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## Guillain-Barre syndrome and its correlation with dengue, Zika and chikungunya viruses infection based on a literature review of reported cases in Brazil

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**Abstract**

Guillain-Barre syndrome (GBS) is one of the main neurologic manifestations of arboviruses, especially Zika virus infection. As known, the prevalence of these diseases is high, so the risk of having an increase on GBS is relevant. The study purposes making a comparative survey between the involvement of dengue, Zika and chikungunya infections in the development of the GBS in Brazil, as well as search in literature resemblances and distinctions between beforehand reported cases. It was performed an electronic search in online databases, with articles published between the years of 2004–2018. A total of 729 articles about the proposed search were found, and 10 were selected according to inclusion and exclusion criteria. The medium age found in Brazilian studies was 429. The time lapse for the neurological symptoms manifest was 6,5–11 days. Facial palsy, paresthesia and member weakness were the main symptoms related. Pediatric cases are rare. There are many studies that implicated the association of GBS and arboviruses and point it to one of the main neurological manifestation of these infections. More research and consistent data are needed to clarify unanswered questions and guide public health measures.

**Keywords:** Guillain-Barre syndrome, Zika virus, Dengue fever, Chikungunya

## Impact of population displacement and forced movements on the transmission and outbreaks of *Aedes*-borne viral diseases: Dengue as a model

Author: Rashad Abdul-Ghani, Mohammed A.K. Mahdy, Samira M.A. Al-Eryani, Florence Fouque

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**Absract**

Population displacement and other forced movement patterns following natural disasters, armed conflicts or due to socioeconomic reasons contribute to the global emergence of *Aedes*-borne viral disease epidemics. In particular, dengue epidemiology is critically affected by situations of displacement and forced movement patterns, particularly within and across borders. In this respect, waves of human movements have been a major driver for the changing epidemiology and outbreaks of the disease on local, regional and global scales. Both emerging dengue autochthonous transmission and outbreaks in countries known to be non-endemic and co-circulation and hyperendemicity with multiple dengue virus serotypes have led to the emergence of severe disease forms such as dengue hemorrhagic fever and dengue shock syndrome. This paper reviews the emergence of dengue outbreaks driven by population displacement and forced movements following natural disasters and conflicts within the context of regional and sub-regional groupings.

**Keywords:** Population displacement, Human forced movement, *Aedes*-borne, disease, Dengue.

## Excito-repellent activity of β-caryophyllene oxide against Aedes aegypti and Anopheles minimus

Author: Jirod Nararak, Sunaiyana Sathantriphop, Monthathip Kongmee

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**Abstract**

Contact irritant and non-contact repellent activities of β-caryophyllene oxide were evaluated against laboratory strains of female *Aedes aegypti* (USDA strain), a major arbovirus vector and *Anopheles minimus* (KU strain), a major malaria parasite vector, compared with the synthetic repellent DEET, using an excito-repellency test system. β-caryophyllene oxide and DEET were tested at concentrations of 0.1, 0.25, 0.5 and 1.0% (v/v). *Anopheles minimus* was found to be more sensitive to β-caryophyllene oxide than that of *Ae. aegypti* and exhibited high avoidance response rates (86–96% escape) at 0.5% and 1.0% concentrations in contact and non-contact trials compared with *Ae. aegypti* (22–59% escape). However, at the same concentrations, DEET displayed lower irritancy and repellency capacities against these two mosquito species (range 0–54% escape) compared to β-caryophyllene oxide. The analysis of escape responses showed significant differences between mosquito species at all concentrations ($P < 0.05$) except for 0.1%. For both species, there were significant differences in irritant and repellent responses between β-caryophyllene oxide and DEET at higher concentrations (0.5 and 1.0%).

**Keywords:** Aedes aegypti, Anopheles minimus, β-Caryophyllene oxide, Contact irritancy, Non-contact repellency

## Paromomycin-loaded mannosylated chitosan nanoparticles: Synthesis, characterization and targeted drug delivery against leishmaniasis

Authors: F. Esfandiari, M.H. Motazedian, Q. Asgari, M.H. Morowvat

Source: Acta Tropica 2019 September; 105045

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### Abstract

Cutaneous leishmaniasis is the most common form of leishmaniasis caused by different species of *Leishmania* parasites. The emergence of resistance, toxicity, long term treatment, high cost of the current drugs, and intracellular nature of the parasite are the major difficulties for the treatment of leishmaniasis. Although the therapeutic effect of paromomycin (PM) on leishmaniasis*Leishmania* parasite). PM-loaded into mannosylated CS (MCS) nanoparticles using dextran (PM-MCS-dex-NPs) was prepared by ionic gelation and then characterized. The particle size and *Zeta* potential of PM-MCS-dex-NPs were obtained as n246 m and +31 mV, respectively. Mannosylation of CS was qualitatively evaluated by Fourier-transform infrared spectroscopy and quantitatively measured by CHNO elemental analysis; also, a mannosylation level of 17% (w) was attained. Encapsulation efficiency (EE), drug release profile, and THP-1 cell uptake potential were determined. A value of 83.5% for EE and a higher release rate in acidic media were achieved. THP-1 cell uptake level of PM-MCS-dex-NPs after 6 h was ˜2.8 and ˜3.9 times of non-mannosylated CS nanoparticles (PM-CS-dex*In vitro*Glucantim, PM-CS-dex-NPs, and PM-MCS-dex-NPs after 48h were obtained as 1846 ± 158, 1234 ± 93, 784 ± 52 and 2714 ± 126 μg $mL^{-1}$Glucantim, PM-CS-dex-NPs, and PM-MCS-dex-NPs after 48h were obtained as 105.0 ± 14.0, 169.5 ± 9.8, 65.8 ± 7.3 and 17.8 ± 1.0 μg $mL^{-1}$Glucantim, PM-CS-dex-NPs and PM-MCS-dexGlucantim, PM-CS-dex-NPs, and PM-MCS-dex-NPs at a typical concentration of 20 μg $mL^{-1}$ were 71.78, 69.94, 83.14 and 33.41%, respectively. While the effect of PM-CS-dex-NPs was more salient on amastigotes, PM-MCS-dex-NPs effectively affected both stages of the parasite, especially the amastigote one. This indicated that the mannosylated formulation acts as a targeted delivery system. The findings of this study revealed that this novel targeted formulation represented a strong anti-leishmanial activity.

**Keywords:** Drug delivery, Macrophage targeting, Mannosylated Nanoparticles, *L. Major*, Aminosidine, MTT Assay

## Entomo-virological surveillance strategy for dengue, Zika and chikungunya arboviruses in field-caught Aedes mosquitoes in an endemic urban area of the Northeast of Brazil

Author: Izabel Cristina dos Reis, Gerusa Gibson, Tania Ayllón

Source: Acta Tropica 2019 September; 197: 105061

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### Abstract

*Aedes* spp. are considered the main vectors of dengue (DENV), Zika (ZIKV) and chikungunya (CHIKV) viruses in the world. Arbovirus detection in *Aedes* mosquitoes can alert authorities to possible outbreaks, reducing the impact of these diseases. The purpose of this study was to perform an operational strategy for virological surveillance of DENV, ZIKV and CHIKV in adult *Aedes aegypti* and *Aedes albopictus* mosquitoes captured at different key-sites in an endemic urban area of the Northeast Region of Brazil, with the prospect of discussing its role as part of an alert system for outbreaks in critical areas. Residential and non-residential premises located in areas of recent of transmission of these arboviruses were selected for adult mosquito collection in the rainy season (July) of 2018. A total of 1068 adult mosquitoes were collected: 946 *Culex quinquefasciatus* (88.6%), 118 *Ae. aegypti* (11.0%), two *Ae. albopictus* (0.2%) and two *Aedes taeniorhynchus* (0.2%). Among the premises surveyed, recycling points (N = 48, 40.7%), municipal schools (N = 36, 30.5%) and junkyards (N = 31, 26.2%) were the places with the highest frequency of adult *Ae. aegypti*. Health units (including primary health care facilities and one hospital) (N = 23; 19.5%) together with residential premises (N = 11; 9. 3%) presented the lowest frequencies. Total RNAs of the samples were extracted from *Aedes* mosquitoes and a nested reverse transcription (RT) polymerase chain reaction (PCR) assay for detecting and typing

DENV, ZIKV and CHIKV was performed. From the 37 *Aedes* spp. pools analyzed (35 *Ae. aegypti*, one *Ae. albopictus* and one *Ae. taeniorhynchus*), seven were positive for DENV-3, including three pools containing *Ae. aegypti* females, one containing an *Ae. aegypti* engorged female and three comprised of *Ae. aegypti* males. The positive pools were composed of mosquitoes collected in public schools, health units, junkyards, recycling points and residential premises. Our findings reinforce the importance of continuous virological surveillance in *Aedes* mosquitoes, as a useful tool for detecting arboviruses circulation in vulnerable areas, even in low infestation seasons.

**Keywords:** Entomo-virological surveillance, Arboviruses *Aedes* spp, Arboviruses, DENV-3, Key-sites

## Biting patterns of malaria vectors of the lower Shire valley, southern Malawi

Author: Monicah M. Mburu, Themba Mzilahowa, Benjamin Amoah

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### Abstract

Assessing the biting behaviour of malaria vectors plays an integral role in understanding the dynamics of malaria transmission in a region. Biting times and preference for biting indoors or outdoors varies among mosquito species and across regions. These behaviours may also change over time in response to vector control measures such as long-lasting insecticidal nets (LLINs). Data on these parameters can provide the sites and times at which different interventions would be effective for vector control. This study assessed the biting patterns of malaria vectors in Chikwawa district southern Malawi. The study was conducted during the dry and wet seasons in 2016 and 2017, respectively. In each season, mosquitoes were collected indoors and outdoors for 24 nights in six houses per night using the human landing catch. Volunteers were organized into six teams of two individuals, whereby three teams collected mosquitoes indoors and the other three collected mosquitoes outdoors each night, and the teams were rotated among twelve houses. All data were analyzed using Poisson log-linear models.

The most abundant species were *Anopheles gambiae* sensu lato (primarily *An. arabiensis*) and *An. funestus* s.l. (exclusively *An. funestus* s.s.). During the dry season, the biting activity

of *An. gambiae* s.l. was constant outdoors across the categorized hours (18:00 h to 08:45 h), but highest in the late evening hours (21:00 h to 23:45 h) during the wet season. The biting activity of *An. funestus* s.l. was highest in the late evening hours (21:00 h to 23:45 h) during the dry season and in the late night hours (03:00 h to 05:45 h) during the wet season. Whereas the number of *An. funestus* s.l. biting was constant ($P = 0.662$) in both seasons, that of *An. gambiae* s.l. was higher during the wet season than in the dry season ($P = 0.001$). *Anopheles gambiae* s.l. was more likely to bite outdoors than indoors in both seasons. During the wet season, *An. funestus* s.l. was more likely to bite indoors than outdoors but during the dry season, the bites were similar both indoors and outdoors.

The biting activity that occurred in the early and late evening hours, both indoors and outdoors coincides with the times at which individuals may still be awake and physically active, and therefore unprotected by LLINs. Additionally, a substantial number of anopheline bites occurred outdoors. These findings imply that LLINs would only provide partial protection from malaria vectors, which would affect malaria transmission in this area. Therefore, protection against bites by malaria mosquitoes in the early and late evening hours is essential and can be achieved by designing interventions that reduce vector-host contacts during this period.

**Keywords:** Anophelines, Culicines, HLC, Biting, Indoors, Outdoors, Malawi.

## Space-time analysis of the incidence of human visceral leishmaniasis (VL) and prevalence of canine VL in a municipality of southeastern Brazil: Identification of priority areas for surveillance and control

Author: Rubiane Mendes Faria de Arruda, Diogo Tavares Cardoso, Rafael ,Gonçalves Teixeira-Neto

Source: Acta Tropica 2019 September;197: 105052

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### Abstract

Human and canine visceral leishmaniasis (HVL and CVL, respectively) represent serious public health issues in Brazil. The surveillance and control measures currently employed have had limited effect in impeding the territorial expansion of the disease and in reducing the number of cases. We have investigated the space-time distribution of HVL incidence rates and CVL prevalence in the coverage areas of the 148 primary healthcare units in Belo Horizonte (MG, Brazil) during a 6-year period in order to identify those that should be prioritized for disease control actions. Data were smoothed using the empirical Bayes method and analyzed by space-time scanning and application of univariate global Moran's I index and local indicators of spatial association (LISA) statistics to identify spatial autocorrelations. Point data of CVL were analyzed using the Kernel method. Bivariate global Moran's I and LISA techniques were employed to identify spatial correlations between HVL and CVL. Based on our results, we were able to formulate two proposals for establishing the prioritization of coverage areas, namely: (i) classification of maximum priority areas as identified by bivariate LISA for HVL and CVL, and (ii) combination of maximum priority areas with high priority areas as identified by univariate LISA for HVL. According to our proposals, 27 coverage areas in Belo Horizonte were categorized as maximum priority and a further 13 were classified as high priority. Our proposals, which are based on practical, feasible and inexpensive statistical tools, will contribute to a better understanding of VL distribution in urban settings and improving the efficiency of governmental control programs.

**Keywords:** Visceral leishmaniasis, Spatial analysis, Zoonoses, Risk assessment, Epidemiology.

## Paromomycin-loaded mannosylated chitosan nanoparticles: Synthesis, characterization and targeted drug delivery against leishmaniasis

Authors: F. Esfandiari, M.H. Motazedian, Q. Asgari, M.H. Morowvat

Source: Acta Tropica 2019 September; 197: 105045

Hyperlinks: https://doi.org/10.1016/j.actatropica.2019.105072

### Abstract

Cutaneous leishmaniasis is the most common form of leishmaniasis caused by different species of *Leishmania* parasites. The emergence of resistance, toxicity, long term treatment, high cost of the current drugs, and intracellular nature of the parasite are the major difficulties for the treatment of leishmaniasis. Although the therapeutic effect of paromomycin (PM) on leishmaniasis has been investigated in different studies, it has a low oral absorption and short half-life, leading to a decreased drug efficacy. Therefore, new and targeted carriers with no such problems are needed. In the present study, PM was loaded into chitosan (CS) nanoparticles

accompanied by targeting to macrophages (as the host of *Leishmania* parasite). PM-loaded into mannosylated CS (MCS) nanoparticles using dextran (PM-MCS-dex-NPs) was prepared by ionic gelation and then characterized. The particle size and zeta potential of PM-MCS-dex-NPs were obtained as 246 nm and +31 mV, respectively. Mannosylation of CS was qualitatively evaluated by Fourier-transform infrared spectroscopy and quantitatively measured by CHNO elemental analysis; also, a mannosylation level of 17% (w) was attained. Encapsulation efficiency (EE), drug release profile, and THP-1 cell uptake potential were determined. A value of 83.5% for EE and a higher release rate in acidic media were achieved. THP-1 cell uptake level of PM-MCS-dex-NPs after 6h was ˜2.8 and ˜3.9 times of non-mannosylated CS nanoparticles (PM-CS-dex-NPs) and PM aqueous solution, respectively. *In vitro* cell cytotoxicity and promastigote and amastigote viabilities were evaluated by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay. Half-maximal inhibitory concentration values toward the THP-1 cells for PM aqueous solution, Glucantim, PM-CS-dex-NPs, and PM-MCS-dex-NPs after 48 h were obtained as 1846 ± 158, 1234 ± 93, 784 ± 52 and 2714 ± 126 μg mL$^{-1}$, respectively. Half-maximal inhibitory concentration values toward the promastigotes for PM aqueous solution, Glucantim, PM-CS-dex-NPs, and PM-MCS-dex-NPs after 48h were obtained as 105.0 ± 14.0, 169.5 ± 9.8, 65.8 ± 7.3 and 17.8 ± 1.0 μg mL$^{-1}$, respectively. Selectivity (therapeutic) indices for PM aqueous solution, Glucantim, PM-CS-dex-NPs and PM-MCS-dex-NPs after 48h were obtained as 24.6, 17.5, 3.7 and 214, respectively. The parasite burden in THP-1 cells after 48h treatment with PM aqueous solution, Glucantim, PM-CS-dex-NPs, and PM-MCS-dex-NPs at a typical concentration of 20μg mL$^{-1}$ were 71.78, 69.94, 83.14 and 33.41%, respectively. While the effect of PM-CS-dex-NPs was more salient on amastigotes, PM-MCS-dex-NPs effectively affected both stages of the parasite, especially the amastigote one. This indicated that the mannosylated formulation acts as a targeted delivery system. The findings of this study revealed that this novel targeted formulation represented a strong anti-leishmanial activity.

**Keywords:** Drug delivery, Macrophage targeting, Mannosylated nanoparticles, *L.* major, Aminosidine, MTT assay

### First record of haemosporidian parasites infecting swifts (Aves: Apodidae)

Author: Daniela de Angeli Dutra, Graziela Tolesano-Pascoli, Frederico Innecco Garcia

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**Abstract**

Avian malaria is a widespread infection caused by parasites from the Order Haemosporida. Indeed, Neotropical swifts are interesting models for host-parasite coevolution studies due to their unique life history that may allow them to escape parasitism. Considering this, we evaluated haemosporidians from Neotropical swifts. We collected blood and prepared smears from 277 individuals from waterfalls in Brazil. Despite low parasitemia or absence of parasites detected by microscopy haemosporidian infection was detected in 44 swifts (15.8%) using a screening PCR that amplifies a 154-nucleotide segment of ribosomal RNA coding sequence within the mitochondrial DNA (mtDNA) of Plasmodium and Haemoproteus. Although previous studies reported absence of these parasites in European and North American swifts our data suggest that Neotropical swifts are susceptible to haemosporidians. Further studies will add information about evolutionary and ecological aspects of avian haemosporidia in Neotropical Cypseloidinae swifts.

**Keywords:** Plasmodium, Neotropics, Cypseloidina, Swifts, Avian malaria

### Developing a dengue prediction model based on climate in Tawau, Malaysia

Author: Vivek Jason Jayaraj, Richard Avoi, Navindran Gopalakrishnan, Dhesi Baha Raja

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**Abstract**

Dengue is fast becoming the most urgent health issue in Malaysia, recording close to a 10-fold increase in cases over the last decade. With much uncertainty hovering over the recently introduced tetravalent vaccine and no effective antiviral drugs, vector control remains the most important strategy in combating dengue. This study analyses the relationship between weather predictors including its lagged terms, and dengue incidence in the District of Tawau over a period of 12 years, from 2006 to 2017. A forecasting model purposed to predict future outbreaks in Tawau was then developed using this data. Monthly dengue incidence data, mean temperature, maximum temperature, minimum temperature, mean relative humidity and mean rainfall over a period of 12 years from 2006 to 2017 in Tawau were retrieved from Tawau District Health Office and the Malaysian Meteorological Department. Cross-correlation analysis between weather predictors, lagged terms of weather predictors and dengue incidences established statistically significant cross-correlation between lagged periods of weather predictors-namely maximum temperature, mean relative humidity and mean rainfall with dengue incidence at time lags of 4–6 months. These variables were then employed into 3 different methods: a multivariate Poisson regression model, a Seasonal Autoregressive Integrated Moving Average (SARIMA) model and a SARIMA with external regressors for selection. Three models were selected but the SARIMA with external regressors model utilising maximum temperature at a lag of 6 months (p-value:0.001), minimum temperature at a lag of 4 months (p-value:0.01), mean relative humidity at a lag of 2 months (p-value:0.001), and mean rainfall at a lag of 6 months (p-value:0.001) produced an AIC of 841.94, and a log-likelihood score of −413.97 establishing it as the best fitting model of the methodologies utilised. In validating the models, they were utilised to develop forecasts with the model selected with the highest accuracy of predictions being the SARIMA model predicting 1 month in advance (MAE: 7.032, MSE: 83.977). This study establishes the effect of weather on the intensity and magnitude of dengue incidence as has been previously studied. A prediction model remains a novel method of evidence-based forecasting in Tawau, Sabah. The model developed in this study, demonstrated an ability to forecast potential dengue outbreaks 1 to 4 months in advance. These findings are not dissimilar to what has been previously studied in many different countries- with temperature and humidity consistently being established as powerful predictors of dengue incidence magnitude. When used in prognostication, it can enhance- decision making and allow judicious use of resources in public health setting. Nevertheless, the model remains a work in progress- requiring larger and more diverse data.

**Keywords:** Dengue fever, Temperature, Rainfall, Forecasting model, Early warning, Epidemic

## Adaptation to temperate climates: Evidence of photoperiod-induced embryonic dormancy in Aedes aegypti in South America

Author: Sylvia Fischer, María Sol De Majo, Cristian M. Di Battista, Pedro Montini, ... Raúl E. Campos

Source: Journal of Insects Physiology 2019 August-Sept: 103887

Hyperlink: https://doi.org/10.1016/j.jinsphys.2019.05.005

### Abstract

Dormancy is a developmental arrest in arthropods, in response to unfavorable conditions in temporally varying environments. In *Aedes aegypti*, the supposed inability of eggs to inhibit hatching has been used to explain the restriction of this species to tropical and subtropical regions. However, the geographic range of *Ae. aegypti* is constantly expanding towards temperate regions. Thus, the aim of the present study was to assess the ability of *Ae. aegypti* individuals from a temperate region (Buenos Aires City, Argentina) to enter photoperiod induced dormancy. To this end, we exposed both the parental generation and the eggs to short-day (SD: 10L:14D) and long-day (LD: 14L:10D) photoperiods, and studied the temporal variation in egg hatching. The experiment consisted of 28 treatment combinations of three factors: parental photoperiod (SD or LD), egg storage photoperiod (SD or LD), and age of eggs (14, 28, 42, 56, 70, 91, and 112 days). The results showed a lower hatching response with the SD parental photoperiod, and a trend to higher hatching with longer egg storage time in all photoperiod treatment combinations. The egg storage photoperiod showed no effect on egg hatching. In both parental photoperiod treatments, egg replicates of most ages from different females showed a large variability, with some replicates with lowest hatching response and others with highest hatching response. Our results show the ability of *Ae. aegypti* to inhibit egg hatching in response to a short-day photoperiod, which could allow the further expansion of this species to regions with colder winters.

**Keywords:** Culicidae, Dormancy, Photoperiod, Overwintering, Hatching, Eggs age

## Induction of RNA interference to block Zika virus replication and transmission in the mosquito Aedes aegypti

Author: Tereza Magalhaes, Nicholas A. Bergren, Susan L. Bennett, Erin M. Borland, Rebekah C. Kading

Source: Insect Biochemistry and Molecular Biology 2019 August; 111:103169

Hyperlink: https://doi.org/10.1016/j.ibmb.2019.05.004

### Abstract

The yellow fever mosquito, *Aedes aegypti*, serves as the primary vector for epidemic transmission of yellow fever, dengue, Zika (ZIKV), and chikungunya viruses to humans. Control of *Ae. aegypti* is currently limited to insecticide applications and larval habitat management; however, to combat growing challenges with insecticide resistance, novel genetic approaches for vector population reduction or transmission interruption are being aggressively pursued. The objectives of this study were to assess the ability of the *Ae. aegypti* antiviral exogenous-small interfering RNA (exo-siRNA) response to inhibit ZIKV infection and transmission, and to identify the optimal RNA interference (RNAi) target region in the ZIKV genome. We accomplished these objectives by *in vitro* transcription of five long double-stranded RNAs (dsRNAs) from the genome region spanning the NS2B-NS3-NS4A genes, which were the most highly conserved among ZIKV RNA sequences representing both East and West African and Asian-American clades, and evaluation of the ability of these dsRNAs to trigger an effective antiviral exo-siRNA response after intrathoracic injection into *Ae. aegypti*. In a pilot study, five ZIKV dsRNAs were tested by intrathoracic inoculation of 250 ng dsRNA into groups of approximately 5-day-old mosquitoes. Three days post-inoculation, mosquitoes were provided an infectious blood-meal containing ZIKV strain PRVABC59 (Puerto Rico), MR766 (Uganda), or 41525 (Senegal). On days 7 and 14 post-infection individual whole mosquito bodies were assessed for ZIKV infectious titer by plaque assays. Based on the results of this initial assessment, three dsRNAs were selected for further evaluation of viral loads of matched body and saliva expectorants using a standardized infectious dose of $1 \times 10^7$ PFU/mL of each ZIKV strain. Fourteen days post-exposure to ZIKV, paired saliva and carcass samples were harvested from individual mosquitoes and assessed for ZIKV RNA load by qRT-PCR. Injection of each of the three dsRNAs resulted in significant inhibition of replication of all three strains of ZIKV in

mosquito bodies and saliva. This study lays critical groundwork for pursuing ZIKV transmission-blocking strategies that exploit the *Ae. aegypti* exo-siRNA response for arbovirus suppression in natural populations.

### The sulcatone receptor of the strict nectar-feeding mosquito Toxorhynchites amboinensis

Author: Amir Dekel, Esther Yakir, Jonathan D. Bohbot

Source: Insect Biochemistry and Molecular Biology 2019 Aug; 111:103174

Hyperlink: https://doi.org/10.1016/j.ibmb.2019.05.009

**Abstract**

Controlling *Ae. aegypti* populations and the prevention of mosquito bites includes the development of monitoring, repelling and attract-and-kill strategies that are based on understanding the chemical ecology of these pests. Olfactory-mediated attraction to mammals has recently been linked to the mosquito *Aedes aegypti* odorant receptor *Or4*, which is activated by animal-released 6-Methyl-5-hepten-2-one (sulcatone). This odorant is also a major component of flower scents and may play a role outside animal-host seeking. To explore the role of this chemical cue, we looked at the interaction between sulcatone and an *Or4* homolog expressed in the antennae of the strict nectar-feeding mosquito *Toxorhynchites amboinensis*. Using the two-electrode voltage clamp of *Xenopus* oocytes as a heterologous expression system, we show that this receptor is a high intensity sulcatone receptor comparable to its *Aedes* counterparts. We also show that OR4 is activated by other aliphatic ketones and is inhibited by DEET. This pharmacological characterization suggests that sulcatone may be operating in more than one context in the Culicidae family.

**Keywords:** Insect repellent, Odorant receptor, Aedes aegypti, Toxorhynchites amboinensis, Olfaction

### A salivary protein of Aedes aegypti promotes dengue-2 virus replication and transmission

Author: Chalida Sri-in, Shih-Che Weng, Wen-Yu Chen, Betty A. Wu-Hsieh, Shin-Hong Shiao

Source: Insect Biochemistry and Molecular Biology 2019 August; 111: 103181

Hyperlink: https://doi.org/10.1016/j.ibmb.2019.103181

### Abstract

Although dengue is the most prevalent arthropod-borne viral disease in humans, no effective medication or vaccine is presently available. Previous studies suggested that mosquito salivary proteins influence infection by the dengue virus (DENV) in the mammalian host. However, the effects of salivary proteins on DENV replication within the *Aedes aegypti* mosquito remain largely unknown. In this study, we investigated the effect of a specific salivary protein (named AaSG34) on DENV serotype 2 (DENV2) replication and transmission. We showed that transcripts of AaSG34 were upregulated in the salivary glands of *Aedes aegypti* mosquitoes after a meal of blood infected with DENV2. Transcripts of the dengue viral genome and envelop protein in the salivary glands were significantly diminished after an infectious blood meal when AaSG34 was silenced. The effect of AaSG34 on DENV2 transmission was investigated in *Stat1*-deficient mice. The intradermal inoculation of infectious mosquito saliva induced hemorrhaging in the *Stat1*-deficient mice; however, saliva from the AaSG34-silenced mosquitoes did not induce hemorrhaging, suggesting that AaSG34 enhances DENV2 transmission. This is the first report to demonstrate that the protein AaSG34 promotes DENV2 replication in mosquito salivary glands and enhances the transmission of the virus to the mammalian host.

**Keywords:** Aedes aegypti, Dengue virus, Mosquito salivary proteins, Transmission, Stat1−/− mice

## Generation and functional characterisation of Plasmodium yoelii csp deletion mutants using a microhomology-based CRISPR/Cas9 method

Author: Ruixue Xu, Yanjing Liu, Ruoxi Fan, Rui Liang, Jian Li

Source: Int. Journal for Parasitology 2019 August; 49(9):705-714

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### Abstract

CRISPR/Cas9 is a powerful genome editing method that has greatly facilitated functional studies in many eukaryotic organisms including malaria parasites. Due to the lack of genes encoding enzymes necessary for the non-homologous end joining DNA repair pathway, genetic manipulation of malaria parasite genomes is generally accomplished through homologous recombination requiring the presence of DNA templates. Recently, an alternative double-strand break repair pathway, microhomology-mediated end joining, was found in the *Plasmodium falciparum* parasite. Taking advantage of the MMEJ pathway, we developed a MMEJ-based CRISPR/Cas9 (mCRISPR) strategy to efficiently generate multiple mutant parasites simultaneously in genes with repetitive sequences. As a proof of principle, we successfully produced various size mutants in the central repeat region of the *Plasmodium yoelii* circumsporozoite surface protein without the use of template DNA. Monitoring mixed parasite populations and individual parasites with different sizes of CSP-CRR showed that the CSP-CRR plays a role in the development of mosquito stages, with severe developmental defects in parasites with large deletions in the repeat region. However, the majority of the *csp* mutant parasite clones grew similarly to the wild type *P. yoelii* 17XL parasite in mice. This study develops a useful technique to efficiently generate mutant parasites with deletions or insertions, and shows that the CSP-CRR plays a role in parasite development in mosquito.

**Keywords:** Rodent malaria, MMEJ,Double strand break,Circumsporozoite surface protein,Mosquito

## Rhoptry neck protein 11 has crucial roles during malaria parasite sporozoite invasion of salivary glands and hepatocytes

Author: Sirasate Bantuchai, Mamoru Nozaki, Amporn Thongkukiatkul, Natcha Lorsuwannarat, Tomoko Ishino

Source: Int. Journal for Parasitology 2019 August; 49(9):725-735

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### Abstract

The malaria parasite sporozoite sequentially invades mosquito salivary glands and mammalian hepatocytes; and is the *Plasmodium* lifecycle infective form mediating parasite transmission by the mosquito vector. The identification of several sporozoite-specific secretory proteins involved in invasion has revealed that sporozoite motility and specific recognition of target cells are crucial for transmission. It has also been demonstrated that some components of the invasion machinery are conserved between erythrocytic asexual and transmission stage parasites. The application of a sporozoite stage-specific gene knockdown system in the rodent malaria parasite, *Plasmodium berghei*, enables us to investigate the roles of such proteins previously intractable to study due to their essentiality for asexual intraerythrocytic stage development, the stage at which transgenic parasites are derived. Here, we focused on the rhoptry neck protein 11 (RON11) that contains multiple transmembrane domains and putative calcium-binding EF-hand domains. *Pb*RON11 is localised to rhoptry organelles in both merozoites and sporozoites. To repress *Pb*RON11 expression exclusively in sporozoites, we produced transgenic parasites using a promoter-swapping strategy. *Pb*RON11-repressed sporozoites showed significant reduction in attachment and motility in vitro, and consequently failed to efficiently invade salivary glands. *Pb*RON11 was also determined to be essential for sporozoite infection of the liver, the first step during transmission to the vertebrate host. RON11 is demonstrated to be crucial for sporozoite invasion of both target host cells – mosquito salivary glands and mammalian hepatocytes – via involvement in sporozoite motility.

**Keywords:** Plasmodium,Sporozoite,Rhoptry,Gliding motility,Conditional knockdown

## Long-term incidence of severe malaria following RTS,S/AS01 vaccination in children and infants in Africa: an open-label 3-year extension study of a phase 3 randomised controlled trial

Author: Halidou Tinto,Walter Otieno,Samwel Gesase,Hermann Sorgho

Source: The Lancet Infectious Disease 2019 August 01;19(8):821-832

Hyperlink: https://doi.org/10.1016/S1473-3099(19)30300-7

### Abstract

**Background:** Results from a previous phase 3 study showed efficacy of the RTS,S/AS01 vaccine against severe and clinical malaria in children (in 11 sites in Africa) during a 3–4-year follow-up. We aimed to investigate malaria incidence up to 7 years postvaccination in three of the sites of the initial study. **Methods:** In the initial phase 3 study, infants aged 6–12 weeks and children aged 5–17 months were randomly assigned (1:1:1) to receive four RTS,S/AS01 doses (four-dose group), three RTS,S/AS01 doses and a comparator dose (three-dose group), or four comparator doses (control group). In this open-label extension study in Korogwe (Tanzania), Kombewa (Kenya), and Nanoro (Burkina Faso), we assessed severe malaria incidences as the primary outcome for 3 additional years (January, 2014, to December, 2016), up to 6 years (younger children) or 7 years (older children) postprimary vaccination in the modified intention-

to-treat population (ie, participants who received at least one dose of the study vaccine). As secondary outcomes, we evaluated clinical malaria incidences and serious adverse events. This trial is registered with ClinicalTrials,govnumber NCT02207816. **Findings:** We enrolled 1739 older children (aged 5–7 years) and 1345 younger children (aged 3–5 years). During the 3-year extension, 66 severe malaria cases were reported, resulting in severe malaria incidence of 0·004 cases per person-years at risk (PPY; 95% CI 0–0·033) in the four-dose group, 0·007 PPY (0·001–0·052) in the three-dose group, and 0·009 PPY (0·001–0·066) in the control group in the older children category and a vaccine efficacy against severe malaria that did not contribute significantly to the overall efficacy (four-dose group 53·7% [95% CI–13·7 to 81·1], p=0·093; three-dose group 23·3% [–67·1 to 64·8], p=0·50). In younger children, severe malaria incidences were 0·007 PPY (0·001–0·058) in the four-dose group, 0·007 PPY (0·001–0·054) in the three-dose group, and 0·011 PPY (0·001–0·083) in the control group. Vaccine efficacy against severe malaria also did not contribute significantly to the overall efficacy (four-dose group 32·1% [–53·1 to 69·9], p=0·35; three-dose group 37·6% [–44·4 to 73·0], p=0·27). Malaria transmission was still occurring as evidenced by an incidence of clinical malaria ranging from 0·165 PPY to 3·124 PPY across all study groups and sites. In older children, clinical malaria incidence was 1·079 PPY (95% CI 0·152–7·662) in the four-dose group, 1·108 PPY (0·156–7·868) in the three-dose group, and 1·016 PPY (0·14–7·213) in the control group. In younger children, malaria incidence was 1·632 PPY (0·23–11·59), 1·563 PPY (0·22–11·104), and 1·686 PPY (0·237–11·974), respectively. In the older age category in Nanoro, clinical malaria incidence was higher in the four-dose (2·444 PPY; p=0·011) and three-dose (2·411 PPY; p=0·034) groups compared with the control group (1·998 PPY). Three cerebral malaria episodes and five meningitis cases, but no vaccine-related severe adverse events, were reported. Interpretation: Overall, severe malaria incidence was low in all groups, with no evidence of rebound in RTS,S/AS01 recipients, despite an increased incidence of clinical malaria in older children who received RTS,S/AS01 compared with the comparator group in Nanoro. No safety signal was identified.

**Parasite Removal for Malaria Elimination in Costa Rica**

Author: Rodrigo Marín Rodríguez, Luis Fernando Chaves

Source: Trends in Parasitology 2019 August;35(8):585-588

Hyperlink: https://doi.org/10.1016/j.pt.2019.04.007

## Abstract

A condition for eliminating malaria is reduction in transmission.The work of Ronald Ross set the stage for the use of vector control as a major tool for reducing malaria transmission.Malaria elimination was achieved for the first time in Mesoamerica when the Panamá Canal, a major interoceanic passage, was built. During the Canal`s construction, William Crawford Gorgas employed different vector-control strategies to reduce and eliminate the transmission of several vector-borne diseases, as these, often lethal, diseases stopped previous attempts to build this major interoceanic passage. Coincidentally, while the theory and scientific evidence that still serve as the basis for mosquito control in mosquito-borne diseases developed, Robert Koch proposed that malaria transmission could be reduced if parasites were removed from human populations through antimalarial drug use Mass drug administration (MDA), the concerted population-wide use of drugs, is not as widely implemented as vector control to reduce malaria transmission, but available evidence supports its potential for eliminating malaria.Indeed, MDA and proper treatments have shown their ability to reduce malaria transmission.Here, we want to highlight the impact that a focalized MDA and treatment shift, both based on supervised 7-day treatments, had on accelerating the malaria elimination process in Costa Rica, where systematic indoor residual spraying stopped in 1990.

**Keywords:** 7-day treatment, Plasmodium vivax, primaquine, breakpoint, regime shift, mass drug administration.

## Tying up Loose Ends in the Malaria Antigenic Variation Story

Authors: David E.Arnot

Source: Trends in Parasitology 2019 August; 35(8):588-590

Hyperlink: https://doi.org/10.1016/j.pt.2019.06.006

## Abstract

A recent paper (Zhang *et al.*, *PLoS Biol.*, 2019) shines remarkable new light onto the malaria antigenic variation story. Using CRISPR/Cas9-targeted chromosome breaks and long-read whole-genome sequencing, they followed the fate of detached subtelomeric *Pf*EMP1/var genes and demonstrated that these initiate cascades of recombination at sites far from the original break.

**Keywords:** malaria, antigenic variation, recombination cascade

## A randomized controlled trial of azithromycin and sulphadoxine–pyrimethamine as prophylaxis against malaria in pregnancy among human immunodeficiency virus–positive women

Author: Oriyomi Akinyotu, Folasade Bello, Rukiyat Abdus-Salam, Ayodele Arowojolu

Source: Transactions of The Royal Society of Tropical Medicine and Hygiene 2019 August; 113(8):463–470

Hyperlink: https://doi.org/10.1093/trstmh/trz028

### Abstract

**Background:** Malaria and human immunodeficiency virus (HIV) infections in pregnancy are important and major contributing factors to maternal morbidity and mortality in sub-Saharan Africa. Prevention of malaria in HIV-positive pregnant woman will reduce the burden of malaria–HIV comorbidity. The objective of this study was to compare effects and safety of azithromycin (AZ) with sulphadoxine–pyrimethamine (SP) for intermittent preventive therapy for malaria in HIV-positive pregnant women. **Methods:** We performed a randomized, controlled, open-label pregnancy trial of 140 HIV-positive pregnant patients attending antenatal clinics at the University College Hospital and Adeoyo Maternity Teaching Hospital, Ibadan, Nigeria. Participants were enrolled from a gestational age of 16 weeks and randomized to receive AZ or SP. The primary outcome was peripheral parasitaemia at delivery. Secondary outcomes were drug tolerability, foetal outcome and birthweight. The $\chi^2$ test (or Fisher's exact test, as appropriate) and Student's t test were used in the per-protocol analysis. The level of statistical significance was $p<0.05$. **Results:** A total of 123 participants (87.9%) completed the study: 60 participants received AZ and 63 received SP. The incidence of malaria parasitaemia at delivery in the AZ group was 6 (10.0%), compared with 7 (11.1%) in the SP group (relative risk 0.89 [95% confidence interval 0.28 to 2.82], $p=0.84$). Placental parasitization was demonstrated in 1 (1.6%) participant in the SP group compared with 3 (5.0%) in the AZ group ($p=0.36$). **Conclusions:** The findings suggest that AZ is comparable to SP in malaria prevention and safety in HIV-positive pregnant women.

**Keywords:** azithromycin, HIV pregnancy, intermittent preventive therapy, malaria in pregnancy, malaria prophylaxis, sulphadoxine–pyrimethamine

## Cutaneous leishmaniasis in north Lebanon: re-emergence of an important neglected tropical disease

Author: Dima El Safadi, Sabah Merhabi, Rayane Rafei, Hassan Mallat, Monzer Hamze

Source: Transactions of The Royal Society of Tropical Medicine and Hygiene 2019 Aug; 113(8):471–476

Hyperlink: https://doi.org/10.1093/trstmh/trz030

### Abstract

**Background:** Cutaneous leishmaniasis (CL) is the most prevalent neglected tropical disease among externally displaced people in the Middle East. In recent years, the Lebanese population has increased >30%, mainly due to a mass influx of Syrian migrants, thousands of them carrying CL, among other infectious diseases. Here we revisit the current CL prevalence among refugees in northern Lebanon. **Methods:** This cohort study was conducted at the Al Bashaer Medical Center in north Lebanon between January and June 2017. A total of 48 randomly selected suspected CL patients were clinically diagnosed by dermatologists and samples were obtained for microscopic examination and molecular identification by polymerase chain reaction restriction fragment length polymorphism. The treatment response to antimonials was assessed each week and was followed for up 6 months. **Results:** *Leishmania tropica* was the predominant species (91.7%) followed by *Leishmania major* (8.3%). Confirmed cases were treated with one to two courses of antimonials and healing was usually achieved after receiving a second course of treatment. Importantly, we show evidence of possible local CL transmission by indigenous sandflies in three separate patients who had no history of recent travel to Syria. **Conclusions:** This highlights the urgent necessity to implement preventive disease strategies to avoid further dispersion of *L. tropica* CL in north Lebanon.

**Keywords:** cutaneous leishmaniasis, Glucantime, Lebanon, Leishmania tropica, PCR-RFLP, Syrian refugees

## Kelch 13 propeller gene polymorphism among Plasmodium falciparum isolates in Lagos, Nigeria: Molecular Epidemiologic Study

Authors: Uche Igbasi, Wellington Oyibo, Sunday Omilabu ,Hong Quan ,Shen-Bo Chen ,Hai-Mo Shen ,Jun-Hu Chen, Xiao-Nong Zhou

Source: Tropical Medicine & International Health 2019 Aug; 24(8):1011–1017.

Hyperlinks: https://doi.org/10.1111/tmi.13273

### Abstract

**Objective:** To assess polymorphism in Kelch 13 gene of Plasmodium falciparum isolates in Lagos, Nigeria. **Methods:** 195 Plasmodium falciparum-positive dried blood spots collected from individuals that accessed diagnostic care at some health facilities and during community surveys across several Local Government Areas of Lagos State, Nigeria, were investigated for the presence of mutations in the K13 gene by nested polymerase chain reaction (PCR) using haplotype-specific probes and sequencing. **Results:** Three mutant genotypes of K13 gene were observed: A578S in 0.5%, D464N in 0.5% and Q613H in 1.5%. The frequency of K13 polymorphism was 3.1%, while the remaining parasite population had the wild K13 propeller genes. **Conclusion:** No validated Kelch 13 polymorphism associated with artemisinin resistance was seen among P. falciparum isolates from Lagos, Nigeria. As no clinical study was done, this could not be correlated with artemisinin sensitivity**.**

**Keywords:** artemisinin ,Plasmodium falciparum ,resistance, Kelch 13 gene,artémisinine Plasmodium falciparum, résistance ,gène Kelch 13

## First Molecular Report of Leishmania (Leishmania) amazonensis and Leishmania (Viannia) guyanensis in Paraguayan Inhabitants Using High-Resolution Melt-PCR

Author: Oscar Daniel Salvioni Recalde1, José Pereira Brunelli2, Miriam Soledad Rolon1, Antonieta Rojas de Arias1, Olga Aldama2, Celeste Vega Gómez1

Source: The American Journal of Tropical Medicine and Hygiene 2019 Oct; 101(4):780-788

Hyperlink: https://doi.org/10.4269/ajtmh.18-0880

### Abstract

American tegumentary leishmaniasis is an endemic anthropozoonosis undergoing expansion on the American continent. The disease is caused by several Leishmania species and it is manifested

as cutaneous and mucocutaneous leishmaniasis. In this study, we evaluate the viability of high-resolution melt polymerase chain reaction (HRM-PCR) analysis to differentiate four closely related Leishmania species as a routine tool for the diagnosis of leishmaniasis. For this purpose, biopsy specimens from cutaneous and mucocutaneous lesions were taken from 132 individuals from endemic and non-endemic areas for leishmaniasis. Each sample was processed for parasitological, histopathological, and molecular analysis. Positive biopsy samples were analyzed by HRM-PCR of a 144-bp heat-shock protein (hsp70) gene fragment, and new cases were confirmed by sequencing. Of the 132 samples analyzed, 36 (27%) were positive for Leishmania spp., of which 86% were from cutaneous lesions and 14% from mucocutaneous lesions. We identified Leishmania (Viannia) braziliensis (84%), Leishmania (Leishmania) infantum (13%), and Leishmania (Leishmania) amazonensis (3%) in cutaneous lesions, and L. (V.) braziliensis (40%), L. (L.) infantum (20%), L. (L.) amazonensis (20%), and Leishmania (Viannia) guyanensis (20%) in mucocutaneous lesions. The main purpose of this research was to report for the first time in Paraguay the presence of L. (L.) amazonensis and L. (V.) guyanensis in patients with cutaneous and mucocutaneous lesions, using the HRM-PCR technique. In addition, we report the presence of additional new cases of L. (L.) infantum in cutaneous lesions.

## Prevalence of Molecular Markers of Antimalarial Drug Resistance across Altitudinal Transmission Zones in Highland Western Uganda

Author: Ross M. Boyce1,2, Nicholas Brazeau3, Travis Fulton1, Nick Hathaway4, Michael Matte2, Moses Ntaro2, Edgar Mulogo2, Jonathan J. Juliano1,3,5

Source: The American Journal of Tropical Medicine and Hygiene 2019 Oct; 101(4):799 - 802

Hyperlinks: https://doi.org/10.4269/ajtmh.19-0081

### Abstract

We explored spatial variation in the prevalence of established molecular markers of antimalarial resistance across a geographically diverse, highland region of western Uganda. We identified Plasmodium falciparum CQ resistance transporter 76T mutations in all pools, but there was no evidence of spatial differences across village-based strata defined by either altitude or river valley. In contrast, we identified a significant inverse association between altitude and the prevalence of Plasmodium falciparum multidrug resistance 1 mutations with the largest proportion of Y184F mutations observed in the low-elevation, high-transmission villages. These results demonstrate the substantial heterogeneity in resistance markers observed across geographic settings, even at relatively small scales, but highlight the complex nature of these ecological relationships.

## Case Report: Cardiac Tamponade in Dengue Hemorrhagic Fever: An Unusual Manifestation of a Common Disease

Author: Sagnik Biswas1, Prabhat Kumar1, Ghazal Tansir1, Ashutosh Biswas1

Source: The American Journal of Tropical Medicine and Hygiene 2019 Aug 07; 101( 2):448-450
Hyperlink: https://doi.org/10.4269/ajtmh.19-0153

### Abstract

Dengue hemorrhagic fever is one of the most commonly encountered mosquito-borne viral infections of humans worldwide with multiple reported outbreaks. Cardiac involvement is a known manifestation of the disease usually presenting as rhythm abnormalities, myocarditis, or pericardial effusion, which may be clinically asymptomatic. We describe a case of a 30-year-old woman who presented to us with high-grade fever, headache, retro-orbital pain, generalized maculopapular rash with bilateral pleural effusion, and hypotension. Dengue non-structural protein 1 (NS1) antigen and IgM antibodies were positive on admission, supporting a diagnosis of dengue hemorrhagic fever. Cardiac troponin-I was elevated on admission (65 ng/L) with diffuse convex ST segment elevations on electrocardiogram, suggestive of possible myopericarditis. Echocardiogram on admission revealed minimal pericardial effusion with preserved ejection fraction. Despite administration of fluids and inotrope use, the patient's hypotension progressively deteriorated over the next 6 hours, associated with decreased urine output and worsening sensorium. Clinical examination revealed muffled heart sounds and raised jugular venous pressure. A repeat echocardiogram confirmed an increase in the pericardial effusion manifesting as cardiac tamponade. Ultrasound-guided pigtail catheter insertion led to a prompt removal of the excessive pericardial fluid and correction of hypotension. Early identification of this uncommon but important complication of dengue hemorrhagic fever led to a good outcome in our case.