



Bulletin 226 | 1 October 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.

Kind regards,  
Inga & Bart

## Publications

### **Abstracts and Reviews: NLRP3 inflammasome in malaria: Role of hemozoin-induced signaling on inflammasome activation**

Marina Tiemi Shio et al.

Cytokine, Volume 48, Issues 1-2, October-November 2009, Page 14, doi: 10.1016/j.cyto.2009.07.059

No abstract

<http://tinyurl.com/ydkwexg>

### **Abstracts and Reviews: Caspase-12 deficiency results in hyperinflammatory responses to lethal malaria**

Jenny Miu, Maya Saleh, Mary M. Stevenson

Cytokine, Volume 48, Issues 1-2, October-November 2009, Page 66, doi: 10.1016/j.cyto.2009.07.211

No abstract

<http://tinyurl.com/yeopvt4>

### **Abstracts and Reviews: The role of immunoglobulin E antibodies in protection against Plasmodium falciparum**

Reem K. Mohamed, Muntaser E. Ibrahim, Ibrahim M. Elhassan

Cytokine, Volume 48, Issues 1-2, October-November 2009, Page 68, doi: 10.1016/j.cyto.2009.07.222

No abstract

<http://tinyurl.com/y8qyr4t>

### **Expression of metallothionein and $\alpha$ -tubulin in heavy metal-tolerant Anopheles gambiae sensu stricto (Diptera: Culicidae)**

Paul O. Mireji et al.

Ecotoxicology and Environmental Safety, In Press, Corrected Proof, Available online 6 September 2009



Anopheles mosquitoes have been shown to adapt to heavy metals in their natural habitats. In this study we explored the possibility of using *Anopheles gambiae* sensu stricto as bio-reporters for environmental heavy metal pollution through expressions of their metal-responsive metallothionein and  $\alpha$ -tubulin genes.

<http://tinyurl.com/ydacjkl>

### **Artemether-lumefantrine: an oral antimalarial for uncomplicated malaria in children**

Adjei GO, Goka BQ, Binka F, Kurtzhals JA

Expert Rev Anti Infect Ther. 2009 Aug;7(6):669-81

In this review, available evidence on efficacy and safety of AL in the treatment of uncomplicated malaria, with emphasis on children where appropriate, and focusing on characteristics that are potentially important for malaria control policy decisions, are presented and discussed.

<http://tinyurl.com/ycu75kl>

### **Meeting report: Malaria genomics meets drug-resistance phenotyping in the field**

Hunt P, MacInnis B, Roper C

Genome Biology 2009, 10:314 (11 August 2009)

No abstract

<http://tinyurl.com/kmvm5r>

### **Clinical case: Pregnancy-associated Plasmodium falciparum malaria discovered fortuitously: About two cases**

I. Poilane, V. Jeantils, L. Carbillon

Gynécologie Obstétrique & Fertilité, In Press, Corrected Proof, Available online 17 September 2009

We report two cases of pregnancy-associated *Plasmodium falciparum* malaria discovered fortuitously. These two women were born in Africa and their last visit in an endemic area was more than one year before. It is well known that pregnancy is one of major risks of late onset of *P. falciparum* malaria. In the two cases reported in this study, clinical signs of malaria were not specific and we will describe the interest to detect more systematically pregnant African women, first arrival immigrants.

<http://tinyurl.com/ycb9z76>

### **Plasmodium falciparum-Specific Cellular Immune Responses after Immunization with the RTS,S/AS02D Candidate Malaria Vaccine in Infants Living in an Area of High Endemicity in Mozambique**

Arnoldo Barbosa et al.

Infect. Immun. 2009;77 4502-4509



Results from clinical trials in areas where malaria is endemic have shown that immunization with RTS,S/AS02A malaria vaccine candidate induces partial protection in adults and children and cellular effector and memory responses in adults. For the first time in a malaria vaccine trial, we sought to assess the cell-mediated immune responses to RTS,S antigen components in infants under 1 year of age participating in a clinical phase I/IIb trial of RTS,S/AS02D in Mozambique.

<http://tinyurl.com/ydau334>

### **Inhibitory Antibodies Specific for the 19-Kilodalton Fragment of Merozoite Surface Protein 1 Do Not Correlate with Delayed Appearance of Infection with Plasmodium falciparum in Semi-Immune Individuals in Vietnam**

E. Elsa Herdiana Murhandarwati, Lina Wang, Casilda G. Black, Doan Hanh Nhan, Thomas L. Richie, and Ross L. Coppel

*Infect. Immun.* 2009;77 4510-4517

Inhibitory antibodies specific for the 19-kDa fragment of merozoite surface protein 1 (MSP119) are a significant component of inhibitory responses in individuals immune to malaria. Nevertheless, conflicting results have been obtained in determining whether this antibody specificity correlates with protection in residents of areas where malaria is endemic. In this study, we examined sera collected from a population of semi-immune individuals living in an area of Vietnam with meso-endemicity during a 6-month period.

<http://tinyurl.com/yeglf8l>

### **Functional and Immunological Characterization of a Duffy Binding-Like Alpha Domain from Plasmodium falciparum Erythrocyte Membrane Protein 1 That Mediates Rosetting**

Alfredo Mayor et al.

*Infect. Immun.* 2009;77 3857-3863

The Duffy binding-like (DBL) domains are common adhesion modules present in Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) variants, which are responsible for immune evasion and cytoadherence. Knowledge about how immune responses are acquired against polymorphic DBL domains of PfEMP1 can aid in the development of vaccines for malaria. A recombinant DBL domain, encoded by R29 var1, which binds complement receptor 1 to mediate rosetting by the P. falciparum laboratory strain R29, was expressed in Escherichia coli, renatured by oxidative refolding to its native form, and purified to homogeneity.

<http://tinyurl.com/n4obq7>

### **Suppression of a Novel Hematopoietic Mediator in Children with Severe Malarial Anemia**

Christopher C. Keller et al.



Infect. Immun. 2009;77 3864-3871

In areas of holoendemic *Plasmodium falciparum* transmission, severe malarial anemia (SMA) is a leading cause of pediatric morbidity and mortality. Although many soluble mediators regulate erythropoiesis, it is unclear how these factors contribute to development of SMA. Investigation of novel genes dysregulated in response to malarial pigment (hemozoin [PfHz]) revealed that stem cell growth factor (SCGF; also called C-type lectin domain family member 11A [CLEC11A]), a hematopoietic growth factor important for development of erythroid and myeloid progenitors, was one of the most differentially expressed genes.

<http://tinyurl.com/knqxdd>

### **Strain-Specific Duffy Binding Protein Antibodies Correlate with Protection against Infection with Homologous Compared to Heterologous *Plasmodium vivax* Strains in Papua New Guinean Children**

Jennifer L. Cole-Tobian, Pascal Michon, Moses Biasor, Jack S. Richards, James G. Beeson, Ivo Mueller, and Christopher L. King

Infect. Immun. 2009;77 4009-4017

Individuals repeatedly infected with malaria acquire protection from infection and disease; immunity is thought to be primarily antibody-mediated and directed to blood-stage infection. Merozoite surface proteins involved in the invasion of host erythrocytes are likely targets of protective antibodies. We hypothesized that Papua New Guinean children (n = 206) who acquire high antibody levels to two *Plasmodium vivax* merozoite proteins, Duffy binding protein region II (PvDBPII) and the 19-kDa C-terminal region of *P. vivax* merozoite surface protein 1 (PvMSP119), would have a delay in the time to reinfection following treatment to clear all blood-stage malaria infections.

<http://tinyurl.com/nwabjw>

### **Annotation and analysis of low-complexity protein families of *Anopheles gambiae* that are associated with cuticle**

R. S. Cornman and J. H. Willis

Insect Molecular Biology, Volume 18 Issue 5, Pages 607 - 622

We have characterized four new families of homologous genes of the mosquito, *Anopheles gambiae*, all of which include members shown by previous work to be cuticular in nature. The CPLCG, CPLCW, CPLCP, and CPLCA families (where CPLC is 'cuticular protein of low complexity') encode proteins with a high proportion of low-complexity sequence. We have also annotated the *An. gambiae* Tweedle genes, a family of cuticular protein genes first described in *Drosophila*, and additional ungrouped *An. gambiae* cuticular proteins identified by proteomics.

<http://tinyurl.com/ye67r36>



### **Simultaneous determination of OZ277, a synthetic 1,2,4-trioxolane antimalarial, and its polar metabolites in rat plasma using hydrophilic interaction chromatography**

Ravi K. Bhamidipati, Julia Morizzi, Francis C.K. Chiu, David M. Shackleford, Susan A. Charman

Journal of Chromatography B, Volume 877, Issue 27, 1 October 2009, Pages 2989-2995, doi:10.1016/j.jchromb.2009.07.015

OZ277 is a synthetic 1,2,4-trioxolane antimalarial currently being evaluated in clinical trials. Biotransformation of OZ277 in rats results in the generation of metabolites with large differences in polarity which complicates the development of a method for the simultaneous analysis of all species. A simple, sensitive and selective hydrophilic interaction liquid chromatography–mass spectroscopy (HILIC/MS) method for simultaneous determination of OZ277 and its major metabolites in rat plasma was developed and validated. <http://tinyurl.com/yc4na95>

### **Development and characterization of novel carrier gel core liposomes based transmission blocking malaria vaccine**

Shailja Tiwari, Amit K. Goyal, Neeraj Mishra, Kapil Khatri, Bhuvaneshwar Vaidya, Abhinav Metha, Yimin Wu, Suresh P. Vyas

Journal of Controlled Release, In Press, Accepted Manuscript, Available online 15 August 2009

The aim of present work was to investigate the potential utility of novel carrier gel core liposomes for intramuscular delivery of transmission blocking malaria antigen Pfs25 and to evaluate the effect of co-administration of vaccine adjuvant CpGODN on immune enhancement of recombinant protein antigen Pfs25. The result indicates high potential of gel core liposomes for their use as a carrier adjuvant for intramuscular delivery of recombinant antigen Pfs25 based transmission blocking malaria vaccine. <http://tinyurl.com/lrus3z>

### **Commentary: Hydroxychloroquine Induces Autophagic Cell Death of Human Dermal Fibroblasts: Implications for Treating Fibrotic Skin Diseases**

Aarne Oikarinen

Journal of Investigative Dermatology 129, 2333-2335 (14 September 2009) doi:10.1038/jid.2009.164

Hydroxychloroquine (HCQ) is widely used to treat rheumatic and inflammatory diseases. It inhibits inflammation by downregulating the effects of inflammatory cells and their mediators. Future studies are needed to determine whether HCQ induces autophagy in vivo and whether antimalarials have antifibrotic effects when used in clinically relevant doses. <http://tinyurl.com/yaqfy56>



### **A host-vector model for malaria with infective immigrants**

J. Tumwiine, J.Y.T. Mugisha, L.S. Luboobi

Journal of Mathematical Analysis and Applications, In Press, Accepted Manuscript, Available online 3 September 2009

This paper considers a host-vector mathematical model for the spread of malaria that incorporates recruitment of human population through a constant immigration, with a fraction of infective immigrants. The model analysis is carried out to find the steady states and their stability. It is found that in the presence of infective immigrant humans, there is no disease-free equilibrium point.

<http://tinyurl.com/y9p5lt6>

### **Imported Malaria in Immigrants to Italy: A Changing Pattern Observed in North Eastern Italy**

Marta Mascarello et al.

Journal of Travel Medicine, Volume 16 Issue 5, Pages 317 - 321

Seventy percent of imported malaria cases in Italy occur in immigrants, generally with milder clinical presentation due to premunition acquired through repeated infections. Nevertheless, premunition could be progressively lost after a long period of nonexposure. We investigated the changing pattern of malaria in immigrants in two definite 5-year periods one decade apart.

<http://tinyurl.com/yatpxq5>

### **Newsdesk: Overprescribing of antimalarials**

Clare Sansom

The Lancet Infectious Diseases, Volume 9, Issue 10, October 2009, Page 596, doi:10.1016/S1473-3099(09)70247-6

No abstract

<http://tinyurl.com/yfssfqq>

### **Identification of mitochondrial Complex II subunits SDH3 and SDH4 and ATP synthase subunits a and b in Plasmodium spp**

Tatsushi Mogi, Kiyoshi Kita

Mitochondrion, In Press, Accepted Manuscript, Available online 12 August 2009

While most protist mitochondrial enzymes could be identified in database, the membrane anchor subunits of Complex II and FoF1-ATP synthase of malaria parasites are not annotated. Based on the presence of structural fingerprints or proteomics data from other protists, here we present their candidates. In contrast to canonical subunits, Plasmodium Complex II anchors have two transmembrane helices and may coordinate heme b via Tyr in place of His.

<http://tinyurl.com/m2yl98>



**Oral: Construction and validation of a detailed kinetic model for glycolysis in the asexual stage of Plasmodium falciparum; application for drug target identification**

J. Snoep, G. Penkler, M. Rautenbach

New Biotechnology, Volume 25, Supplement 1, September 2009, Page S354

No abstract

<http://tinyurl.com/mjlule>

**Malaria, sexual development and transmission: retrospect and prospect**

R. E. Sinden

Parasitology, Volume 136, Issue 12, October 2009, pp 1427 - 1434

doi:10.1017/S0031182009990667

It is difficult to recapture the excitement of recent research into the malaria parasites. Plasmodium has shown itself to be a most elegant, resourceful and downright devious cell. To reveal any of its manifold secrets is a hard-won privilege. The thrill of this intellectual endeavour, however, has to be tempered by the realism that we have made unremarkable progress in attacking malaria in the field, where it remains almost as omnipresent as it ever was in the 19th and 20th centuries, and both the parasite and vector have become more difficult to control than ever before. This personal view looks back at the significant progress made, and forward to the challenges of the future, focusing on work on sexual development.

<http://tinyurl.com/yb2de6h>

**The malaria merozoite, forty years on**

L. H. Bannister and G. H. Mitchell

Parasitology, Volume 136, Issue 12, October 2009, pp 1435 - 1444

doi:10.1017/S0031182009990734

The invasive blood stage of malaria parasites, merozoites, are complex entities specialized for the capture and entry of red blood cells. Their potential for vaccination and other anti-malaria strategies have attracted much research attention over the last 40 years, and there is now a considerable body of data relating to their biology. In this article some of the major advances over this period and remaining challenges are reviewed.

<http://tinyurl.com/y8baepr>

**The carboxy-terminus of merozoite surface protein 1: structure, specific antibodies and immunity to malaria**

A. A. Holder

Parasitology, Volume 136, Issue 12, October 2009, pp 1445 - 1456

doi:10.1017/S0031182009990515

Now that clinical trials of MSP1 vaccines are underway and the early results have been disappointing, it is increasingly clear that we need to know more



about the mechanisms of immunity, because a better understanding will highlight the limitations of our current assays and identify the improvements required. Understanding the structure of MSP1 will help us design and engineer better antigens that are more effective than the first generation of vaccine candidates. This review is focused on the carboxy-terminus of MSP1.  
<http://tinyurl.com/yeugb3l>

### **Along a TNF-paved road from dead parasites in red cells to cerebral malaria, and beyond**

I. A. Clark

Parasitology, Volume 136, Issue 12, October 2009, pp 1457 - 1468  
doi:10.1017/S0031182009006088

This is a personal account of how tumour necrosis factor (TNF) the prototype of a group of host-origin mediators, often known as pro-inflammatory cytokines, came into parasitology, and was subsequently realised to be central to the pathogenesis of most disease pathology. This contribution summarizes an example of how a curiosity-driven outsider, with initially no intention of heading this way, and no relevant experience, and with no more than the simplest of plans but an ambition to read as widely as it takes, and (most importantly) allowed to follow his head, can be what is required to give fresh insight into understanding a disease. It also gives the author's views on aspects of how the field of malaria disease pathogenesis seems to be developing. The hope is to inspire another generation to follow a similarly original course.

<http://tinyurl.com/yatqpw5>

### **Population dynamics of genetically diverse Plasmodium falciparum lineages: community-based prospective study in rural Amazonia**

P. Orjuela-Sanchez, M. da Silva-Nunes, N. S. da Silva, K. K. G. Scopel, R. M. Goncalves, R. S. Malafronte and M. U. Ferreira

Parasitology, Volume 136, Issue 10, September 2009, pp 1097-1105, doi: 10.1017/S0031182009990539

Temporal changes in the prevalence of antigenic variants in Plasmodium falciparum populations have been interpreted as evidence of immune-mediated frequency-dependent selection, but evolutionarily neutral processes may generate similar patterns of serotype replacement. Over 4 years, we investigated the population dynamics of P. falciparum polymorphisms at the community level by using 11 putatively neutral microsatellite markers.

<http://tinyurl.com/luhmar>

### **Effects of CD4+CD25+Foxp3+regulatory T cells on early Plasmodium yoelii 17XL infection in BALB/c mice**

Guang Chen, Jun Liu, Qing-Hui Wang, Yi Wu, Hui Feng, Wei Zheng, Sheng-Yu Guo, Dong-Mei Li, Ji-Chun Wang and Ya-Ming Cao



Parasitology, Volume 136, Issue 10, September 2009, pp 1107-1120, doi: 10.1017/S0031182009990370

The outcome of Plasmodium yoelii 17XL-infected BALB/c and DBA/2 mice, ranging from death to spontaneous cure, respectively, depends largely on the establishment of effective pro-inflammatory type 1 responses during the early stages of infection and associates with CD4+CD25+Foxp3+regulatory T cells (Tregs). Here, effects of Tregs were analysed on early P. yoelii 17XL infection in BALB/c and DBA/2 mice.

<http://tinyurl.com/lstjz>

### **Spatial distribution, blood feeding pattern, and role of Anopheles funestus complex in malaria transmission in central Kenya**

Ephantus J. Muturi, Luna Kamau, Benjamin G. Jacob, Simon Muriu, Charles M. Mbogo, Josephat Shililu, John Githure, Robert J. Novak

Parasitology Research, Volume 105, Number 4 / October, 2009 : 1041-1046

Studies were conducted to determine the role of sibling species of Anopheles funestus complex in malaria transmission in three agro-ecosystems in central Kenya. We conclude that agricultural practices have significant influence on distribution and blood feeding behavior of A. funestus complex. Although none of the species was implicated with malaria transmission, these results may partly explain why non-irrigated agro-ecosystems are associated with higher risk of malaria transmission by this species compared to irrigated agro-ecosystems.

<http://tinyurl.com/kwbu9p>

### **Short Communication: Plasmodium falciparum and Plasmodium vivax: so similar, yet very different**

Aparup Das, Meenu Sharma, Bhavna Gupta, Aditya Prasad Dash

Parasitology Research, Volume 105, Number 4 / October, 2009 : 1169-1171

The recently published whole genome sequence information of one of the human malaria parasites, Plasmodium vivax, have provided opportunities to compare similar features with Plasmodium falciparum that causes the most deadly form of human malaria. We herewith present comparative genomic insights into the whole genome of the two parasites and also to several other characteristics in terms of disease pathogenicity, evolution, etc. We show that while high similarities exist at the functional gene level, several contrasting features for other characteristics are hallmarks of these two human malaria parasites.

<http://tinyurl.com/mh95km>

### **Commentary: Human-specific evolution of sialic acid targets: Explaining the malignant malaria mystery?**

Ajit Varki and Pascal Gagneux

PNAS September 1, 2009 vol. 106 no. 35 14739-14740



Malaria caused by *Plasmodium falciparum* ("malignant malaria") is one of the most devastating pathogens of humans (1). *Plasmodium reichenowi*, which infects chimpanzees and gorillas, is the closest relative of *P. falciparum* (2). In early 20th-century experiments (never to be replicated), blood from *P. reichenowi*-infected chimpanzees was injected into humans, but failed to produce infections (3). Conversely, chimpanzees injected with *P. falciparum*-infected human blood suffered no infection. Taken together, these data suggested that each parasite had coevolved with its host, but did not rule out chimpanzee to human transmission, or vice versa. In this issue of PNAS, Rich et al. (4) provide an answer to this malignant malaria "mystery" and confirm a prediction that we and our colleagues made earlier (5).  
<http://tinyurl.com/yc8blya>

### **Inhibiting *Plasmodium falciparum* growth and heme detoxification pathway using heme-binding DNA aptamers**

Jacquin C. Niles, Joseph L. DeRisi, and Michael A. Marletta

PNAS August 11, 2009 vol. 106 no. 32 13266-13271

In this report, we demonstrate that heme-binding DNA aptamers efficiently inhibit in vitro hemozoin formation catalyzed by either a model lipid system or parasite-derived extracts just as or more potently than chloroquine. Altogether, these data demonstrate that aptamers can be versatile tools with applicability in functionally dissecting important *P. falciparum*-specific pathways both in vitro and in vivo.  
<http://tinyurl.com/nwsuux>

### **Commentary: Underestimating malaria risk under variable temperatures**

Mercedes Pascual, Andrew P. Dobson, and Menno J. Bouma

PNAS August 18, 2009 vol. 106 no. 33 13645-13646

The paper by Paaijmans et al. (3) in this issue of PNAS suggests that the relationship between climate and malaria is even more subtle than previously appreciated. If we are to assess the impact of both climate and weather on malaria transmission, we need a deeper understanding of the nonlinear ways in which the biology of the parasite and its mosquito vector integrates temperature fluctuations.  
<http://tinyurl.com/m4xc6j>

### **The malarial parasite *Plasmodium falciparum* imports the human protein peroxiredoxin 2 for peroxide detoxification**

Sasa Koncarevic et al.

PNAS August 11, 2009 vol. 106 no. 32 13323-13328

Coevolution of the malarial parasite and its human host has resulted in a complex network of interactions contributing to the homeodynamics of the host-parasite unit. As a rapidly growing and multiplying organism, *Plasmodium*



falciparum depends on an adequate antioxidant defense system that is efficient despite the absence of genuine catalase and glutathione peroxidase. Using different experimental approaches, we demonstrate that *P. falciparum* imports the human redox-active protein peroxiredoxin 2 (hPrx-2, hTPx1) into its cytosol.

<http://tinyurl.com/murzpl>

### **Distillery: Therapeutics: Malaria, Trypanosomiasis - Falcipain; rhodesain**

Science-Business eXchange 2, (24 September 2009) doi:10.1038/scibx.2009.1414

SAR studies identified fumaric acid-based cysteine protease (EP-B2) inhibitors that could help treat malaria and African trypanosomiasis. Further details on the research, next steps and licensing status are discussed in the article.

<http://tinyurl.com/y8axnbb>

### **Antimalarial compounds from *Schefflera umbellifera***

X.S. Mthembu, F.R. Van Heerden, G. Fouché

South African Journal of Botany, In Press, Corrected Proof, Available online 27 August 2009

The organic extract of the leaves of *Schefflera umbellifera* exhibited good antimalarial activity when tested against the chloroquine-susceptible strain (D10). Bioassay-guided fractionation of the dichloromethane fraction of the dichloromethane/methanol extract yielded an active compound, betulin, which exhibited good antiplasmodial activity with an IC<sub>50</sub> value of 3.2 µg/ml. The reference compound, chloroquine gave an IC<sub>50</sub> value of 27.2 ng/ml. Two other compounds were also isolated from the dichloromethane extract namely, 7-hydroxy-6-methoxycoumarin and ent-kaur-16-en-19-oic acid. These two compounds did not exhibit any significant antiplasmodial activity.

<http://tinyurl.com/nr6am7>

### **Malaria zoonoses**

J. Kevin Baird

Travel Medicine and Infectious Disease, Volume 7, Issue 5, September 2009, Pages 269-277, doi:10.1016/j.tmaid.2009.06.004

The genus *Plasmodium* includes many species that naturally cause malaria among apes and monkeys. The 2004 discovery of people infected by *Plasmodium knowlesi* in Malaysian Borneo alerted to the potential for non-human species of plasmodia to cause human morbidity and mortality. Subsequent work revealed what appears to be a surprisingly high risk of infection and relatively severe disease, including among travelers to Southeast Asia. The biology and medicine of this zoonosis is reviewed here, along with an examination of the spectrum of *Plasmodium* species that may cause infection of humans.



<http://tinyurl.com/y9j7t5q>

**Update: Virulence and drug resistance in malaria parasites**

Wilfred D. Stein, Cecilia P. Sanchez, Michael Lanzer

Trends in Parasitology, Volume 25, Issue 10, October 2009, Pages 441-443, doi:10.1016/j.pt.2009.07.003

Virulence and drug resistance are traits that pathogens can acquire independently, albeit these traits can influence each other. A recent publication has reported on the co-evolution of virulence and pyrimethamine resistance in malaria parasites. Here, we discuss this finding in the context of the folate biosynthesis pathway and explain how mutational changes in this pathway can affect both parasite replication rates and the development of drug resistance.

<http://tinyurl.com/yecbcpl>

**Opinion: Why is it important to study malaria epidemiology in India?**

Vineeta Singh, Neelima Mishra, Gauri Awasthi, Aditya P. Dash, Aparup Das

Trends in Parasitology, Volume 25, Issue 10, October 2009, Pages 452-457, doi:10.1016/j.pt.2009.06.004

Malaria is a major vector-borne disease in India. Based on vast geographic areas with associated topographic and climatic diversity, the variable malaria epidemiology in India is associated with high parasite genetic diversity and rapidly evolving drug resistance, differential distribution of vector species and emerging insecticide resistance and underlying human genetic diversity and past evolutionary histories.

<http://tinyurl.com/y96jbku>

**Review: Plasmodium falciparum biology: analysis of in vitro versus in vivo growth conditions**

Michele LeRoux, Viswanathan Lakshmanan, Johanna P. Daily

Trends in Parasitology, Volume 25, Issue 10, October 2009, Pages 474-481, doi:10.1016/j.pt.2009.07.005

We review the differences between *P. falciparum* in vitro culture systems and in vivo host environments, as well as evidence that host conditions can alter pathogen biology. For select biological questions, the incorporation of naturally occurring conditions into in vitro experimental manipulation of microbes may provide novel insight into pathogen biology.

<http://tinyurl.com/yd7jkaq>

**Monitoring for multidrug-resistant Plasmodium falciparum isolates and analysis of pyrimethamine resistance evolution in Uige province, Angola**

Michela Menegon et al.

Tropical Medicine & International Health, Volume 14 Issue 10, Pages 1251 - 1257



he parasite population of Uige Angola has high frequency mutations in pfcr, dhfr and dhps associated with resistance to chloroquine and sulphadoxine pyrimethamine, reflecting past reliance on these two drugs which were the mainstay of treatment until recently. Our findings show that drug resistance in Uige has occurred through a combination of local drug pressure and the regional and international dispersal of resistance mutant alleles.  
<http://tinyurl.com/yeffr6z>

**Clinical Microbiology: Environmental, socio-demographic and behavioural determinants of malaria risk in the western Kenyan highlands: a case-control study**

Kacey C. Ernst, Kim A. Lindblade, David Koech, Peter O. Sumba, Dickens O. Kuwuor, Chandy C. John, Mark L. Wilson

Tropical Medicine & International Health, Volume 14, Issue 10, Date: October 2009, Pages: 1258-1265, DOI 10.1111/j.1365-3156.2009.02370.x

Objective: To identify risk factors for uncomplicated malaria in highland areas of East Africa at higher risk of malaria epidemics, in order to design appropriate interventions.

Conclusions: In this East African highland area, risk of developing uncomplicated malaria was multifactorial with a risk factor profile similar to that in endemic regions. Households within close proximity to forest and swamp borders are at higher risk of malaria and should be included in indoor residual spraying campaigns.

<http://tinyurl.com/ye86wle>

**Clinical Microbiology: Molecular assessment of Plasmodium falciparum resistance to antimalarial drugs in China**

G. Q. Zhang, Y. Y. Guan, B. Zheng, S. Wu, L. H. Tang

Tropical Medicine & International Health, Volume 14, Issue 10, Date: October 2009, Pages: 1266-1271, DOI 10.1111/j.1365-3156.2009.02342.x

In China, Chloroquine (CQ) and sulfadoxine-pyrimethamine (SP) were abandoned for the treatment of falciparum malaria 20 years ago due to resistance. Subsequent field studies showed a trend of declining CQ and SP resistance in the country. The main purpose of this study was to analyse the molecular markers of antimalarial resistance and thereby to assess the possibility of reintroduction of CQ or SP for falciparum malaria treatment.

<http://tinyurl.com/y8b5g9e>

**Conference Report: Report of a Consultation on the Optimization of Clinical Challenge Trials for Evaluation of Candidate Blood Stage Malaria Vaccines, 18-19 March 2009, Bethesda, MD, USA**

V.S. Moorthy et al.

Vaccine, Volume 27, Issue 42, 25 September 2009, Pages 5719-5725, doi: 10.1016/j.vaccine.2009.07.049



Development and optimization of first generation malaria vaccine candidates has been facilitated by the existence of a well-established *Plasmodium falciparum* clinical challenge model in which infectious sporozoites are administered to human subjects via mosquito bite. While ideal for testing pre-erythrocytic stage vaccines, some researchers believe that the sporozoite challenge model is less appropriate for testing blood stage vaccines. Here we report a consultation, co-sponsored by PATH MVI, USAID, EMVI and WHO, where scientists from all institutions globally that have conducted such clinical challenges in recent years and representatives from regulatory agencies and funding agencies met to discuss clinical malaria challenge models. <http://tinyurl.com/yax49ua>

## Reports & Manuals

Open access

### **ExxonMobil, UCSF Global Health Group Co-Host Wilton Park Conference: New Report Released**

In April 2009, a diverse group of global health leaders came together to attend the "Malaria: Getting to Zero" conference at Wilton Park, U.K., sponsored by the Exxon Mobil Corporation and the UCSF Global Health Group. Country leaders, private sector partners, funders, implementers, researchers and journalists convened to discuss two ambitious global goals: achieving zero deaths from malaria in high-burden countries, and achieving zero transmission of malaria (elimination) in low-burden countries. The new report is a digest of the participants' conversations, exploring current progress, future challenges, and long and short-term control and elimination strategies.

<http://tinyurl.com/y9j4eqn>

Open access

### **RDT transport and storage guides**

Pocket-guides designed for malaria programme managers, medical stores and transport personnel, and clinic workers on transport and storage of malaria rapid diagnostic tests. The separate guides concentrate on central transport and stage, and remote transport and storage, respectively. Many of the principles are applicable to other perishable medical supplies transported to, and used in, clinics in tropical and sub-tropical areas. The guides are developed jointly by FIND, WHO/WPRO, USAID/Deliver, the RBM Partnership and UNICEF.

<http://tinyurl.com/ybgamco>

### **WHO malaria microscopy quality assurance manual**

The first comprehensive guide to development and maintenance of national malaria microscopy quality assurance programmes, and development of



external programmes for quality assurance and accreditation of microscopists. Developed by the WHO-Regional Office for the Western Pacific in collaboration with multiple partners including WHO/GMP, MSF, KEMRI, AMREF and several malaria control programmes in Asia and Africa, with support from USAID and FIND.

<http://tinyurl.com/ycngf7m>

### **Lot-testing access guide**

A guide for malaria programmes and other procurement agencies to access the malaria RDT lot-testing process of the WHO-FIND malaria RDT evaluation programme. This programme provides rapid testing of batches of malaria RDTs to confirm acceptable performance prior to release to the field, and is open to all procurers of malaria RDTs.

<http://tinyurl.com/y9luelw>

### **Malaria RDT field trial guide**

A field guide developed from the malaria RDT field trial recommendations previously published by WHO/WPRO and WHO/TDR in Nature Microbiological Reviews, adapted by WHO/WPRO with support from FIND. The booklet outlines a clear minimum standard protocol to ensure quality and comparability of field trials of malaria RDTs, to guide trial protocol development, and analysis, reporting and publication of results.

<http://tinyurl.com/y9n86wh>

## **Online Exhibition**

### **Online Exhibit of Modern Chinese Anti-Malaria Posters**

This exhibit represents the work of Chinese public health historian Dr. Liping Bu, who has been in residence at the History of Medicine Division for the summer. Roxanne Beatty did the work of preparing the on-line exhibit.

Malaria control in modern China was a resounding success. According to the exhibition introduction, "In 1998, there were 31 thousand malaria cases in China, with a morbidity of 0.25 per ten thousand, a drop of 99% compared to 1954." The great reduction in disease was due to concentrated and coordinated programs in public health control and prevention. The exhibit's gallery of images presents classic posters, from the early 1950s through the early 1970s, at the peak of the campaign.

<http://tinyurl.com/yeg2wyu>



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