AP4b is likely due to inhibition of hemozoin formation and that the efficacy of these compounds against the CQ-resistant strains can be ascribed to their hydrophobicity and capacity to accumulate in the vacuolar lipid (elevated lipid accumulation ratios). <http://tinyurl.com/yblzmvo>

### **Experimental Therapeutics: Antimalarial Activity of Simalikalactone E, a New Quassinoid from Quassia amara L. (Simaroubaceae)**

N. Cachet et al.

Antimicrob. Agents Chemother. 2009 53: 4393-4398, doi:10.1128/AAC.00951-09

We report the isolation and identification of a new quassinoid named simalikalactone E (SkE), extracted from a widely used Amazonian antimalarial remedy made out of *Quassia amara* L. (Simaroubaceae) leaves.

The contribution of quassinoids as a source of antimalarial molecules needs therefore to be reconsidered. <http://tinyurl.com/yaok9dj>



**Experimental Therapeutics: Improved Murine Model of Malaria Using Plasmodium falciparum Competent Strains and Non-Myelodepleted NOD-scid IL2R $\gamma$ null Mice Engrafted with Human Erythrocytes**

María Belén Jiménez-Díaz et al.

Antimicrob. Agents Chemother. 2009 53: 4533-4536, doi:10.1128/AAC.00519-09

Murine models of Plasmodium falciparum malaria may become crucial tools in drug discovery. Here we show that non-myelodepleted NOD-scid IL2R $\gamma$ null mice engrafted with human erythrocytes support an infectious burden up to tenfold higher than that supported by engrafted NOD-scid  $\beta$ 2microglobulinnull mice. The new model was validated for drug discovery and was used to assess the therapeutic efficacy of 4-pyridones, selective inhibitors of P. falciparum cytochrome bc1. <http://tinyurl.com/ydyg4hc>

**Letter: New PfATP6 Mutations Found in Plasmodium falciparum Isolates from Vietnam**

Lionel Bertaux, Le Hong Quang, Véronique Sinou, Nguyen Xuan Thanh, and Daniel Parzy

Antimicrob. Agents Chemother. 2009 53: 4570-4571, doi:10.1128/AAC.00684-09

No abstract. <http://tinyurl.com/y9brd9q>

**Structure and function of Plasmodium falciparum malate dehydrogenase: Role of critical amino acids in co-substrate binding pocket**

Anupam Pradhan, Abhai K. Tripathi, Prashant V. Desai, Prasenjit K. Mukherjee, Mitchell A. Avery, Larry A. Walker, Babu L. Tekwani

Biochimie, In Press, Accepted Manuscript, Available online 20 September 2009

These studies provide critical insights into the co-substrate binding pocket of PfMDH, which may be important in design of selective PfMDH/PfLDH inhibitors as potential antimalarials. <http://tinyurl.com/ybua5mh>

**Analytical Chemistry: Simple and rapid micro-scale quantification of artemisinin in living Artemisia annua L. by improved gas chromatography with electron-capture detection**

Shuoqian Liu, Na Tian, Juan Li, Jianan Huang, Zhonghua Liu

Biomedical Chromatography, Volume 23, Issue 10, Date: October 2009, Pages: 1101-1107, DOI 10.1002/bmc.1230

Artemisinin has been widely used as part of the artemisinin-based combination therapies against malaria. The present work developed a simple, fast and low toxic micro-scale analysis procedure for determination of artemisinin in a single leaf or flower of living Artemisia annua using improved gas chromatography with electron-capture detection. This method provides a powerful tool for biosynthesis study of artemisinin, high-throughput screening high-yield clone in



an early stage, or real-time quality control of *Artemisia annua* crop. <http://tinyurl.com/y9rdapb>

### **Synthesis and in vitro DMPK profiling of a 1,2-dioxolane-based library with activity against *Plasmodium falciparum***

Derek C. Martyn et al.

Bioorganic & Medicinal Chemistry Letters, Volume 19, Issue 19, 1 October 2009, Pages 5657-5660, doi:10.1016/j.bmcl.2009.08.024

A 43-member 1,2-dioxolane library was synthesized by coupling a 1,2-dioxolane-3-acetic acid derivative to a range of amines. Ten compounds had EC50s less-than-or-equals, slant 30 nM against *Plasmodium falciparum* 3D7 and Dd2 strains, and another 15 compounds had EC50s less-than-or-equals, slant 50 nM against both 3D7 and Dd2. The library was then subjected to a range of in vitro DMPK assays, which revealed that side chains with a heteroatom were required for favorable solubility, Log D and membrane permeability. CYP450 inhibition was isoform dependent, with 2C19 and 3A4 particularly susceptible, and the majority of compounds tested against rat and human microsomes were metabolized rapidly. <http://tinyurl.com/ycl6mt5>

### ***Plasmodium berghei*-infection induces volume-regulated anion channel-like activity in human hepatoma cells**

Miguel Prudêncio, Elvira T. Derbyshire, Catarina A. Marques, Sanjeev Krishna, Maria M. Mota, Henry M. Staines

Cellular Microbiology, Volume 11 Issue 10, Pages 1492 - 1501

Parasite infection can lead to alterations in the permeability of host plasma membranes. Presented here is the first demonstration that this phenomenon occurs in *Plasmodium*-infected liver cells. <http://tinyurl.com/ybszh8d>

### **Research Letter: Cell and Molecular Biology: Antimalarial Activity of the Novel Quinoline/6-Thiopurine Conjugate in *Gallus gallus* Linnaeus, Infected Experimentally by *Plasmodium (Novyella) juxtancleare***

Usha Vashist, Rafael Carvalhaes, Marta D'agosto, Adilson David da Silva

Chemical Biology & Drug Design, Volume 74, Issue 4, Date: October 2009, Pages: 434-437, DOI 10.1111/j.1747-0285.2009.00877.x

This study aimed to evaluate the 4-(6'-thiopurine)-7-chloroquinoline, a novel quinoline/6-thiopurine conjugate, for the treatment of *Gallus gallus* experimentally infected with *Plasmodium juxtancleare*, an avian malaria agent. The avian group treated with 4-(6'-thiopurine)-7-chloroquinoline showed a significant parasite clearance and maintained a low level of parasitaemia, when compared with the untreated control group and to the chloroquine treated avian group. <http://tinyurl.com/ybt6xhx>

### **DDT residues in water, sediment, domestic and indigenous biota from a currently DDT-sprayed area**



I.E.J. Barnhoorn, M.S. Bornman, C. Jansen van Rensburg, H. Bouwman  
Chemosphere, In Press, Corrected Proof, Available online 25 September 2009  
DDT is used for indoor residual spraying (IRS) in Limpopo Province, northern South Africa to control malaria. Through IRS, DDT may reach the outdoor environment via dust and air and from possible spillages during application. These findings raise concern that both water and food may be major routes of human exposure to DDT and metabolites, thereby posing possible adverse human health implications to the local communities. <http://tinyurl.com/ybfXuU9>

### **Parasite detection and identification for automated thin blood film malaria diagnosis**

F. Boray Tek, Andrew G. Dempster, Izzet Kale  
Computer Vision and Image Understanding, In Press, Accepted Manuscript, Available online 24 August 2009

This paper investigates automated detection and identification of malaria parasites in images of Giemsa-stained thin blood film specimens. The Giemsa stain highlights not only the malaria parasites but also the white blood cells, platelets, and artefacts. We propose a complete framework to extract these stained structures, determine whether they are parasites, and identify the infecting species and life-cycle stages. <http://tinyurl.com/mp695s>

### **Abstracts and Reviews: Immune responses in experimental human malaria infections**

Robert Sauerwein  
Cytokine, Volume 48, Issues 1-2, October-November 2009, Page 13, doi: 10.1016/j.cyto.2009.07.053  
No abstract. <http://tinyurl.com/ydenejtc>

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