



Bulletin 206 | 27 April 2009

Announcement: Do you have a great idea how to solve the malaria problem? – Click [here](#)



Call for Proposals Grand Challenges Explorations Grants, The Bill & Melinda Gates Foundation

Closing date for applications: May 28, 2009

The Bill & Melinda Gates Foundation is now accepting grant proposals for Round 3 of Grand Challenges Explorations, a US\$100 million initiative to help scientists pursue innovative ideas for solving major global health problems.

Grant proposals are being accepted online at <http://www.grandchallenges.org/Explorations/MalariaWorld> until May 28, 2009, on the following topics:

- **New!** Create Low-Cost Diagnostics for Priority Global Health Conditions
- **New!** Create New Ways to Induce Mucosal Immunity
- Create New Vaccines for Diarrhea, HIV, Malaria, Pneumonia and Tuberculosis
- Create New Tools to Accelerate the Eradication of Malaria

Initial grants will be \$100,000 each, and projects showing promise may have the opportunity to receive additional funding of \$1 million or more.

Full descriptions of the topics and application instructions are available at <http://www.grandchallenges.org/Explorations/MalariaWorld>

One great idea - Two pages to fill out - \$100.000,= to prove it

Anyone can apply, regardless of education or experience level

Publications

Open access | Chloroquine-Resistant Haplotype Plasmodium falciparum Parasites, Haiti

B.L. Londono et al.

EID, Volume 15, Number 5–May 2009

Plasmodium falciparum parasites have been endemic to Haiti for >40 years without evidence of chloroquine (CQ) resistance. In 2006 and 2007, we obtained blood smears for rapid diagnostic tests (RDTs) and filter paper blots of blood from 821 persons by passive and active case detection. P. falciparum infections diagnosed for 79 persons by blood smear or RDT were confirmed by PCR for the small subunit rRNA gene of P.

falciparum. These results indicate that CQ-resistant haplotype P. falciparum malaria parasites are present in Haiti.

Open access | CME Activity: Increased Risk for Severe Malaria in HIV-1–Infected Adults, Zambia

V. Chalwe et al.

EID, Volume 15, Number 5–May 2009

Medscape, LLC is pleased to provide online continuing medical education (CME) for this journal article, allowing clinicians the opportunity to earn CME credit. This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Medscape, LLC and Emerging Infectious Diseases. Medscape, LLC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Open access | Near-Fatal Multiple Organ Dysfunction Syndrome Induced by Plasmodium malariae

P.-N. Descheemaeker et al.

EID, Volume 15, Number 5–May 2009

We report a case of Plasmodium malariae–related multiple organ dysfunction syndrome (MODS) in a healthy immunocompetent patient. Despite extensive investigation, P. malariae was the only pathogen identified. The patient's isolates had a combination of mutant alleles that could possibly explain the severity of the infection.

Open access | A supervised land cover classification of a western Kenya lowland endemic for human malaria: associations of land cover with larval Anopheles habitats

Mutuku FM, Bayoh MN, Hightower AW, Vulule JM, Gimnig JE, Mueke JM, Amimo FA, Walker ED

International Journal of Health Geographics 2009, 8:19 (16 April 2009)

A supervised land cover classification was developed from very high resolution IKONOS satellite data and extensive ground truth sampling of a ca. 10 sq km malaria-endemic lowland in western Kenya. The classification was then applied to an investigation of distribution of larval Anopheles habitats. The hypothesis was that the distribution and abundance of aquatic habitats of larvae of various species of mosquitoes in the genus Anopheles is associated with identifiable landscape features.

Open access | Research: The effect of varying analytical methods on estimates of anti-malarial clinical efficacy

Wendy J Verret, Grant Dorsey, Francois Nosten, Ric N Price

Malaria Journal 2009, 8:77 (22 April 2009)

Anti-malarial drug clinical trials are conducted both to monitor anti-malarial drug resistance and to compare treatment regimens. Estimates of anti-malarial clinical efficacy vary significantly depending on the analytical methodology from which they are derived. This paper compares different ways to estimate the risk of failure in 65 treatment arms from 29 clinical trials.

Open access | Research: High retention and appropriate use of insecticide-treated nets distributed to HIV-affected households in Rakai, Uganda: results from interviews and home visits

Lauren Cohee, Lisa A Mills, Joseph Kagaayi, Ilana Jacobs, Ronald M Galiwango, James Ludigo, Joseph Ssekasanvu, Steven J Reynolds

Malaria Journal 2009, 8:76 (22 April 2009)

HIV patients in malaria-endemic areas have fewer and less severe episodes of malaria if they use ITNs and PEPFAR-funded HIV care programmes are now implementing ITN distribution as part of comprehensive HIV care. The paper assesses knowledge, retention

and appropriate use of ITNs distributed to HIV-positive adults as a part of a community-based outpatient HIV care programme in Uganda.

Open access | Research: Ecological and genetic relationships of the Forest-M form among chromosomal and molecular forms of the malaria vector *Anopheles gambiae sensu stricto*

Yoosook Lee, Anthony J Cornel, Claudio R Meneses, Abdrahamane Fofana, Aurelie G Andrianarivo, Rory D McAbee, Etienne Fondjo, Sekou F Traore, Gregory C Lanzaro
Malaria Journal 2009, 8:75 (21 April 2009)

Chromosome inversions, microsatellite allele frequencies and habitat preference all indicate that the Forest M form of *Anopheles gambiae* is genetically distinct from the other recognized forms within the taxon, particularly the M form found in Mali and elsewhere in West Africa

Open access | Research: A country-wide malaria survey in Mozambique II - Malaria attributable proportion of fever and establishment of malaria case definition in children across different epidemiological settings

Samuel Mabunda, John J Aponte, Armindo Tiago, Pedro Alonso
Malaria Journal 2009, 8:74 (21 April 2009)

Paper on a classical problem related to malaria-endemic areas, namely how much of fevers in children are attributed to malaria; this problem is still topical even if malaria is declining in many parts of sub-Saharan Africa. Overall more than 50% of children had *P. falciparum* parasitaemia, but only less than 10% had fever.

Open access | Research: Morphological features and differential counts of *Plasmodium knowlesi* parasites in naturally acquired human infections

Kim-Sung Lee, Janet Cox-Singh, Balbir Singh
Malaria Journal 2009, 8:73 (21 April 2009)

The morphological resemblance of early trophozoites of *P. knowlesi* to *P. falciparum* and later erythrocytic stages to *P. malariae* makes it extremely difficult to identify *P. knowlesi* infections by microscopy alone. This is the first, extensive description of the various stages of the parasite as seen in stained blood films.

Open access | Research: Thermal behaviour of *Anopheles stephensi* in response to infection with malaria and fungal entomopathogens

Simon Blanford, Andrew F Read, Matthew B Thomas
Malaria Journal 2009, 8:72 (20 April 2009)

Temperature is a critical determinant of the development of malaria parasites in mosquitoes, and hence the geographic distribution of malaria risk, but little is known about the thermal preferences of *Anopheles*. A number of other insects modify their thermal behaviour in response to infection. These alterations can be beneficial for the insect or for the infectious agent. Given current interest in developing fungal biopesticides for control of mosquitoes, *Anopheles stephensi* were examined to test whether mosquitoes showed thermally-mediated behaviour in response to infection with fungal entomopathogens and the rodent malaria, *Plasmodium yoelii*.

Open access | Case report: Malaria transmission in non-endemic areas: case report, review of the literature and implications for public health management

Thomas Zoller et al.

Malaria Journal 2009, 8:71 (20 April 2009)

In non-endemic areas, malaria is rare and locally acquired infections, particularly with *Plasmodium falciparum*, are exceptional events. The diagnosis is, therefore, likely to be delayed or missed in patients without a relevant travel history. This report describes a case of *falciparum* malaria in Berlin, Germany, in a patient who had not been to an endemic area for more than a decade.

Open access | Research: Ace-1 duplication in Anopheles gambiae: a challenge for malaria control

Luc Djogbenou, Pierrick Labbe, Fabrice Chandre, Nicole Pasteur, Mylene Weill

Malaria Journal 2009, 8:70 (18 April 2009)

Using molecular phenotype data collected from natural populations from West Africa, the frequency of this duplicated allele was investigated by statistical inference. This method is based on the departure from Hardy-Weinberg phenotypic frequency equilibrium caused by the presence of this new allele. The spread of this less costly resistance allele could represent a major threat to public health, as it may impede An. gambiae control strategies, and thus increases the risk of malaria outbreaks.

Open access | Research: A systematic classification of Plasmodium falciparum P-loop NTPases: structural and functional correlation

Deepti Gangwar, Mridul K Kalita, Dinesh Gupta, Virander S Chauhan, Asif Mohmmmed

Malaria Journal 2009, 8:69 (18 April 2009)

The study suggests a strong correlation between sequence and secondary structure profile of P-loop domains and functional roles of these proteins and thus provides an opportunity to speculate the role of many hypothetical proteins. The study provides a methodical framework for the characterization of biologically diverse NTPases in the P. falciparum genome. The efforts made in the analysis are first of its kind; and the results augment to explore the functional role of many of these proteins from the parasite that could provide leads to identify novel drug targets against malaria.

Open access | Research: Using the SaTScan method to detect local malaria clusters for guiding malaria control programmes

Marlize Coleman, Michael Coleman, Aaron M Mabuza, Gerdalize Kok, Maureen Coetzee, David N Durrheim

Malaria Journal 2009, 8:68 (17 April 2009)

Understanding the clustering of malaria cases is important for targeting control efforts at local levels, especially in areas of low malaria transmission.

Open access | Research: Structural insights into chondroitin sulphate A binding Duffy-binding-like domains from Plasmodium falciparum: implications for intervention strategies against placental malaria

Jasmita Gill, Chetan E Chitnis, Amit Sharma

Malaria Journal 2009, 8:67 (17 April 2009)

The work is focused on a sequence and structural comparison of the DBL domains (based on crystal structures) found in PfEMP1 protein that bind to placental endothelial cells via chondroitin sulphate A (CSA). The main conclusion suggests that PfEMP1 protein that binds to CSA have non-identical ligand binding sites and that the CSA binding sites may interact with their ligands differently. This has implications for vaccine/drug design.

Open access | Research: Malaria misdiagnosis in Uganda - implications for policy change

Joan Nankabirwa, Dejan Zurovac, Julius N Njogu, John B Rwakimari, Helen Counihan, Robert W Snow, James K Tibenderana

Malaria Journal 2009, 8:66 (16 April 2009)

An important study which shows very poor adherence to microscopy results, (much lower than expected malaria prevalence among sick people, and very poor field microscopy standards. The implications of these findings are discussed in a context where RDTs are likely to replace microscopy in some settings.

Open access | Research: Equity and coverage of insecticide-treated bed nets in an area of intense transmission of Plasmodium falciparum in Tanzania

Jubilate Bernard, George Mtove, Renata Mandike, Frank Mtei, Caroline Maxwell, Hugh Reyburn

Malaria Journal 2009, 8:65 (16 April 2009)

Marked inequity persists with the poorest households still experiencing the highest risk of malaria and the lowest ITN coverage. Abolition of this inequity within the foreseeable future is likely to require mass interventions.

Open access | Research: Bed net use and associated factors in a rice farming community in central Kenya

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

Malaria Journal 2009, 8:64 (16 April 2009)

This paper reports the findings of a study conducted in an irrigated agro-ecosystem in central Kenya, to investigate the local knowledge of malaria and mosquitoes as well as bed net use, prior to large scale distribution of long-lasting ITNs.

Open access | Hemoglobin Cleavage Site-Specificity of the Plasmodium falciparum Cysteine Proteases Falcipain-2 and Falcipain-3

Subramanian S, Hardt M, Choe Y, Niles RK, Johansen EB, et al.

PLoS ONE 4(4): e5156. doi:10.1371/journal.pone.0005156

The Plasmodium falciparum cysteine proteases falcipain-2 and falcipain-3 degrade host hemoglobin to provide free amino acids for parasite protein synthesis. Hemoglobin hydrolysis has been described as an ordered process initiated by aspartic proteases, but cysteine protease inhibitors completely block the process, suggesting that cysteine proteases can also initiate hemoglobin hydrolysis. To characterize the specific roles of falcipains, we used three approaches.

Open access | High Throughput Functional Assays of the Variant Antigen PfEMP1 Reveal a Single Domain in the 3D7 Plasmodium falciparum Genome that Binds ICAM1 with High Affinity and Is Targeted by Naturally Acquired Neutralizing Antibodies

Oleinikov AV, Amos E, Frye IT, Rosnagle E, Mutabingwa TK, et al.

PLoS Pathog 5(4): e1000386. doi:10.1371/journal.ppat.1000386

Plasmodium falciparum-infected erythrocytes bind endothelial receptors to sequester in vascular beds, and binding to ICAM1 has been implicated in cerebral malaria. Binding to ICAM1 may be mediated by the variant surface antigen family PfEMP1: for example, 6 of 21 DBL β C2 domains from the IT4 strain PfEMP1 repertoire were shown to bind ICAM1, and the PfEMP1 containing these 6 domains are all classified as Group B or C type. In this study, we surveyed binding of ICAM1 to 16 DBL β C2 domains of the 3D7 strain PfEMP1 repertoire, using a high throughput Bioplex assay format.

Open access | Brief Communication: Relationship between plasma and red blood cell concentrations of quinine in Brazilian children with uncomplicated Plasmodium falciparum malaria on oral therapy

Vieira, José L.F.; Gomes, Andreza L.S.; Borges, Larissa M.G.; Guimarães, Erika R.

Rev. Inst. Med. trop. S. Paulo vol.51 no.2 São Paulo Mar./Apr. 2009

We determined the relationship between plasma and red blood cell concentrations of quinine in children with uncomplicated falciparum malaria from an endemic area of Amazonian region. This result demonstrated that quinine do not concentrate in red blood cell of Brazilian children and characterize the absence of interracial difference in this relationship.

Southeast Asian AE1 associated renal tubular acidosis: Cation leak is a class effect

Stephen Walsh, Franck Borgese, Nicole Gabillat, Helene Guizouarn

Biochemical and Biophysical Research Communications, Volume 382, Issue 4, 15 May 2009, Pages 668-672, doi:10.1016/j.bbrc.2009.03.062

Anion Exchanger 1 (AE1) is present in the erythrocyte and also in the α -intercalated cell; different mutations can cause either red cell disease or distal renal tubular acidosis (dRTA). Recently, we described a cation leak property in four dRTA-causing AE1 mutants, three autosomal dominant (AD) European mutants, one autosomal recessive (AR) from Southeast Asia, G701D. G701D had a very large leak property and is unusually common in SE Asia. We hypothesized that this property might confer a survival advantage. We characterized three other AR dRTA-associated AE1 mutants found in SE Asia, S773P, Δ 850 and A858D via transport experiments in AE1-expressing *Xenopus* oocytes. These three SE Asian mutants also had cation leaks of similar magnitude to that seen in G701D, a property that distinguishes them as a discrete group. The clustering of these cation-leaky AE1 mutations to malarious areas of SE Asia suggests that they may confer malaria resistance.

Early Production of γ -Interferon in Clinical Malaria: Role of Interleukin-18 and Interleukin-12

Donato Torre

Clinical Infectious Diseases. Volume 48, Issue 10, Page 1481–1482, May 2009, DOI: 1058-4838/2009/4810-0025

No abstract available

Correspondence: Mechanisms Underlying Early Interferon- γ Production in Human *Plasmodium falciparum* Malaria

Marthe C. D’Ombrian, Leanne J. Robinson, Ivo Mueller, and Louis Schofield

Clinical Infectious Diseases. Volume 48, Issue 10, Page 1482–1483, May 2009, DOI: 1058-4838/2009/4810-0026

No Abstract available

A phosphatidylcholine-BODIPY 581/591 conjugate allows mapping of oxidative stress in *P. falciparum*-infected erythrocytes

Ying Fu, Nectarios Klonis, Cacang Suarna, Ghassan J. Maghzal, Roland Stocker, Leann Tilley

Cytometry Part A, Volume 75A, Issue 5, Date: May 2009, Pages: 390-404, DOI: 10.1002/cyto.a.20704

The chromophore, BODIPY 581/591, has an extended conjugated system that reacts with oxygen centered-radicals leading to changes in its spectral characteristics. Fatty acid-conjugated BODIPY 581/591 transfers readily between membrane bilayers and can be used as a sensor of oxidative stress in cell populations. We report here the use of a phosphatidylcholine (PC) derivative of BODIPY 581/591, which transfers much less rapidly between membranes. This allows the analysis of oxidative stress in individual cells and in different compartments within cells.

Primaquine dipeptide derivatives bearing an imidazolidin-4-one moiety at the N-terminus as potential antimalarial prodrugs

Nuno Vale, Fátima Nogueira, Virgílio E. do Rosário, Paula Gomes, Rui Moreira

European Journal of Medicinal Chemistry, Volume 44, Issue 6, June 2009, Pages 2506-2516, doi:10.1016/j.ejmech.2009.01.018

Primaquine dipeptide derivatives bearing an imidazolidin-4-one moiety at the N-terminus were synthesized and evaluated as potential transmission-blocking antimalarial prodrugs. The imidazolidin-4-one derived from Ala-Ala–primaquine and acetone reduced the transmission of the infection to mosquitoes more efficiently than primaquine as shown by the significant decrease in the number of oocysts in the midguts of the mosquitoes at 10 and 50 μ mol/kg when compared to the control.

Preliminary Communication: New antimalarial and cytotoxic 4-nerolidylcatechol derivatives

Rúbia Silva Melo et al.

European Journal of Medicinal Chemistry, Volume 44, Issue 6, June 2009, Pages 2731-2735, doi:10.1016/j.ejmech.2008.10.025

4-Nerolidylcatechol (1) was isolated from cultivated *Pothomorphe peltata* root on a multigram scale using straight-forward solvent extraction-column chromatography. New semi-synthetic derivatives of 1 were prepared and tested in vitro against multidrug-resistant *Plasmodium falciparum* K1 strain.

Minireview: Malaria sporozoite proteome leaves a trail

Vignali M, Speake C, Duffy PE

Genome Biology 2009, 10:216 (21 April 2009)

The malaria parasite sporozoite proteome changes during maturation, revealing proteins specifically expressed in the stage that infects the human host.

Short Communication: Genomic resources for invertebrate vectors of human pathogens, and the role of VectorBase

K. Megy, M. Hammond, D. Lawson, R.V. Bruggner, E. Birney, F.H. Collins

Infection, Genetics and Evolution, Volume 9, Issue 3, May 2009, Pages 308-313, doi: 10.1016/j.meegid.2007.12.007

High-throughput genome sequencing techniques have now reached vector biology with an emphasis on those species that are vectors of human pathogens. The first mosquito to be sequenced was *Anopheles gambiae*, the vector for *Plasmodium* parasites that cause malaria. The proliferation of genomic data creates the need for efficient and accessible storage. We present VectorBase, a genomic resource centre that is both involved in the annotation of vector genomes and act as a portal for access to the genomic information.

Plasmodium possesses dynein light chain classes that are unique and conserved across species

Elijah K. Githui, Etienne P. De Villiers, Andrew G. McArthur

Infection, Genetics and Evolution, Volume 9, Issue 3, May 2009, Pages 337-343, doi: 10.1016/j.meegid.2008.03.002

In this study, we analyzed the cytoplasmic dynein light chains (Dlcs) of *P. falciparum* since they provide adaptor surface to the cargoes and are likely to be involved in differential transport. Dlcs consist of three different families: TcTex1/2, LC8 and LC7/roadblock. The data presented demonstrate that *P. falciparum* Dlcs sequences and functional domains show high sequence similarity within the species, but that only the Dlc group 1 (LC8) has a high similarity to human orthologues. TcTex1 and LC7/roadblock have low similarity to human orthologues. This sequence variation could be targeted for vaccine or drug development.

Estimating novel potential drug targets of Plasmodium falciparum by analysing the metabolic network of knock-out strains in silico

Segun Fatumo, Kitiporn Plaimas, Jan-Philipp Mallm, Gunnar Schramm, Ezekiel Adebisi, Marcus Oswald, Roland Eils, Rainer König

Infection, Genetics and Evolution, Volume 9, Issue 3, May 2009, Pages 351-358, doi: 10.1016/j.meegid.2008.01.007

We have established a simple computational tool which analyses the topology of the metabolic network of *P. falciparum* to identify essential enzymes as possible drug targets. We investigated the essentiality of a reaction in the metabolic network by deleting (knocking-out) such a reaction in silico. The algorithm selected neighbouring compounds of the investigated reaction that had to be produced by alternative biochemical pathways.

Discussion: Potential and limits of in silico target discovery—Case study of the search for new antimalarial chemotherapeutic targets

Nadia Saïdani, Delphine Grando, Hélène Valadié, Olivier Bastien, Eric Maréchal

Infection, Genetics and Evolution, Volume 9, Issue 3, May 2009, Pages 359-367, doi: 10.1016/j.meegid.2008.01.001

In this brief review, we describe how in silico organization of genomic and post-genomic information of all partners involved in malaria (human patient, Plasmodium parasite and Anopheles vector), complying with knowledge of the disease in etiologic terms, appears as an efficient source of information not only to help selecting but also discarding target candidates. Some limitations in our capacity to explore the stored biological information, due to the current quality of genomic annotation, level of database integration, or to the performances of existing analytic and mining tools, are discussed. In silico strategies to assess the feasibility of bringing a target to a therapeutic development pipeline, in terms of target "druggability", are introduced.

A Baculovirus Dual Expression System-Based Malaria Vaccine Induces Strong Protection against Plasmodium berghei Sporozoite Challenge in Mice

Shigeto Yoshida, Masanori Kawasaki, Norimitsu Hariguchi, Kuniko Hirota, and Makoto Matsumoto

Infect. Immun. 2009;77 1782-1789

We have previously shown that a recombinant baculovirus that displays Plasmodium berghei circumsporozoite protein (PbCSP), a homolog of the leading human malaria vaccine candidate, on the viral envelope protected 60% of mice against P. berghei infection. Here, we describe a second-generation baculovirus vaccine based on the "baculovirus dual expression system," which drives PbCSP expression by a dual promoter that consists of tandemly arranged baculovirus-derived polyhedrin and mammal-derived cytomegalovirus promoters.

Polymeric Linear Peptide Chimeric Vaccine-Induced Antimalaria Immunity Is Associated with Enhanced In Vitro Antigen Loading

Luciana M. Silva-Flannery, Monica Cabrera-Mora, Megan Dickherber, and Alberto Moreno

Infect. Immun. 2009;77 1798-1806

Immunization of mice with Plasmodium berghei or Plasmodium yoelii synthetic linear peptide chimeras (LPCs) based on the circumsporozoite protein protects against experimental challenge with viable sporozoites. The immunogenicity of LPCs is significantly enhanced by spontaneous polymerization. To better understand the antigenic properties of polymeric antimalarial peptides, we studied the immune responses elicited in mice immunized with a polymer or a monomer of a linear peptide construct specific for P. yoelii and compared the responses of antigen-presenting cells following incubation with both peptide species.

Variant-Specific Immunity to Plasmodium berghei in Pregnant Mice

Rosette Megnekou, Lars Hviid, and Trine Staalsoe

Infect. Immun. 2009;77 1827-1834

We have investigated the immunological basis of pregnancy-related Plasmodium berghei recrudescence in immune mice with substantial preexisting immunity. Specifically, we examined the relevance of this experimental model to the study of pregnancy-associated malaria (PAM) caused by P. falciparum in women with substantial preexisting protective immunity.

Analysis of Immunity to Febrile Malaria in Children That Distinguishes Immunity from Lack of Exposure

Philip Bejon, George Warimwe, Claire L. Mackintosh, Margaret J. Mackinnon, Sam M. Kinyanjui, Jennifer N. Musyoki, Peter C. Bull, and Kevin Marsh

Infect. Immun. 2009;77 1917-1923

In studies of immunity to malaria, the absence of febrile malaria is commonly considered evidence of "protection." However, apparent "protection" may be due to a lack of exposure to infective mosquito bites or due to immunity. We studied a cohort that was

given curative antimalarials before monitoring began and documented newly acquired asymptomatic parasitemia and febrile malaria episodes during 3 months of surveillance.

Antimicrobial activity of Acacia mellifera extracts and lupane triterpenes

Charles Mutai, Christine Bii, Constantinos Vagias, Dennis Abatis, Vassilios Roussis

Journal of Ethnopharmacology, Volume 123, Issue 1, 4 May 2009, Pages 143-148, doi: 10.1016/j.jep.2009.02.007

Acacia mellifera (Vahl) Benth (Leguminosae) is a subtropical medicinal plant that is widely used in traditional African medicines against various diseases such as pneumonia and malaria. The present study was performed to evaluate the antimicrobial effects of extracts from the stem bark of Acacia mellifera.

Serological evidence for long-term Epstein-Barr virus reactivation in children living in a holoendemic malaria region of Kenya

Erwan Piriou, Rhonda Kimmel, Kiprotich Chelimo, Jaap M. Middelorp, Peter Sumba Odada, Robert Ploutz-Snyder, Ann M. Moormann, Rosemary Rochford

Journal of Medical Virology, Volume 81, Issue 6, Date: June 2009, Pages: 1088-1093, DOI: 10.1002/jmv.21485

To study the long term the effects of chronic exposure to *P. falciparum* malaria on Epstein-Barr virus (EBV) reactivation in children, EBV-specific antibody levels were measured in a cross-sectional survey of two groups of Kenyan children with divergent malaria exposure, varying in age from 1 to 14 years. These data suggest that chronic exposure to malaria may lead to long-term EBV reactivation.

Short Communication: Differential sub-nuclear localisation of repressive and activating histone methyl modifications in *P. falciparum*

Neha Issar, Stuart A. Ralph, Liliana Mancio-Silva, Catherine Keeling, Artur Scherf

Microbes and Infection, Volume 11, Issue 3, March 2009, Pages 403-407, doi:10.1016/j.micinf.2008.12.010

Post-translational histone modifications and sub-nuclear organization epigenetically influence gene regulation, especially those implicated in antigenic variation of *Plasmodium falciparum*. Here we screened for histone methylation modifications and determined, for the first time, their spatial nuclear localisation.

Short Communication: Enhanced antibody responses to Plasmodium falciparum Pfs28 induced in mice by conjugation to ExoProtein A of Pseudomonas aeruginosa with an improved procedure

Feng Qian et al.

Microbes and Infection, Volume 11, Issue 3, March 2009, Pages 408-412, doi:10.1016/j.micinf.2008.12.009

In this paper we report our efforts to enhance the immunogenicity of Pfs28, a transmission blocking vaccine candidate of *Plasmodium falciparum*, using a strategy of chemical conjugation. With an improved procedure, Pfs28 was covalently coupled to the mutant and non-toxic ExoProtein A of *Pseudomonas aeruginosa* by the reaction between thiolated antigen and maleimide modified carrier protein. The optimized process resulted in a higher antigen-carrier conjugation ratio, and the conjugation product could be purified using single-step size-exclusion chromatography. A significant increase in immunogenicity measured by ELISA was observed in mice immunized with conjugated Pfs28 as compared to unconjugated Pfs28.

Review: The iron trap: iron, malaria and anemia at the mother-child interface

Jennifer F. Friedman, Jonathan D. Kurtis, Edward R. Kabyemela, Michal Fried, Patrick E. Duffy

Microbes and Infection, Volume 11, Issue 4, April 2009, Pages 460-466, doi:10.1016/j.micinf.2009.02.006

Iron deficiency causes anemia, but prevents malaria for unknown reasons, thus hindering iron supplementation programs for mothers and children. Iron homeostasis is tightly regulated, including at the mother–fetus interface where iron–malaria relationships are complex. Improved iron status assays, and understanding of malaria protection mechanisms, are needed to manage these disorders.

Cooperativity between Plasmodium falciparum adhesive proteins for invasion into erythrocytes

Tiffany M. DeSimone, et al.

Molecular Microbiology, Volume 72, Issue 3, Date: May 2009, Pages: 578-589, DOI: 10.1111/j.1365-2958.2009.06667.x

Here we report the targeted gene disruption of PfRh2b and PfRh2a in W2mef, a parasite strain that is heavily dependent on sialic-acid receptors for invasion, and show that the PfRh2b ligand is functional in this parasite background. Our results reveal the importance of genetic background in ligand–receptor usage by *P. falciparum* parasites, and suggest that the co-ordinate expression of PfRh2a, PfRh2b together mediate efficient sialic acid-independent erythrocyte invasion.

Editorial: Malaria: health is wealth

Nature Reviews Microbiology 7, 322-322 (30 April 2009), doi: 10.1038/nrmicro2144

On 25 April, we celebrate World Malaria Day, an occasion to look at the burden of malaria on the populations in endemic areas. The human cost of malaria is well known, and the link between poverty and malaria is well established. Crucially, decreasing, and possibly eliminating, malaria will have a beneficial economic effect on endemic areas. Therefore, increased funding of malaria research can provide wide-ranging economic benefits beyond the obvious alleviation of human suffering.

Review: Malaria parasite proteins that remodel the host erythrocyte

Alexander G. Maier, Brian M. Cooke, Alan F. Cowman, Leann Tilley

Nature Reviews Microbiology 7, 341-354 (30 April 2009), doi: 10.1038/nrmicro2110

Exported proteins of the malaria parasite *Plasmodium falciparum* interact with proteins of the erythrocyte membrane and induce substantial changes in the morphology, physiology and function of the host cell. These changes underlie the pathology that is responsible for the deaths of 1–2 million children every year due to malaria infections. The advent of molecular transfection technology, including the ability to generate deletion mutants and to introduce fluorescent reporter proteins that track the locations and dynamics of parasite proteins, has increased our understanding of the processes and machinery for export of proteins in *P. falciparum*-infected erythrocytes and has provided us with insights into the functions of the parasite protein exportome. We review these developments, focusing on parasite proteins that interact with the erythrocyte membrane skeleton or that promote delivery of the major virulence protein, PfEMP1, to the erythrocyte membrane.

Immunogenicity and protection-inducing ability of recombinant Plasmodium vivax rhoptry-associated protein 2 in Aotus monkeys: A potential vaccine candidate

Jose Rojas-Caraballo, Alvaro Mongui, Manuel A. Giraldo, Gabriela Delgado, Diana Granados, Diana Millan-Cortes, Paola Martinez, Raul Rodriguez, Manuel A. Patarroyo

Vaccine, Volume 27, Issue 21, 11 May 2009, Pages 2870-2876, doi:10.1016/j.vaccine.2009.02.083

Rhoptry proteins have been extensively shown to be important in invasion and parasitophorous vacuole (PV) formation. This work evaluates the immunogenicity and protective efficacy of *Plasmodium vivax* RAP2 in the non-human *Aotus* primate model, when expressed as a recombinant molecule in *E. coli* and formulated in Freund and Alum hydroxide adjuvants. Our results show that rPvRAP2 is immunogenic in both formulations, finding a trend of higher cytokine levels in immunized monkeys, specially in

IL-4 levels (using Freund's adjuvant) and IL-5 (using Alum hydroxide). RAP2 is suggested as a *P. vivax*-vaccine candidate since immunized monkeys exhibited lower parasitemias than control groups after being experimentally challenged with the *P. vivax* VCG-I strain.

Evaluation of two long synthetic merozoite surface protein 2 peptides as malaria vaccine candidates

Christian Flueck et al.

Vaccine, Volume 27, Issue 20, 5 May 2009, Pages 2653-2661, doi:10.1016/j.vaccine.2009.02.081

Here we present the evaluation of two long synthetic peptides representing both allelic families of MSP2 as potential vaccine candidates. The constructs were well recognized by human immune sera from different locations and different age groups. Furthermore, peptide-specific antibodies in human immune sera were associated with protection from clinical malaria. The synthetic fragments share major antigenic properties with native MSP2. Immunization of mice with these antigens yielded high titre antibody responses and monoclonal antibodies recognized parasite-derived MSP2. Our results justify taking these candidate poly-peptides into further vaccine development.

Training



The second multi-disciplinary and multi-cultural training workshop on reducing Plasmodium transmission and malaria burden by integrated vector control (insecticide treated bed nets / indoor

residual spraying)

'Progress in ITNs and IRS implementation and perspectives on genetically modified Mosquitoes'

Date: 6-11 July 2009

Location: Camerino (Marche Region), Italy

The training event is organized in the frame of the PhD Programme on Malaria and Human Development supported by WHO, Global Malaria Programme, the University of Camerino and the Italian Malaria Network. It is targeted to doctoral candidates (whatever their disciplinary background), working in the field of malaria or who plan to be involved from various perspectives and with different approaches in research and control of poverty-related diseases in their future.

The workshop, - structured in plenary lectures, working group sessions and poster discussions - can rely upon the expertise of lecturers and facilitators from research and control institutions from different malaria endemic countries, from WHO, UNOPS, the Italian Malaria Network and other institutions focusing on malaria / vector research.

For detailed information on the workshop programme, participating experts, application modalities, the PhD programme on Malaria, outcomes of the first workshop conducted in 2008, please view our website: <http://web.unicam.it/laureati/dottorato/index.asp>

News

Africa

21 April 2009, Ghanaian Chronicle

Ghana: World Malaria Day Marked

The District Malaria Advocacy Teams (DMAT), which includes eleven districts in various parts of Ghana, last Friday, marked World Malaria Day, with the theme "District Leadership Involvement in Counting Malaria Out" in Accra.

21 April 2009, ANGOP

Angola: Over Three Million Cases of Malaria Recorded in 2008

About three million simple cases and 200,000 of serious cases with 9,000 deaths were registered in the country, in 2008, ANGOP learnt this Tuesday here from a source of the National Malaria Control Programme (PNCM).

21 April 2009, Daily Trust

Nigeria: Health Minister in UK to Share Nigeria's Malaria Experience

Minister of Health, Professor Babatunde Osotomehin is to speak at a conference on Malaria which will be taking place between Wednesday 15th and Friday 17th April 2009 at Wilton Park, United Kingdom.

21 April 2009, AllAfrica.com

Mozambique: Further Efforts Urged in Anti-Malaria Struggle

The president of the Roll Back Malaria (RBM) movement in Mozambique, Anglican Bishop Dinis Sengulane, on Tuesday declared that, despite all the encouraging results achieved to date, civil society should still undertake further efforts in the fight against malaria.

21 April 2009, IPPmedia

United Republic of Tanzania: Mama Kikwete attends African First Ladies meet in US

The First Lady Mama Salma Kikwete yesterday left the country for the US to attend the African First Ladies' Leadership for Health Summit to be held in Los Angeles, California. During the two-day summit, participants would discuss a number of things, including multi-partnered approaches in combating HIV/Aids and malaria, maternal health as one of the keystones of the Millennium Development Goals (MDGs), safer pregnancies and moving beyond rhetoric to improve women`s lives.

21 April 2009, Cameroon Tribune

Cameroon: Dr Celestin Kouambeng - Auto-Medication Can Kill (interview)

Dr Celestin Kouambeng, in charge of Monitoring and Evaluation at the National Malaria Control Programme.

20 April 2009, Daily Observer

Gambia: Farafenni to Host World Malaria Day Celebrations

As the World Malaria Day celebrations gets closer, the National Malaria Control Programme (NMCP), on Monday, organised a press briefing on the upcoming celebrations and the significance of the day, at the National Malaria Control Programme conference hall in Kanifing.

20 April 2009, New Times

Rwanda: IRS Exercise Starts in August

The fourth Indoor Residual Spraying exercise by Research Triangle Institute International (RTI) will start in August.

20 April 2009, This Day

Nigeria: Scientists Record Breakthrough in Fight Against Malaria

Mustapha Shehu in Abuja with Agency Reports

20 April 2009, AngolaPress

Angola: Chevron donates USD 5 million to combat malaria

At least USD five million were donated Monday in Luanda by Chevron Cabinda Gulf Oil Company, through the Global Fund, to the Health Ministry's National Programme to fight malaria.

20 April 2009, AngolaPress

Angola: Malaria main cause of school, professional absenteeism - vice-minister

The deputy-minister of Health, Carlos Maseca Monday in Luanda said that malaria was the leading cause of school and professional absenteeism among the country's population.

20 April 2009, New Vision

Uganda: Hima cement company begins sh500m malaria programme

HIMA Cement has launched a two-year community malaria prevention campaign worth sh500m in Kasese district. The campaign will benefit at least 28,000 residents of Hima town.

20 April 2009, New Vision

Uganda: Country Gets Sh800 Million China Malaria Drugs

UGANDA has received malaria drugs worth \$400,000 (about sh860m) from China.

20 April 2009, Daily Nation

Kenya: Why malaria kills so many children

Some 72 children in Kenya aged below five years die every day from malaria, doctors have said.

20 April 2009, Standard

Kenya: New drug a boost for malaria treatment

A Chinese pharmaceutical company has introduced a new malaria drug that would treat the disease in one day into the Kenyan market.

19 April 2009, Daily Nation

Kenya: Anti-malaria drug trials set to kick off in Kenya

Trials for a new anti-malaria drug are set to begin at Rusinga Island of Suba District.

19 April 2009, New Vision

Uganda: Malaria - People Still Think It is Caused By Witchcraft, Eating Mangoes

On 25 April this week, Uganda joins the World in marking 'World Malaria Day' under the theme: "Counting Malaria Out". Malaria is predictable, preventable and curable.

19 April 2009, New Vision

Uganda: \$225m malaria project launched

Uganda is among 11 countries to benefit from a \$225m initiative to provide effective anti-malaria drugs.

18 April 2009, UGPulse.com

Uganda: Uganda Health News: HIV/Malaria cost Uganda \$200m annually

The for Head of Health Services in the Ministry of Health, Prof. Francis Omaswa says Uganda spends 200 million dollars in the fight against HIV/Aids and Malaria every year.

17 April 2009, Vanguard

Nigeria: Country Urges Regional Effort to Fight Malaria

Minister of Health, Professor Babatunde Osotimehin, has canvassed for a sub-regional effort among West African states to jointly fight the malaria scourge in the region.

17 April 2009, Modern Ghana

Ghana: Accra Brewery assists Malaria Control

Accra Brewery Limited (ABL) has donated chemicals and spraying machines worth over 10,000 Ghana cedis to the Health Directorate of the Accra Metropolitan Authority. The donation is in support of the directorate's malaria prevention exercise in the central business district of Accra.

17 April 2009, The Citizen Daily

United Republic of Tanzania: Bank step up war on malaria

Standard Chartered Bank Tanzania has launched a campaign against malaria under which it will spend \$1 million (about Sh1.3 billion) to distribute impregnated mosquito nets across the country.

16 April 2009, Vanguard

Nigeria: Osotimehin in London for malaria talk

Global attention focuses on Nigeria today as the Minister of Health, Prof. Babatunde Osotimehin, speaks on malaria control efforts in the country at a conference titled "Malaria: Getting to Zero" holding at Wilton Park in the United Kingdom.

16 April 2009, Ghana News

Ghana: Schools hold inter-school drama competition on malaria eradication

Even though stringent measures have been put in place to control the menace of malaria, the disease still remained a major health challenge.

15 April 2009, SciDev.Net

Tanzania: Fish to Fight Malaria

Scientists are developing a biological control method for malaria that uses larvae-eating fish to control mosquito populations in rain-fed pools.

Asia

20 April 2009, Hindu

India: Drive for low-cost malaria drugs

United Nations: Anti-malaria drugs, more powerful than previous versions, will be put within reach of millions of people in Africa and Asia as part of an initiative launched by the U.N.-backed fund that fights major epidemics.

19 April 2009, Xinhua

China: Zambian Health Authorities advised to fight against malaria

The health authorities in Zambia's Southern Province have been advised to start planning and budgeting for the construction of facilities for safe storage of toxic chemicals used for the residential indoor spray against malaria, Zambia News and Information Service (ZANIS) reported on Sunday.

19 April 2009, Hindu

India: Cambodia to provide anti-mosquito nets to counter malaria

The Cambodian government will soon dispatch to the public 1,500 nets soaked with mosquito-killing liquid amid rising danger of malaria during the rainy season, national media said on Sunday.

18 April 2009, Ceylon Daily News

Sri Lanka: Malaria almost eradicated

Sri Lanka has almost eradicated Malaria and no Malaria deaths have been reported during last three years. It has also resulted in an unprecedented 99 per cent decrease in the reported incidence of Malaria during the last 10 years.

Oceania

17 April 2009, Melbourne Herald Sun

Australia: Ashton Kutcher live on Twitter to raise money for malaria fight

Ashton Kutcher has succeeded in reaching a million viewers live on his Twitter blog, to raise money for charity.

Americas

22 April 2009, NJ.com

USA: Rutgers senior selected for interfaith effort against malaria

He was chosen yesterday as one of 30 recipients -- 12 of them American -- of a fellowship from the Tony Blair Faith Foundation. The former British prime minister started the foundation to raise awareness about efforts to fight malaria in Africa.

20 April 2009, Kaiser network.org

USA: Shortage of HIV/AIDS, TB, Malaria Drugs in Ugandan District Could ...

A shortage of HIV/AIDS, tuberculosis and malaria medications in Uganda's northern Gulu district could cause patients to interrupt treatment and lead to drug resistance, Paul Onek, Gulu director of health services, said recently, IRIN/PlusNews reports.

17 April 2009, Scientific American

USA: Money for cheaper herb-based malaria meds

A subsidy program intended to drive down the cost of lifesaving malaria drugs called artemisinin-based combination therapies—now considered the most effective treatment against the parasitic disease—was unveiled today in Norway.

17 April 2009, Voice of America

USA: Malaria-Control Scheme Targets Older Mosquitoes

Despite new drugs and strategies for combating malaria, this infectious illness remains one of the world's most dangerous and deadly diseases. Now, some researchers think they have a strategy to produce a new, more environmentally friendly insecticide that targets geriatric mosquitoes.

16 April 2009, PR Newswire (press release)

USA: Every 30 Seconds an African Child Dies from Malaria; Education Key to Prevention

An African child dies every 30 seconds from this same disease; nearly a half billion people become ill because of it. About 1 million children under the age of 5 die each year from malaria- a disease that is entirely preventable. As World Malaria Day approaches April 25, Christian Children's Fund Senior Program Health Specialist David Shanklin stresses the importance of education about the disease.

16 April 2009, Christian Post

USA: Malaria – A global affordable healthcare crisis

As we come upon World Malaria Day, the world is reminded it has only two years to meet the 2010 targets of delivering effective and affordable protection and treatment to all people at risk of malaria. Malaria is the Democratic Republic of Congo's (DRC) most common killer disease. One in five children does not make it to their fifth birthday because of it. Five-year-old Deux-Anges is now sitting up in bed and beaming after she received a course of quinine by infusion – a treatment which cost her mother the family's monthly income.

15 April 2009, Christian Post

USA: Anti-Malaria Campaign Mobilizes Thousands of Teens to 'Bite Back'

An initiative to mobilize teens in the fight against malaria has raised nearly half a million dollars since its launch – most of which came in over the past four months.

15 April 2009, SmartBrief

USA: Study: Home-based malaria treatment not effective

A recent study involving African children showed that home-based malaria treatment in cities isn't effective since most fevers usually aren't caused by the disease. The study found that parents tended to treat their children with malaria drugs for fevers before they are diagnosed with the disease.

15 April 2009, Exchange Morning Post

Canada: MEDA casts wider (malaria) net to save more young lives in Tanzania

MEDA (Mennonite Economic Development Associates) is on the front lines of a new \$21 million project in Tanzania to get young children sleeping under life-protecting malaria nets over the next two years.

14 April 2009, Danville News

USA: Malaria may meet its match

Killing just the older mosquitoes would be a more sustainable way of controlling malaria, according to entomologists who add that the approach may lead to evolution-proof insecticides that never become obsolete.

Europe

21 April 2009, Times Online

UK: UN envoy: big business must help end malaria

Efforts to control malaria and cut its colossal death toll on the young and poor will fail if governments and big business retreat into self-interest during the economic downturn, one of Wall Street's pioneers has told The Times.

17 April 2009, Financial Times

UK: Malaria treatment made more affordable

Patients in poor countries could gain easier access to effective malaria treatments at a fraction of current prices under a pioneering subsidy mechanism unveiled on Friday.

16 April 2009, Earthtimes (press release)

UK: Stanford Study of Malaria Vaccine Needs Participants

Researchers at the Stanford University School of Medicine need additional participants to complete the first study of a new vaccine against malaria.

16 April 2009, Look To The Stars

UK: Ashton Kutcher Challenges CNN For Malaria Nets

Earlier this month, Ashton Kutcher used Twitter to encourage his fans to support World Malaria Day on April 25. Now he has challenged CNN to a popularity race to get 1 million followers on the micro-blogging site. And he'll make a charity donation if he wins.

MalariaWorld - Knowledge for Solutions

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

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