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Dengue, chikungunya et maladie à virus Zika.....	2
Rage	8
Trachome	8
Ulcère de Buruli.....	9
Pian	9
Lèpre	9
Trypanosomes (trypanosomiase et maladie de Chagas)	10
Leishmaniose.....	12
Cysticercose	14
Dracunculose	15
Echinococcoses	15
Trématodes d'origine alimentaire (clonorchiase, opisthorchiase, fasciolase et paragonimose)	16
Filariose lymphatique	17
Mycétome.....	17
Onchocercose	17
Schistosomiase.....	18
Helminthiases transmises par le sol (ascaridiose, trichuriase, ankylostomiasis)	19
Gale	19
Morsures de serpent.....	19

DENGUE, CHIKUNGUNYA ET MALADIE A VIRUS ZIKA

Molecular docking analysis of Adhatoda Vasica with Thromboxane A2 receptor (TXA2R) (6IIU) and Antiviral molecules for possible dengue complications.

Thangaraju, P., N, G., Ar, V., Gurunthalingam, M., Ty, S., Venkatesan, S., Thangaraju, E.

18-07-2022

Infect Disord Drug Targets

<https://doi.org/10.2174/187152652266220718101544>

Objective The present study is an in-silicomodel of platelet amplification potential of Adhatoda vasica which can be used to treat thrombocytopenia in Dengue complications. Methods Docking studies are proved to be an essential tool that facilitates the structural diversity of natural products to be harnessed in an organized manner. In the present study, vasicine containing natural anti-dengue potential was subjected to docking studies using Schrodinger glides software (ver.11.1). The docking study was carried out to find out the potential molecular targets for selected protein. The docking was carried out on different ligands like vasicine, ramatroban, Chloroquine, Celgosivir and standard elthrombopag downloaded from the PubChem and retrieved to glide software and ligands prepared using lig prep wizard. Docking was performed using the ligand docking wizard of Glide-maestro 2018. Results The docking score of vasicine (-5.27) is nearly identical to the standard used elthrombopag (-6.08) and both ligands bind with one hydrogen bond. The validation ramatroban score is -12.39 and bind with five hydrogen bonds, Celgosivir had a docking score of -7.3 with three hydrogen bonds, and Chloroquine has no hydrogen bond but a docking score of -4.6. Conclusion Vasicine was found to be the most suitable target of platelet amplification potential from Adhatoda vasica. However, the molecular docking results are preliminary and it indicated that vasicine could be one of the potential ligands to treat the thrombocytopenia of dengue and experimental evaluation will be carried out in near future.

Experiences of women raising children with congenital Zika syndrome along a trajectory of prevention, care and support in Brazil.

Morris, M., Brito, A., Malta, M., Jacques, I., Rocha, G., Novaes, R., Mantsios, A., Kerrigan, D.

18-07-2022

Glob Public Health

<https://doi.org/10.1080/17441692.2022.2098999>

Social science research investigating the social dynamics of Zika and congenital Zika syndrome (CZS) is essential to inform future services related to Zika and other infectious diseases. We sought to understand lived experiences with Zika during pregnancy, birth, and post-partum by conducting in-depth interviews with a sample of 31 women infected with Zika during the 2015-16 outbreak who had a child with CZS in

Pernambuco, Brazil. Transcripts were coded using thematic content analysis. Many women experienced shock when their children were born with CZS given the lack of information they were provided during the antenatal period. Stigma from loved ones and community members was a salient theme as were financial difficulties arising from women having to stop working to care for their child. While women experienced significant challenges caring for a child with CZS, they also exhibited resiliency in their ability to move from shock and sorrow to focusing on the needs of their child. While support services were generally available, they were often located at a significant distance. Results underscore the need for interventions to improve patient-provider communication, address socio-structural stressors, and support individual and collective resilience in women and families affected by Zika in lower resource settings.

A controlled effects approach to assessing immune correlates of protection.

Gilbert, P., Fong, Y., Kenny, A., Carone, M.

15-07-2022

Biostatistics

<https://pubmed.ncbi.nlm.nih.gov/35848843>

An immune correlate of risk (CoR) is an immunologic biomarker in vaccine recipients associated with an infectious disease clinical endpoint. An immune correlate of protection (CoP) is a CoR that can be used to reliably predict vaccine efficacy (VE) against the clinical endpoint and hence is accepted as a surrogate endpoint that can be used for accelerated approval or guide use of vaccines. In randomized, placebo-controlled trials, CoR analysis is limited by not assessing a causal vaccine effect. To address this limitation, we construct the controlled risk curve of a biomarker, which provides the causal risk of an endpoint if all participants are assigned vaccine and the biomarker is set to different levels. Furthermore, we propose a causal CoP analysis based on controlled effects, where for the important special case that the biomarker is constant in the placebo arm, we study the controlled vaccine efficacy curve that contrasts the controlled risk curve with placebo arm risk. We provide identification conditions and formulae that account for right censoring of the clinical endpoint and two-phase sampling of the biomarker, and consider G-computation estimation and inference under a semiparametric model such as the Cox model. We add modular approaches to sensitivity analysis that quantify robustness of CoP evidence to unmeasured confounding. We provide an application to two phase 3 trials of a dengue vaccine indicating that controlled risk of dengue strongly varies with 50% neutralizing antibody titer. Our work introduces controlled effects causal mediation analysis to immune CoP evaluation.

Molecular adaptations during viral epidemics.

Revue de littérature

Rochman, N., Wolf, Y., Koonin, E.

Dengue, chikungunya et maladie à virus Zika

18-07-2022

EMBO Rep

<https://doi.org/10.15252/embr.202255393>

In 1977, the world witnessed both the eradication of smallpox and the beginning of the modern age of genomics. Over the following half-century, 7 epidemic viruses of international concern galvanized virologists across the globe and led to increasingly extensive virus genome sequencing. These sequencing efforts exerted over periods of rapid adaptation of viruses to new hosts, in particular, humans provide insight into the molecular mechanisms underpinning virus evolution. Investment in virus genome sequencing was dramatically increased by the unprecedented support for phylogenomic analyses during the COVID-19 pandemic. In this review, we attempt to piece together comprehensive molecular histories of the adaptation of variola virus, HIV-1 M, SARS, H1N1-SIV, MERS, Ebola, Zika, and SARS-CoV-2 to the human host. Disruption of genes involved in virus-host interaction in animal hosts, recombination including genome segment reassortment, and adaptive mutations leading to amino acid replacements in virus proteins involved in host receptor binding and membrane fusion are identified as the key factors in the evolution of epidemic viruses.

Assessing the impact of SARS-CoV-2 infection on the dynamics of dengue and HIV via fractional derivatives.

Omame, A., Abbas, M., Abdel-Aty, A.

11-07-2022

Chaos Solitons Fractals

<https://doi.org/10.1016/j.chaos.2022.112427>

A new non-integer order mathematical model for SARS-CoV-2, Dengue and HIV co-dynamics is designed and studied. The impact of SARS-CoV-2 infection on the dynamics of dengue and HIV is analyzed using the tools of fractional calculus. The existence and uniqueness of solution of the proposed model are established employing well known Banach contraction principle. The Ulam-Hyers and generalized Ulam-Hyers stability of the model is also presented. We have applied the Laplace Adomian decomposition method to investigate the model with the help of three different fractional derivatives, namely: Caputo, Caputo-Fabrizio and Atangana-Baleanu derivatives. Stability analyses of the iterative schemes are also performed. The model fitting using the three fractional derivatives was carried out using real data from Argentina. Simulations were performed with each non-integer derivative and the results thus obtained are compared. Furthermore, it was concluded that efforts to keep the spread of SARS-CoV-2 low will have a significant impact in reducing the co-infections of SARS-CoV-2 and dengue or SARS-CoV-2 and HIV. We also highlighted the impact of three different fractional derivatives in analyzing complex models dealing with the co-dynamics of different diseases.

A replication competent luciferase-secreting DENV2 reporter for sero-epidemiological surveillance of neutralizing and enhancing antibodies.

Saipin, K., Thaisomboonsuk, B., Siridechadilok, B., Chaitaveep, N., Ramasoota, P., Puttikhunt, C., Sangiambut, S., Jones, A., Kraivong, R., Sriburi, R., Keelapang, P., Sittisombut, N., Junjhon, J.

14-07-2022

J Virol Methods

<https://pubmed.ncbi.nlm.nih.gov/35843366>

Dengue virus (DENV) specific neutralizing and enhancing antibodies play crucial roles in dengue disease prevention and pathogenesis. DENV reporters are gaining popularity in the evaluation of these antibodies; their accessibility and acceptance may improve with more efficient production systems and indications of their antigenic equivalence to the wild-type virus. This study aimed to generate a replication competent luciferase-secreting DENV reporter (LucDENV2) and evaluate its feasibility in neutralizing and infection-enhancing antibody assays in comparison with wild-type DENV2, strain 16681, and a luciferase-secreting, single-round infectious DENV2 reporter (LucSIP). LucDENV2 replicated to similarly high levels as that of the parent 16681 virus in a commonly used mosquito cell line. LucDENV2 was neutralized in an antibody concentration-dependent manner by a monoclonal antibody specific to the flavivirus fusion loop and two antibodies specific to the E domain III, which closely resembled the neutralization patterns employing the LucSIP and wild-type DENV2. Parallel analysis of LucDENV2 and wild-type DENV2 revealed good agreement between the luciferase-based and focus-based neutralization and enhancement assays in a 96-well microplate format when employed against a set of clinical sera, suggesting comparable antigenic properties of LucDENV2 with those of the parent virus. The high-titer, replication competent, luciferase-secreting DENV reporter presented here should be a useful tool for fast and reliable quantitation of neutralizing and infection-enhancing antibodies in populations living in DENV-endemic areas.

Control of the COVID-19 pandemic is derailing the fight against typhoid, dengue, and measles in Pakistan.

Rana, M., Usman, M., Alzahrani, K., Alam, M., Ikram, A., Salman, M., Umair, M.

16-07-2022

J Glob Health

<https://doi.org/10.7189/jogh.12.03040>

Theoretical studies on RNA recognition by Musashi 1 RNA-binding protein.

Darai, N., Mahalapbutr, P., Wolschann, P., Lee, V., Wolfinger, M., Rungrotmongkol, T.

15-07-2022

Sci Rep

<https://doi.org/10.1038/s41598-022-16252-w>

The Musashi (MSI) family of RNA-binding proteins, comprising the two homologs Musashi-1 (MSI1) and Musashi-2 (MSI2), typically regulates translation and is involved in cell proliferation and tumorigenesis. MSI proteins contain two ribonucleoprotein-like RNA-binding domains, RBD1 and RBD2, that bind single-stranded RNA motifs with a central UAG trinucleotide with high affinity and specificity. The finding that MSI also promotes the replication of Zika virus, a neurotropic Flavivirus, has triggered further investigations of the biochemical principles behind MSI-RNA interactions. However, a detailed molecular understanding of the specificity of MSI RBD1/2 interaction with RNA is still missing. Here, we performed computational studies of MSI1-RNA association complexes, investigating different RNA pentamer motifs using molecular dynamics simulations with binding free energy calculations based on the solvated interaction energy method. Simulations with AlphaFold2 suggest that predicted MSI protein structures are highly similar to experimentally determined structures. The binding free energies show that two out of four RNA pentamers exhibit a considerably higher binding affinity to MSI1 RBD1 and RBD2, respectively. The obtained structural information on MSI1 RBD1 and RBD2 will be useful for a detailed functional and mechanistic understanding of this type of RNA-protein interactions.

FIRST REPORT OF AEDES VITTATUS IN ISLAMABAD, PAKISTAN.

Jabeen, A., Ansari, J., Ikram, A., Khan, M.

15-07-2022

J Am Mosq Control Assoc

<https://doi.org/10.2987/22-7067>

Aedes vittatus is distributed throughout Asia, Africa, and Europe and can transmit dengue, chikungunya, yellow fever, and Zika viruses. Like other Aedes species, larvae develop in both natural and artificial containers in urban, suburban, and rural areas. In September 2021, an entomological survey was conducted at the National Institute of Health of Pakistan (NIH) and adjacent housing within the NIH colony. All containers with water were examined for Aedes mosquitoes at 150 locations, including residential properties, a plant nursery, junkyards, and recreational parks and playgrounds. A total of 103 larvae, 37 pupae, 5 female and 2 male Ae. vittatus were collected from a fountain. This was the first detection of Ae. vittatus in urban Islamabad. Additional vector surveillance is needed to better understand the geographical distribution, ecology, and behavior of this invasive species and to understand its possible role in the transmission of dengue and chikungunya viruses in Pakistan.

Multiple chikungunya virus introductions in Lao PDR from 2014 to 2020.

Calvez, E., Bounmany, P., Somlor, S., Xaybounousou, T., Viengphouthong, S., Keosenghom, S., Brey, P., Lacoste, V., Grandadam, M.

15-07-2022

PLoS One

<https://doi.org/10.1371/journal.pone.0271439>

The first documented chikungunya virus (CHIKV) outbreak in Lao People's Democratic Republic (Lao PDR) occurred in 2012–2013. Since then, several imported and a few autochthonous cases were identified by the national arbovirus surveillance network. The present study aimed to summarize the main genetic features of the CHIKV strains detected in Lao PDR between 2014 and 2020. Samples from Lao patients presenting symptoms compatible with a CHIKV infection were centralized in Vientiane Capital city for real-time RT-PCR screening. Molecular epidemiology was performed by sequencing the E2-6K-E1 region. From 2014 to 2020, two Asian lineage isolates (e.g. French Polynesia; Indonesia), one ECSA-IOL lineage isolate (e.g. Thailand) and one unclassified (e.g. Myanmar) were imported in Vientiane Capital city. Sequences from the autochthonous cases recorded in the Central and Southern parts of the country between July and September 2020 belonged to the ECSA-IOL lineage and clustered with CHIKV strains recently detected in neighboring countries. These results demonstrate the multiple CHIKV introductions in Lao PDR since 2014 and provide evidence for sporadic and time-limited circulation of CHIKV in the country. Even if the circulation of CHIKV seems to be geographically and temporally limited in Lao PDR, the development of international tourism and trade may cause future outbreaks of CHIKV in the country and at the regional level.

Immunoglobulin G Subclass Response After Chikungunya Virus Infection.

Patil, H., Gosavi, M., Kulkarni, R., Mishra, A., Arankalle, V.

15-07-2022

Viral Immunol

<https://doi.org/10.1089/vim.2022.0055>

Various vaccines are under development to prevent chikungunya (CHIKV) infection. For the assessment of the CHIKV vaccine-induced antibody response, it is extremely important to understand antibody response after the infection has occurred. Previously, we assessed IgG response in samples from healthy donors using I-CHIKV and found that IgG1 was the predominant subclass induced after CHIKV infection followed by IgG4. However, IgG3 subclass induction is reported in serum samples from patients with acute CHIKV infection. Therefore, in this study, we evaluated serum/plasma from samples of patients with acute CHIKV infection for the presence of IgG and IgG subclasses against I-CHIKV and recombinant E2 protein (rE2). Out of 44 samples that were positive against I-CHIKV, 43 were found reactive against rE2. The positivity of IgG1 either alone or together with other IgG subclasses using I-CHIKV was 89% samples, while 86% samples were positive using rE2. High titers of IgG1 are obtained with I-CHIKV (67%), while raised IgG4 levels are detected using rE2p (72%) in the samples that are positive for both these subclasses. Testing of 22 samples for neutralizing antibodies revealed 100% IgG1 positivity and neutralizing antibodies in 21, 1 sample negative for both. Overall, these data will be useful in assessing IgG subclass-specific CHIKV neutralization and response after CHIKV immunization.

Condom use among women of reproductive age (18-49 years) in Puerto Rico during the 2016 Zika virus outbreak: secondary analysis of data from a cross-sectional, population-based, cell-phone survey.

Chang, K., Snead, M., Serrano Rodriguez, R., Bish, C., Shapiro-Mendoza, C., Ellington, S.

14-07-2022

BMJ Open

<https://doi.org/10.1136/bmjopen-2022-065592>

Objectives: Zika virus (ZIKV) can be sexually transmitted, and ZIKV infection during pregnancy can cause birth defects. Contraception is a medical countermeasure to reduce unintended pregnancy and ZIKV-associated birth defects. We estimated the prevalence of condom use and associated factors among women at risk for unintended pregnancy in Puerto Rico during the 2016 ZIKV outbreak. **Design:** Secondary analysis of a cross-sectional, population-based, cell-phone survey. **Setting and participants:** Women, 18-49 years, living in Puerto Rico during July–November 2016. We limited our analytical sample ($n=1840$) to women at risk for unintended pregnancy, defined as those who were sexually active with a man in the last 3 months and did not report menopause, hysterectomy, current pregnancy or desiring pregnancy. **Outcome measures:** We estimated the weighted prevalence of any condom use among women at risk for unintended pregnancy. We calculated crude and adjusted prevalence ratios (aPRs) to examine the association between condom use and ZIKV-related factors, stratified by use of more effective versus less effective or no contraception. **Results:** Overall, 32.7% (95% CI: 30.2% to 35.1%) of women reported any condom use in the last 3 months. Among women using more effective contraception, condom use was higher for women who received ZIKV counselling (aPR: 1.61, 95% CI: 1.15 to 2.25) and those worried about having a child with a ZIKV-associated birth defect (aPR: 1.47, 95% CI: 1.03 to 2.10). Among women using less effective or no contraception, condom use was associated with being worried (aPR: 1.20, 95% CI: 1.01 to 1.43) compared with those not worried about ZIKV infection or with a previous known infection. **Conclusions:** During the 2016 ZIKV outbreak, one in three women at risk for unintended pregnancy reported any condom use. Counselling to promote consistent and correct condom use may address concerns regarding ZIKV among women of reproductive age, which may differ by use of effective contraception.

A specific EMC subunit supports Dengue virus infection by promoting virus membrane fusion essential for cytosolic genome delivery.

Bagchi, P., Speckhart, K., Kennedy, A., Tai, A., Tsai, B.

14-07-2022

PLoS Pathog

<https://doi.org/10.1371/journal.ppat.1010717>

Dengue virus (DENV) represents the most common human arboviral infection, yet its cellular entry mechanism remains unclear. The multi-subunit endoplasmic reticulum membrane

complex (EMC) supports DENV infection, in part, by assisting the biosynthesis of viral proteins critical for downstream replication steps. Intriguingly, the EMC has also been shown to act at an earlier step prior to viral protein biogenesis, although this event is not well-defined. Here we demonstrate that the EMC subunit EMC4 promotes fusion of the DENV and endosomal membranes during entry, enabling delivery of the viral genome into the cytosol which is then targeted to the ER for viral protein biosynthesis. We also found that EMC4 mediates ER-to-endosome transfer of phosphatidylserine, a phospholipid whose presence in the endosome facilitates DENV-endosomal membrane fusion. These findings clarify the EMC-dependent DENV early entry step, suggesting a mechanism by which an ER-localized host factor can regulate viral fusion at the endosome.

Human immune globulin treatment controls Zika viremia in pregnant rhesus macaques.

Dudley, D., Koenig, M., Stewart, L., Semler, M., Newman, C., Shepherd, P., Yamamoto, K., Breitbach, M., Schotzko, M., Kohn, S., Antony, K., Qiu, H., Tunga, P., Anderson, D., Guo, W., Dennis, M., Singh, T., Rybarczyk, S., Weiler, A., Razo, E., Mitzey, A., Zeng, X., Eickhoff, J., Mohr, E., Simmons, H., Fritsch, M., Mejia, A., Aliota, M., Friedrich, T., Golos, T., Kodihalli, S., Permar, S., O'Connor, D.

14-07-2022

PLoS One

<https://doi.org/10.1371/journal.pone.0266664>

There are currently no approved drugs to treat Zika virus (ZIKV) infection during pregnancy. Hyperimmune globulin products such as VARIZIG and WinRho are FDA-approved to treat conditions during pregnancy such as Varicella Zoster virus infection and Rh-incompatibility. We administered ZIKV-specific human immune globulin as a treatment in pregnant rhesus macaques one day after subcutaneous ZIKV infection. All animals controlled ZIKV viremia following the treatment and generated robust levels of anti-Zika virus antibodies in their blood. No adverse fetal or infant outcomes were identified in the treated animals, yet the placebo control treated animals also did not have signs related to congenital Zika syndrome (CZS). Human immune globulin may be a viable prophylaxis and treatment option for ZIKV infection during pregnancy, however, more studies are required to fully assess the impact of this treatment to prevent CZS.

Biocidal action, characterization, and molecular docking of *Mentha piperita* (Lamiaceae) leaves extract against *Culex quinquefasciatus* (Diptera: Culicidae) larvae.

Iqbal, A., Qureshi, N., Alhewairini, S., Shaheen, N., Hamid, A., Qureshi, M.

14-07-2022

PLoS One

<https://doi.org/10.1371/journal.pone.0270219>

Mosquitoes are found in tropical and subtropical areas and are the carriers of a variety of diseases that are harmful to

people's health. e.g., malaria, filariasis, chikungunya, dengue fever, etc. Although several insecticides are available, however, due to insect resistance and environmental hazards, more eco-friendly chemicals are needed for insect control. So, the current research was planned to explore the prospective of *Mentha piperita* to be used for the formulation of larvicides against mosquito *Culex quinquefasciatus*. The ethanolic and water extracts of *M. piperita* leaves were prepared using the soxhlet apparatus. The extracts were dried and subjected to prepare five concentrations multiple of 80 ppm. Each concentration was applied for its larvicidal efficacy setting an experiment (in triplicate) in plastic containers of 1000 ml with extracts, 30 larvae of all four instars separately, and fed with dog biscuits along with controls. Observations were taken after each 12 hrs. till 72 hrs. The antioxidant perspective of *M. piperita* was determined by DPPH radical scavenging, total antioxidant capacity, and ferric reducing power assays. Using brine shrimp lethality bioactivity, the cytotoxic study was perceived. Standard techniques were used to classify the *M. piperita* extract using preliminary qualitative and quantitative phytochemicals, UV-Vis spectroscopy, FT-IR, and GC-MS analysis. *M. piperita* ethanolic leaves extract after 24 hrs. of exposure in 400 ppm showed 93% ($LC_{50} = 208.976$ ppm) mortality in ethanolic extract and 80% ($LC_{90} = 246.900$ ppm) in the water extract. In treated larvae, biochemical examination revealed a substantial ($P < 0.05$) decrease in proteins, carbohydrates, and fat contents. The ethanol extract of *M. piperita* was the most efficient, killing brine shrimp nauplii in 50% to 90% of cases. TAC (125.4 3.5gAAE/mg DW) and FRP (378.1 1.0gAAE/mg DW) were highest in the ethanolic extract of *M. piperita*. The presence of medicinally active components such as alkaloids, carbohydrates, flavonoids, and others in *M. piperita* leaves extract in ethanol was discovered. The UV-Vis spectrum showed two peaks at 209.509 and 282.814 nm with the absorption of 2.338 and 0.796 respectively. The FT-IR consequences exhibited the occurrence of alcohols, alkanes, aldehyde, aromatic rings, ether linkage, ester, and halo- compounds. The GC-MS analysis according to peak (%) area and retention time showed ten phytochemicals consisting of six major and four minor compounds. Among all the compounds, 1, 2-benzene dicarboxylic acid, and 3-ethyl-5, 5-dimethyl -6-phenyl bound well to the NS3 protease domain with PDB ID: 2FOM. Hence, for the prevention of health hazards and mosquito control, *M. Piperita* is a potential source of chemicals for insecticide formulation.

Linguistic Pattern-Infused Dual-Channel Bidirectional Long Short-term Memory With Attention for Dengue Case Summary Generation From the Program for Monitoring Emerging Diseases-Mail Database: Algorithm Development Study.

Chang, Y., Chiu, Y., Chuang, T.

13-07-2022

JMIR Public Health Surveill

<https://doi.org/10.2196/34583>

Background: Globalization and environmental changes have intensified the emergence or re-emergence of infectious diseases worldwide, such as outbreaks of dengue fever in Southeast Asia. Collaboration on region-wide infectious disease surveillance systems is therefore critical but difficult to achieve because of the different transparency levels of health information systems in different countries. Although the Program for Monitoring Emerging Diseases (ProMED)-mail is the most comprehensive international expert-curated platform providing rich disease outbreak information on humans, animals, and plants, the unstructured text content of the reports makes analysis for further application difficult.

Objective: To make monitoring the epidemic situation in Southeast Asia more efficient, this study aims to develop an automatic summary of the alert articles from ProMED-mail, a huge textual data source. In this paper, we proposed a text summarization method that uses natural language processing technology to automatically extract important sentences from alert articles in ProMED-mail emails to generate summaries. Using our method, we can quickly capture crucial information to help make important decisions regarding epidemic surveillance. **Methods:** Our data, which span a period from 1994 to 2019, come from the ProMED-mail website. We analyzed the collected data to establish a unique Taiwan dengue corpus that was validated with professionals' annotations to achieve almost perfect agreement (Cohen $\kappa=90\%$). To generate a ProMED-mail summary, we developed a dual-channel bidirectional long short-term memory with attention mechanism with infused latent syntactic features to identify key sentences from the alerting article. **Results:** Our method is superior to many well-known machine learning and neural network approaches in identifying important sentences, achieving a macroaverage F1 score of 93%. Moreover, it can successfully extract the relevant correct information on dengue fever from a ProMED-mail alerting article, which can help researchers or general users to quickly understand the essence of the alerting article at first glance. In addition to verifying the model, we also recruited 3 professional experts and 2 students from related fields to participate in a satisfaction survey on the generated summaries, and the results show that 84% (63/75) of the summaries received high satisfaction ratings. **Conclusions:** The proposed approach successfully fuses latent syntactic features into a deep neural network to analyze the syntactic, semantic, and contextual information in the text. It then exploits the derived information to identify crucial sentences in the ProMED-mail alerting article. The experiment results show that the proposed method is not only effective but also outperforms the compared methods. Our approach also demonstrates the potential for case summary generation from ProMED-mail alerting articles. In terms of practical application, when a new alerting article arrives, our method can quickly identify the relevant case information, which is the most critical part, to use as a reference or for further analysis.

Development and Characterization of an Inducible

Assay System to Measure Zika Virus Capsid Interaction.

Yu, J., Huang, C., Wang, Z., Kaushik, R., Sheng, Z., Li, F., Wang, D.
12-07-2022
J Med Virol
<https://doi.org/10.1002/jmv.27991>

The global spread of the mosquito-borne Zika virus (ZIKV) infection and its complications including Guillain-Barré syndrome and fetus microcephaly in 2015 have made ZIKV as a significant public health threat. The capsid protein plays crucial roles in ZIKV replication and thus represents an attractive therapeutic target. However, inhibitors of ZIKV capsid assembly have not been rigorously identified due to the lack of a target-based screening system. In this study, we developed a novel ZIKV capsid interaction method based on a split-luciferase complementation assay (SLCA), which can be used to measure and quantify ZIKV capsid-capsid interaction by the restored luciferase signal when capsid proteins interact with each other. Furthermore, a Tet-on inducible stable cell line was generated to screen inhibitors of capsid dimerization. By using of this system, peptides (Pep.15-24 in the N-terminal region of ZIKV capsid protein and Pep.44-58 in the α 2 helix of ZIKV capsid protein) were identified to inhibit ZIKV capsid-capsid interaction. Overall, this study developed a novel inducible assay system to measure ZIKV capsid interaction and identify ZIKV capsid multimerization inhibitors, which will be applied for future discovery of ZIKV assembly inhibitors. This article is protected by copyright. All rights reserved.

The 2021 Zika outbreak in Uttar Pradesh state of India: Tackling the emerging public health threat.

Khan, E., Jindal, H., Mishra, P., Suvvari, T., Jonna, S.
12-07-2022
Trop Doct
<https://doi.org/10.1177/00494755221113285>

Zika virus is an RNA virus belonging to the Flavivirus family that is chiefly transmitted by the female Aedes mosquito. The Zika virus first infected humans in Uganda and Tanzania in 1952. Since, it has spread to several parts of the world causing outbreaks of variable extent. In India, these outbreaks have been reported from Gujarat, Tamil Nadu, Madhya Pradesh, Rajasthan, Kerala, and Maharashtra. The most recent outbreak is from the most populous state of India, Uttar Pradesh, where the climate is conducive to the breeding and transmission of other arboviral infections such as Dengue, Chikungunya, and Malaria. These infections also happen to share similar incubation periods and overlapping clinical manifestations with Zika virus (ZIKV) infection, leading to misdiagnoses or delayed diagnosis. We aim to provide an account of the outbreak, its repercussions, errors made in attempting to contain the spread of the disease, and, measures to be taken in the future.

Zika virus induces FOXG1 nuclear displacement and

downregulation in human neural progenitors.

Lottini, G., Baggiani, M., Chesi, G., D'Orsi, B., Quaranta, P., Lai, M., Pancrazi, L., Onorati, M., Pistello, M., Freer, G., Costa, M.
16-06-2022
Stem Cell Reports
<https://pubmed.ncbi.nlm.nih.gov/35714598>

Congenital alterations in the levels of the transcription factor Forkhead box g1 (FOGX1) coding gene trigger "FOGX1 syndrome," a spectrum that recapitulates birth defects found in the "congenital Zika syndrome," such as microcephaly and other neurodevelopmental conditions. Here, we report that Zika virus (ZIKV) infection alters FOXG1 nuclear localization and causes its downregulation, thus impairing expression of genes involved in cell replication and apoptosis in several cell models, including human neural progenitor cells. Growth factors, such as EGF and FGF2, and Thr271 residue located in FOXG1 AKT domain, take part in the nuclear displacement and apoptosis protection, respectively. Finally, by progressive deletion of FOXG1 sequence, we identify the C-terminus and the residues 428-481 as critical domains. Collectively, our data suggest a causal mechanism by which ZIKV affects FOXG1, its target genes, cell cycle progression, and survival of human neural progenitors, thus contributing to microcephaly.

Natural Aedes-Borne Virus Infection Detected in Male Adult Aedes aegypti (Diptera: Culicidae) Collected From Urban Settings in Mérida, Yucatán, México.

Kirstein, O., Talavera, G., Wei, Z., Ciau-Carrillo, K., Koyoc-Cardeña, E., Puerta-Guardo, H., Rodríguez-Martín, E., Medina-Barreiro, A., Mendoza, A., Piantadosi, A., Manrique-Saide, P., Vazquez-Prokope, G.

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J Med Entomol
<https://doi.org/10.1093/jme/tjac048>

Aedes-borne viruses (ABVs) such as dengue (DENV), chikungunya (CHIKV), and Zika (ZIKV) contribute significantly to the global burden of infectious diseases, disproportionately affecting disadvantaged populations from tropical and subtropical urban areas. ABVs can be transmitted from female mosquitoes to their progeny by vertical transmission via transovarial and/or trans-egg vertical transmission and contribute to the maintenance of infected-mosquito populations year-round in endemic regions. This study describes the natural infection rate of DENV, CHIKV, and ZIKV in field-caught male Aedes (*Sergentomyia*) aegypti (*Linnaeus*) mosquitoes from Mérida, Yucatán, México, as a proxy for the occurrence of vertical virus transmission. We used indoor sequential sampling with Prokopack aspirators to collect all mosquitoes inside houses from ABV hotspots areas. Collections were performed in a DENV and CHIKV post-epidemic phase and during a period of active ZIKV transmission. We individually RT-qPCR tested all indoor collected Ae. aegypti males (1,278) followed by Sanger sequencing analysis for final confirmation. A total of 6.7% male mosquitoes were positive for ABV (CHIKV = 5.7%; DENV =

Rage

0.9%; ZIKV = 0.1%) and came from 21.0% (30/143) houses infested with males. Most ABV-positive male mosquitoes were positive for CHIKV (84.8%). The distribution of ABV-positive Ae. aegypti males was aggregated in a few households, with two houses having 11 ABV-positive males each. We found a positive association between ABV-positive males and females per house. These findings suggested the occurrence of vertical arbovirus transmission within the mosquito populations in an ABV-endemic area and, a mechanism contributing to viral maintenance and virus re-emergence among humans in post-epidemic periods.

RAGE

A country classification system to inform rabies prevention guidelines and regulations.

Henry, R., Blanton, J., Angelo, K., Pieracci, E., Stauffer, K., Jentes, E., Allen, J., Glynn, M., Brown, C., Friedman, C., Wallace, R.

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J Travel Med

<https://pubmed.ncbi.nlm.nih.gov/35348741>

Background: Assessing the global risk of rabies exposure is a complicated task requiring individual risk assessments, knowledge of rabies epidemiology, surveillance capacity and accessibility of rabies biologics on a national and regional scale. In many parts of the world, availability of this information is limited and when available is often dispersed across multiple sources. This hinders the process of making evidence-based health and policy recommendations to prevent the introduction and spread of rabies. **Methods:** CDC conducted a country-by-country qualitative assessment of risk and protective factors for rabies to develop an open-access database of core metrics consisting of the presence of lyssaviruses (specifically canine or wildlife rabies virus variants or other bat lyssaviruses), access to rabies immunoglobulins and vaccines, rabies surveillance capacity and canine rabies control capacity. Using these metrics, we developed separate risk scoring systems to inform rabies prevention guidance for travelers and regulations for the importation of dogs. Both scoring systems assigned higher risk to countries with enzootic rabies (particularly canine rabies), and the risk scoring system for travelers also considered protective factors such as the accessibility of rabies biologics for post-exposure prophylaxis. Cumulative scores were calculated across the assessed metrics to assign a risk value of low, moderate or high. **Results:** A total of 240 countries, territories and dependencies were assessed, for travelers, 116 were identified as moderate to high risk and 124 were low or no risk; for canine rabies virus variant importation, 111 were identified as high-risk and 129 were low or no risk. **Conclusions:** We developed a comprehensive and easily accessible source of information for assessing the rabies risk for individual countries that included a database of rabies risk and protective factors based on

enzootic status and availability of biologics, provided a resource that categorizes risk by country and provided guidance based on these risk categories for travelers and importers of dogs into the United States.

Two-year immunogenicity of a pre-exposure rabies vaccination administered as a two-dose schedule.

Windels, L., Naneix-Laroche, V., Pasquier, C., Delobel, P., Parize, P., Martin-Blondel, G.

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J Travel Med

<https://pubmed.ncbi.nlm.nih.gov/35238924>

TRACHOME

Risk of seroconversion and seroreversion of antibodies to Chlamydia trachomatis pgp3 in a longitudinal cohort of children in a low trachoma prevalence district in Tanzania.

Chen, X., Munoz, B., Mkocha, H., Gaydos, C., Dize, L., Quinn, T., West, S.

13-07-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010629>

Background: Serologic testing for chlamydial antibodies is one potential tool for trachoma monitoring. Understanding the dynamics of seroconversion and seroreversion in low endemic districts is critical for determining the value of using serology.

Methodology/Principal findings: We surveyed a random sample of 2536 children aged 1-9 years in Kongwa, Tanzania, over three years; 1719 (67.8%) participants had all three follow-ups. Surveys assessed trachomatous inflammation-follicular (TF), Chlamydia trachomatis infection, and anti-pgp3 antibodies. Mass drug administration occurred immediately after the first and second follow-up surveys. The cohort was classified into trajectories of change in serostatus, and risk factors were evaluated for seroconversion and seroreversion. We found that 86.2% of seropositives remained seropositive throughout the study, whereas 12.1% seroreverted. Seroreverters were younger (Odds Ratio [OR] = 0.88 for every one-year increase in age, 95% CI = 0.79-0.99). 84.5% of seronegatives remained seronegative, and 13.0% seroconverted. Seroconverters were also younger (OR = 0.92, 95% CI = 0.87-0.98). Seroconversion and seroreversion were not explained by indeterminate values for the intensity of antibody response. Less than 1% of the cohort had unstable changes in serostatus, mostly explained by values in the indeterminate range. TF and infection in the cohort declined over time, while seropositivity increased from 31.5% to 36.4%. **Conclusions/Significance:** Antibody status is relatively stable over time. Both seroconversion and seroreversion occurred over the three years in this low endemic district, especially in

Ulcère de Buruli

younger children. Modeling seroreversion is important for accurate determination of seroconversion. The use of serology as a monitoring tool should target the younger aged children as they will most likely capture recent changes in serostatus.

Forecasting the elimination of active trachoma: An empirical model.

Renneker, K., Emerson, P., Hooper, P., Ngondi, J.

11-07-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010563>

Background: Great progress has been made toward the elimination of trachoma as a public-health problem. Mathematical and statistical models have been used to forecast when the program will attain the goal of the elimination of active trachoma, defined as prevalence of trachomatous inflammation-follicular in 1-9 year olds (TF1-9) <5%. Here we use program data to create an empirical model predicting the year of attaining global elimination of TF1-9.

Methodology/Principal findings: We calculated the mean number of years (95% CI) observed for an implementation unit (IU) to move from a baseline TF1-9 prevalence $\geq 5\%$ to the elimination threshold, based on the region (Ethiopia vs. non-Ethiopia) and baseline prevalence category. Ethiopia IUs had significantly different rates of reaching the TF1-9 elimination threshold after a trachoma impact survey (TIS) compared to non-Ethiopia IUs across all baseline categories. We used those estimates to predict when remaining active trachoma-endemic IUs (TF1-9 $\geq 5\%$) would have their last round of mass drug administration (MDA) based on the mean number of years required and number of MDA rounds already completed. Our model predicts that elimination of TF1-9 will be achieved in 2028 in Ethiopia (95% CI: 2026-2033) and 2029 outside of Ethiopia (95% CI: 2023-2034), with some IUs in East Africa predicted to be the last requiring MDA globally.

Conclusions/Significance: Our empirical estimate is similar to those resulting from previous susceptible-infectious-susceptible (SIS) and mathematical models, suggesting that the forecast achievement of TF1-9 elimination is realistic with the caveat that although disease elimination progress can be predicted for most IUs, there is an important minority of IUs that is not declining or has not yet started trachoma elimination activities. These IUs represent an important barrier to the timely global elimination of active trachoma.

ULCERE DE BURULI

PIAN

Reviewing the Past, Present, and Future Risks of Pathogens in Ghana and What This Means for Rethinking Infectious Disease Surveillance for Sub-Saharan Africa.

Revue de littérature

Mahama, P., Kabo-Bah, A., Blanford, J., Yamba, E., Antwi-Agyei, P.

14-07-2022

J Trop Med

<https://doi.org/10.1155/2022/4589007>

The current epidemiological transition makes us wonder how the parallel of infectious diseases (IDs) might be at the end of each passing year. Yet, the surveillance of these IDs continues to focus on high-profile diseases of public health importance without keeping track of the broad spectrum of the IDs we face. Here, we presented the prevalence of the broad spectrum of IDs in Ghana. Data from the annual reports on Gold Coast now Ghana, Global Infectious Diseases and Epidemiology Network (GIDEON), and the District Health Information Management System II (DHIMS2) databases were examined for records of ID prevalence in Ghana. Using the IDs from these databases, the paper assessed the epidemiological transition, pathogen-host interactions, spatiotemporal distribution, transmission routes, and their potential areas of impact in Ghana. The topmost ID recorded in health facilities in Ghana transitioned from yaws in the 1890s to malaria in the 1950s through 2020. We then presented the hosts of a pathogen and the pathogens of a host, the administrative districts where a pathogen was found, and the pathogens found in each district of Ghana. The highest modes of transmission routes were through direct contact for bacteria and airborne or droplet-borne for viral pathogens. From GIDEON, 226 IDs were identified as endemic or potentially endemic in Ghana, with 42% cited in peer-reviewed articles from 2000 to 2020. From the extent of risk of endemic or potentially endemic IDs, Ghana faces a high risk of ID burden that we should be mindful of their changing patterns and should keep track of the state of each of them.

LEPRE

Investigating drug resistance of Mycobacterium leprae in the Comoros: an observational deep-sequencing study.

Marijke Braet, S., Jouet, A., Aubry, A., Van Dyck-Lippens, M., Lenoir, E., Assoumani, Y., Baco, A., Mzemba, A., Cambau, E., Vasconcellos, S., Rigouts, L., Suffys, P., Hasker, E., Supply, P., de Jong, B.

15-07-2022

Lancet Microbe

<https://pubmed.ncbi.nlm.nih.gov/35850123>

Background: Despite strong leprosy control measures, including effective treatment, leprosy persists in the Comoros.

Trypanosomes (trypanosomiase et maladie de Chagas)

As of May, 2022, no resistance to anti-leprosy drugs had been reported, but there are no nationally representative data. Post-exposure prophylaxis (PEP) with rifampicin is offered to contacts of patients with leprosy. We aimed to conduct a countrywide drug resistance survey and investigate whether PEP led to the emergence of drug resistance in patients with leprosy. **Methods:** In this observational, deep-sequencing analysis we assessed *Mycobacterium leprae* genomes from skin biopsies of patients in Anjouan and Mohéli, Comoros, collected as part of the ComLep (NCT03526718) and PEOPLE (NCT03662022) studies. Skin biopsies that had sufficient *M leprae* DNA (>2000 bacilli in 2 µl of DNA extract) were assessed for the presence of seven drug resistance-associated genes (ie, *rpoB*, *ctpC*, *ctpl*, *folP1*, *gyrA*, *gyrB*, and *nth*) using Deeplex Myc-Lep (targeted next generation deep sequencing), with a limit of detection of 10% for minority *M leprae* bacterial populations bearing a polymorphism in these genes. All newly registered patients with leprosy for whom written informed consent was obtained were eligible for inclusion in the survey. Patients younger than 2 years or with a single lesion on the face did not have biopsies taken. The primary outcome of our study was the proportion of patients with leprosy (ie, new cases, patients with relapses or reinfections, patients who received single (double) dose rifampicin-PEP, or patients who lived in villages where PEP was distributed) who were infected with *M leprae* with a drug-resistant mutation for rifampicin, fluoroquinolone, or dapsone in the Comoros. **Findings:** Between July 1, 2017, and Dec 31, 2020, 1199 patients with leprosy were identified on the basis of clinical criteria, of whom 1030 provided a skin biopsy. Of these 1030 patients, 755 (73·3%) tested positive for the *M leprae*-specific repetitive element-quantitative PCR (qPCR) assay. Of these 755 patients, 260 (34·4%) were eligible to be analysed using Deeplex Myc-Lep. 251 (96·5%) were newly diagnosed with leprosy, whereas nine (3·4%) patients had previously received multidrug therapy. 45 (17·3%) patients resided in villages where PEP had been administered in 2015 or 2019, two (4·4%) of whom received PEP. All seven drug resistance-associated targets were successfully sequenced in 216 samples, 39 samples had incomplete results, and five had no results. No mutations were detected in any of the seven drug resistance-related genes for any patient with successfully sequenced results. **Interpretation:** This drug resistance survey provides evidence to show that *M leprae* is fully susceptible to rifampicin, fluoroquinolones, and dapsone in the Comoros. Our results also show, for the first time, the applicability of targeted sequencing directly on skin biopsies from patients with either paucibacillary or multibacillary leprosy. These data suggest that PEP had not selected rifampicin-resistant strains, although further support for this finding should be confirmed with a larger sample size. **Funding:** Effect:Hope, The Mission To End Leprosy, the Fonds Wetenschappelijk Onderzoek, the EU.

TRYPANOSOMES (TRYPANOSOMIASE ET MALADIE DE CHAGAS)

A novel approach for assessment of antitrypanosomal activity of sesquiterpene lactones through additive and non-additive molecular structure parameters.

Keshavarz, M., Shirazi, Z., Sayehvand, F.

17-07-2022

Mol Divers

<https://doi.org/10.1007/s11030-022-10495-5>

Human African trypanosomiasis (HAT) or sleeping sickness is a protozoan neglected tropical disease, which is the main health worry in more than 20 countries in Africa. A novel approach is presented to predict the antitrypanosomal activity of sesquiterpene lactones (STLs) in terms of biological activity (pIC_{50}). The largest reported data set of pIC_{50} for *Trypanosoma brucei rhodesiense* (Tbr) as one form of HAT are used to derive and test the new model. The new model is based on five additive and two non-additive molecular structural parameters in several frameworks where it can be easily applied through a computer code. It is derived and tested based on 125 and 31 experimental data, respectively, with different types of statistical parameters. The high reliability of the novel model is compared with the best available QSAR models, which use "classical" molecular descriptors, and 3D pharmacophore features. The values of R^2 (correlation coefficient), root mean squared error (RMSE), and RMSEP (root mean square error of prediction) of the new model are 0.77, 0.38, and 0.35, respectively. Meanwhile, R^2 , RMSE, and RMSEP of comparative QSAR models based on complex descriptors are in the ranges 0.71-76, 0.46-0.4, and 0.51-0.44, respectively. The predictive results of the novel approach confirm its high simplicity, reliability, precision, accuracy, and goodness-of-fit.

Chagas disease in children from the Gran Chaco region: A bibliographic appraisal.

Mendicino, D., Bottasso, O.

15-07-2022

Trop Doct

<https://doi.org/10.1177/00494755221103002>

In the Gran Chaco region, the Pan American Health Organization (PAHO) declared the interruption of vector transmission of Chagas Disease in Paraguay and some district of Argentina. After a bibliographic search, by using the words "Chagas, prevalence, children, Chaco", on scientific articles indexed in Pubmed and Lilacs during the 2010-2021 period, we found nine studies which dealt with entomological data seroprevalence surveys of Chagas Disease in Argentine children and three studies in Bolivian children. More field studies need to be published to better understand the epidemiological situation in children from the region. Due to its social and ecological characteristics, the Gran Chaco region remains a hotspot for Chagas Disease affecting

Trypanosomes (*trypanosomiase et maladie de Chagas*)

disproportionally rural communities and certain vulnerable ethnic groups.

Treatment of dogs with fluralaner reduced pyrethroid-resistant *Triatoma infestans* abundance, *Trypanosoma cruzi* infection and human-triatomine contact in the Argentine Chaco.

Gürtler, R., Laiño, M., Alvedro, A., Enriquez, G., Macchiaverna, N., Gaspe, M., Cardinal, M.

13-07-2022

Parasit Vectors

<https://doi.org/10.1186/s13071-022-05343-2>

Background: Triatomine elimination efforts and the interruption of domestic transmission of *Trypanosoma cruzi* are hampered by pyrethroid resistance. Fluralaner, a long-lasting ectoparasiticide administered to dogs, substantially reduced site infestation and abundance of pyrethroid-resistant *Triatoma infestans* Klug (Heteroptera: Reduviidae) in an ongoing 10-month trial in Castelli (Chaco Province, Argentina). We assessed the effects of fluralaner on vector infection with *T. cruzi* and blood meal sources stratified by ecotope and quantified its medium-term effects on site infestation and triatomine abundance. **Methods:** We conducted a placebo-controlled, before-and-after efficacy trial of fluralaner in 28 infested sites over a 22-month period. All dogs received either an oral dose of fluralaner (treated group) or placebo (control group) at 0 month post-treatment [MPT]. Placebo-treated dogs were rescue-treated with fluralaner at 1 MPT, as were all eligible dogs at 7 MPT. Site-level infestation and abundance were periodically assessed by timed manual searches with a dislodging aerosol. Vector infection was mainly determined by kDNA-PCR and blood meal sources were determined by enzyme-linked immunosorbent assay. **Results:** In fluralaner-treated households, site infestation dropped from 100% at 0 MPT to 18-19% over the period 6-22 MPT while mean abundance plummeted from 5.5 to 0.6 triatomines per unit effort. In control households, infestation dropped similarly post-treatment. The overall prevalence of *T. cruzi* infection steadily decreased from 13.8% at 0-1 MPT (baseline) to 6.4% and subsequently 2.3% thereafter, while in domiciles, kitchens and storerooms it dropped from 17.4% to 4.7% and subsequently 3.3% thereafter. Most infected triatomines occurred in domiciles and had fed on humans. Infected-bug abundance plummeted after fluralaner treatment and remained marginal or nil thereafter. The human blood index of triatomines collected in domiciles, kitchens and storerooms highly significantly fell from 42.9% at baseline to 5.3-9.1% over the period 6-10 MPT, increasing to 36.8% at 22 MPT. Dog blood meals occurred before fluralaner administration only. The cat blood index increased from 9.9% at baseline to 57.9-72.7% over the period 6-10 MPT and dropped to 5.3% at 22 MPT, whereas chicken blood meals rose from 39.6% to 63.2-88.6%. **Conclusion:** Fluralaner severely impacted infestation- and transmission-related indices over nearly 2 years, causing evident effects at 1 MPT, and deserves larger efficacy trials.

The IMD and Toll canonical immune pathways of *Triatoma pallidipennis* are preferentially activated by Gram-negative and Gram-positive bacteria, respectively, but cross-activation also occurs.

Alejandro, A., Lilia, J., Jesús, M., Henry, R.

12-07-2022

Parasit Vectors

<https://doi.org/10.1186/s13071-022-05363-y>

Background: Antimicrobial peptides (AMPs) participate in the humoral immune response of insects eliminating invasive microorganisms. The immune deficiency pathway (IMD) and Toll are the main pathways by which the synthesis of these molecules is regulated in response to Gram-negative (IMD pathway) or Gram-positive (Toll pathway) bacteria. Various pattern-recognition receptors (PRRs) participate in the recognition of microorganisms, such as pgrp-lc and toll, which trigger signaling cascades and activate NF- κ B family transcription factors, such as relish, that translocate to the cell nucleus, mainly in the fat body, inducing AMP gene transcription. **Methods:** *T. pallidipennis* inhibited in Tppgrp-lc, Tptoll, and Tprelisch were challenged with *E. coli* and *M. luteus* to analyze the expression of AMPs transcripts in the fat body and to execute survival assays. **Results:** In this work we investigated the participation of the pgrp-lc and toll receptor genes and the relish transcription factor (designated as Tppgrp-lc, Tptoll, and Tprelisch), in the transcriptional regulation of defensin B, prolixin, and lysozyme B in *Triatoma pallidipennis*, one of the main vectors of Chagas disease. AMP transcript abundance was higher in the fat body of blood-fed than non-fed bugs. Challenge with *Escherichia coli* or *Micrococcus luteus* induced differential increases in AMP transcripts. Additionally, silencing of Tppgrp-lc, Tptoll, and Tprelisch resulted in reduced AMP transcription and survival of bugs after a bacterial challenge. **Conclusions:** Our findings demonstrated that the IMD and Toll pathways in *T. pallidipennis* preferentially respond to Gram-negative and Gram-positive bacteria, respectively, by increasing the expression of AMP transcripts, but cross-induction also occurs.

Evaluation of Selective Deltamethrin Application with Household and Community Awareness for the Control of Chagas Disease in Southern Ecuador.

Grijalva, M., Moncayo, A., Yumiseva, C., Ocaña-Mayorga, S., Baus, E., Villacís, A.

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J Med Entomol

<https://doi.org/10.1093/jme/tjac050>

Chagas disease is endemic in ~70% of Ecuador. *Rhodnius ecuadoriensis* and *Triatoma carrioni* (Hemiptera: Reduviidae) are the primary vectors of Chagas disease in Southern Ecuador. This study tested the effectiveness of selective deltamethrin application of Domiciliary Units (DUs) infested with triatomines, coupled with community education activities and a community-based surveillance system. Ten communities were selected in Loja Province, 466 DUs were examined, of these, 5.6% were infested with *R. ecuadoriensis* (Density [D] =

Leishmaniose

4 triatomines/DUs searched, Crowding [CR] = 71 triatomines/infested house, Colonization Index [CI] = 77% infested DUs with nymphs) and 8% with *T. carrioni* (D = 0.6, CR = 7, CI = 64%). Infested DUs were sprayed with deltamethrin. Subsequent visits were conducted at 6 and 12 mo after spraying. At each time point, new entomological searches were carried out in all DUs. All entomological indexes dropped significantly for the primary vector species one year after the initial intervention (*R. ecuadoriensis*: I = 2%, D = 0.1, CR = 7, CI = 100%; *T. carrioni*: I = 1.6%, D = 0.1, CR = 5.5, CI = 50%). Fifteen min educational talks were conducted in every DUs and workshops for schoolchildren were organized. Community-based surveillance system was established. However, there is a high risk of DUs reinfestation, possibly from sylvatic habitats (especially of *R. ecuadoriensis*) and reinforcing educational and surveillance activities are necessary.

LEISHMANIOSE

Immune recovery-related patterns of post kala-azar dermal and ocular leishmaniasis in people living with HIV: a national survey and literature review.

Rousset, S., Zenou, M., Saunier, A., Varenne, F., Soler, V., Tournier, E., Legrand, L., Lachaud, L., Buffet, P., Berry, A., Delobel, P., Martin-Blondel, G.

18-07-2022

AIDS

<https://doi.org/10.1097/QAD.0000000000003336>

Objective: Post kala-azar dermal leishmaniasis (PKDL) is a rare complication of visceral leishmaniasis. We aimed at reporting PKDL cases in people living with HIV (PLHIV) and compare their characteristics based on whether PKDL occurred in the context of immune recovery under antiretroviral therapy (ART) or not.

Design: National survey and literature review. **Methods:** We called for observations in France in October 2020 and performed a literature review from PubMed (Medline) and Web of Science up to December 2020. Two groups of patients were defined based on whether PKDL occurred in the context of immune recovery under ART (group 1) or not (group 2), and compared. **Results:** Three PLHIV with PKDL identified in France in the last decade were described and added to 33 cases from the literature. Compared with group 2 (16/36, 44.4%), patients from group 1 (20/36, 55.6%) originated more frequently from Europe (12/20, 60% vs. 2/16, 12.5%; P=0.0038), had higher median blood CD4+ cell counts (221/ μ l vs. 61/ μ l; P=0.0005) and increase under ART (122/ μ l, interquartile range 73-243 vs. 33/ μ l, interquartile range 0-53; P=0.0044), had less frequently concomitant visceral leishmaniasis (3/20, 15% vs. 8/12, 66.7%; P=0.006), and a trend to more frequent ocular involvement (7/20, 35% vs. 1/16, 6.25%; P=0.0531). **Conclusion:** In PLHIV, PKDL occurs after a cured episode of visceral leishmaniasis as part of an immune restoration disease under ART, or concomitant to a

visceral leishmaniasis relapse in a context of AIDS. For the latter, the denomination 'disseminated cutaneous lesions associated with visceral leishmaniasis' seems more accurate than PKDL.

Leishmania tarentolae: A new frontier in the epidemiology and control of the leishmaniases?

Revue de littérature

Mendoza-Roldan, J., Votýpka, J., Bandi, C., Epis, S., Modrý, D., Tichá, L., Wolf, P., Otranto, D.

15-07-2022

Transbound Emerg Dis

<https://doi.org/10.1111/tbed.14660>

Leishmaniasis (or the leishmaniases), classified as a neglected tropical parasitic disease, is found in parts of the tropics, subtropics and southern Europe. Leishmania parasites are transmitted by the bite of phlebotomine sand flies and million cases of human infection occur annually. *Leishmania tarentolae* has been historically considered a non-pathogenic protozoan of reptiles, which has been studied mainly for its potential biotechnological applications. However, some strains of *L. tarentolae* appear to be transiently infective to mammals. In areas where leishmaniasis is endemic, recent molecular diagnostics and serological positivity to *L. tarentolae* in humans and dogs have spurred interest in the interactions between these mammalian hosts, reptiles and *Leishmania infantum*, the main aetiologic agent of human and canine leishmaniasis. In this review, we discuss the systematics and biology of *L. tarentolae* in the insect vectors and the vertebrate hosts and address questions about evolution of reptilian leishmaniae. Furthermore, we discuss the possible usefulness of *L. tarentolae* for new vaccination strategies. This article is protected by copyright. All rights reserved.

Promising molecular targets related to polyamine biosynthesis in drug discovery against leishmaniasis.

Santiago-Silva, K., Camargo, P., Bispo, M.

13-07-2022

Med Chem

<https://doi.org/10.2174/1573406418666220713145446>

Leishmaniasis is a neglected tropical disease widely distributed worldwide, caused by parasitic protozoa of the genus *Leishmania*. Despite representing a significant public health problem, the therapeutic options are old, with several reported adverse effects, have high costs, with administration mainly by parenteral route, which makes treatment difficult, increasing dropout and, consequently, the emergence of resistant strains. Thus, the research and development of new antileishmanial therapies become necessary. In this field, inhibiting essential targets that affect the parasite's growth, survival, and infectivity represents an attractive therapeutic strategy. With this in mind, this review addresses the main structural, functional characteristics and recent reports of the discovery of promising inhibitors of the enzymes arginase (ARG) and trypanothione synthase (TryS), which are involved

Leishmaniose

in the biosynthesis of polyamines and trypanothione and trypanothione reductase (TR), responsible for the reduction of trypanothione thiol.

ELISA based evaluation of antibody response to Leishmania in a region endemic for cutaneous leishmaniasis.

Piyasiri, S., Samaranayake, T., Silva, H., Manamperi, N., Karunaweera, N.

14-07-2022

Parasite Immunol

<https://doi.org/10.1111/pim.12940>

Aims: Leishmaniasis includes several clinical forms. While routine diagnosis of cutaneous leishmaniasis (CL) is by microscopy, an antibody response to CL has been reported in several recent studies. This study evaluated anti-leishmanial IgG antibody responses as a biomarker of active leishmaniasis and a measure of exposure to Leishmania. **Methods and results:** Sera from 50 untreated CL patients, 140 patients under treatment and 280 healthy individuals residing in endemic regions collected as part of an epidemiological survey, was analysed with an ELISA established in-house using receiver-operator-characteristic (ROC) curve at optimised cut-off value. The assay showed high performance as a diagnostic tool in identifying exposure in endemic individuals (sensitivity: 98%, specificity: 90.3%). All patients showed lower antibody levels over time since onset of lesion/s. Antibody levels were higher ($p < 0.01$) and persisted for a longer period in untreated patients. In patients under treatment, the level of anti-IgG antibodies was negatively correlated with the total duration the patient had been on treatment. **Conclusion:** The anti-leishmanial IgG response in *L. donovani* induced CL is transient and is unlikely to confer protective immunity. Optimised serological assays may be useful in endemic settings for diagnosis and monitoring the treatment response in CL.

Susceptibility status of the wild-caught *Phlebotomus argentipes* (Diptera: Psychodidae: Phlebotominae), the sand fly vector of visceral leishmaniasis, to different insecticides in Nepal.

Roy, L., Uranw, S., Cloots, K., Smekens, T., Kiran, U., Pyakurel, U., Das, M., S Yadav, R., Van Bortel, W.

14-07-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010304>

Background: Visceral leishmaniasis (VL) is targeted for elimination as a public health problem in Nepal by 2023. For nearly three decades, the core vector control intervention in Nepal has been indoor residual spraying (IRS) with pyrethroids. Considering the long-term use of pyrethroids and the possible development of resistance of the vector *Phlebotomus argentipes* sand flies, we monitored the susceptibility status of their field populations to the insecticides of different classes, in villages with and without IRS activities in recent years. **Methodology/Principal findings:** Sand flies were collected from villages with and without IRS in

five VL endemic districts from August 2019 to November 2020. The WHO susceptibility test procedure was adopted using filter papers impregnated at the discriminating concentrations of insecticides of the following classes: pyrethroids (alpha-cypermethrin 0.05%, deltamethrin 0.05%, and lambda-cyhalothrin 0.05%), carbamates (bendiocarb 0.1%) and organophosphates (malathion 5%). Pyrethroid resistance intensity bioassays with papers impregnated with 5x of the discriminating concentrations, piperonyl butoxide (PBO) synergist-pyrethroid bioassays, and DDT cross-resistance bioassays were also performed. In the IRS villages, the vector sand flies were resistant (mortality rate <90%) to alpha-cypermethrin and possibly resistant (mortality rate 90–97%) to deltamethrin and lambda-cyhalothrin, while susceptibility to these insecticides was variable in the non-IRS villages. The vector was fully susceptible to bendiocarb and malathion in all villages. A delayed knockdown time (KDT50) with pyrethroids was observed in all villages. The pyrethroid resistance intensity was low, and the susceptibility improved at 5x of the discriminating concentrations. Enhanced pyrethroid susceptibility after pre-exposure to PBO and the DDT-pyrethroid cross-resistance were evident. **Conclusions/Significance:** Our investigation showed that *P. argentipes* sand flies have emerged with pyrethroid resistance, suggesting the need to switch to alternative classes of insecticides such as organophosphates for IRS. We strongly recommend the regular and systematic monitoring of insecticide resistance in sand flies to optimize the efficiency of vector control interventions to sustain VL elimination efforts in Nepal.

Bromodomain factor 5 is an essential regulator of transcription in Leishmania.

Jones, N., Geoghegan, V., Moore, G., Carnielli, J., Newling, K., Calderón, F., Gabarró, R., Martín, J., Prinjha, R., Rioja, I., Wilkinson, A., Mottram, J.

13-07-2022

Nat Commun

<https://doi.org/10.1038/s41467-022-31742-1>

Leishmania are unicellular parasites that cause human and animal diseases. Like other kinetoplastids, they possess large transcriptional start regions (TSRs) which are defined by histone variants and histone lysine acetylation. Cellular interpretation of these chromatin marks is not well understood. Eight bromodomain factors, the reader modules for acetyl-lysine, are found across Leishmania genomes. Using *L. mexicana*, Cas9-driven gene deletions indicate that BDF1-5 are essential for promastigotes. Dimerisable, split Cre recombinase (DiCre)-inducible gene deletion of BDF5 show it is essential for both promastigotes and murine infection. ChIP-seq identifies BDF5 as enriched at TSRs. XL-BioID proximity proteomics shows the BDF5 landscape is enriched for BDFs, HAT2, proteins involved in transcriptional activity, and RNA processing; revealing a Conserved Regulators of Kinetoplastid Transcription (CRKT) Complex. Inducible deletion of BDF5 causes global reduction in RNA polymerase II transcription. Our results indicate the requirement of Leishmania to

Cysticercose

interpret histone acetylation marks through the bromodomain-enriched CRKT complex for normal gene expression and cellular viability.

Impact of collaborative actions of *Leishmania (Viannia) braziliensis* subpopulations on the infection profile.

de Albuquerque-Melo, B., Cysne-Finkelstein, L., Gonçalves-Oliveira, L., Cascabulho, C., Henriques-Pons, A., Pereira, M., Alves, C., Dias-Lopes, G.

13-07-2022

Parasitology

<https://doi.org/10.1017/S003118202200097X>

The repellency effect of icaridin nanostructural solution applied on cotton knitting fabric against *Lutzomyia longipalpis*.

Ferreira, H., Cabral, R., Queiroga, T., Guedes, P., Lourenço de Assis, A., de Moura Barbosa, T., do Nascimento, J., Gama, R.

12-07-2022

Parasitol Res

<https://doi.org/10.1007/s00436-022-07595-4>

The use of repellents is considered an alternative against biting insects, including *Lutzomyia longipalpis* (Diptera: Psychodidae), the main vector of the protozoan *Leishmania infantum*, visceral leishmaniasis's (VL) etiologic agent in the Americas. This study aimed to evaluate the repellent efficacy of icaridin nanostructured solution applied on cotton knitting fabric against *L. longipalpis*. Arm-in-cage tests were performed in eight volunteers at different concentrations (5%, 10%, 25%, and 50%), using *L. longipalpis* ($n=30$). The bioassay was performed in 1, 24, 48, 72, 96, 120, and 144 h after impregnation and one test after washing the fabrics with icaridin. The total repellency rate (%R)>95% was used as a reference to define a minimum effective concentration (MEC). The results revealed that the insects' landing mean decreased significantly in different icaridin concentrations, compared with the control tests ($p<0.05$) and the 25% and 50% concentrations compared to lower concentration (5%) ($p<0.05$). The higher concentrations (25% and 50%) provided longer complete protection times (CPTs) with 120 and 144 h of protection, respectively and the %R of 100% for 72 and 96 h after impregnation, respectively. The 25% was the MEC (%R Total=98.18%). Our results indicate, for the first time, that icaridin nanostructured solution applied on cotton knitting fabric proved to be an efficient repellent against *L. longipalpis* with the presence of repellent action even after washing. The concentration of 25% showed better efficiency and may become an efficient method for *L. longipalpis* biting control.

Molecular and Biochemical Detection of Insecticide Resistance in the *Leishmania* Vector, *Phlebotomus papatasii* (Diptera: Psychodidae) to Dichlorodiphenyltrichloroethane and Pyrethroids, in Central Iran.

Shirani-Bidabadi, L., Oshaghi, M., Enayati, A., Akhavan, A., Zahraei-Ramazani, A., Yaghoobi-Ershadi, M., Rassi, Y., Aghaei-Afshar, A., Koosha, M., Arandian, M., Ghanei, M., Ghassemi, M., Vatandoost, H.

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J Med Entomol

<https://doi.org/10.1093/jme/tjac031>

The aim of the present study was to explore resistance markers and possible biochemical resistance mechanisms in the Phlebotomine sand fly *Phlebotomus papatasii* in Esfahan Province, central Iran. Homogenous resistant strains of sand flies were obtained by exposing *P. papatasii* collected from Esfahan to a single diagnostic dose of DDT. The adults from the colony were tested with papers impregnated with four pyrethroid insecticides: Permethrin 0.75%, Deltamethrin 0.05%, Cyfluthrin 0.15%, and Lambdacyhalothrin 0.05% to determine levels of cross-resistance. To discover the presence of mutations, a 440 base pair fragment of the voltage gated sodium channel (VGSC) gene was amplified and sequenced in both directions for the susceptible and resistant colonies. We also assayed the amount of four enzymes that play a key role in insecticide detoxification in the resistant colonies. A resistance ratio (RR) of 2.52 folds was achieved during the selection of resistant strains. Sequence analysis revealed no knockdown resistance (kdr) mutations in the VGSC gene. Enzyme activity ratio of the resistant candidate and susceptible colonies were calculated for α -esterases (3.78), β -esterases (3.72), mixed function oxidases (MFO) (3.21), and glutathione-S-transferases (GST) (1.59). No cross-resistance to the four pyrethroids insecticides was observed in the DDT resistant colony. The absence of kdr mutations in the VGSC gene suggests that alterations in esterase and MFO enzymes are responsible for the resistant of *P. papatasii* to DDT in central Iran. This information could have significant predictive utility in managing insecticide resistant in this *Leishmania* vector.

CYSTICERCOSE

The burden of *T. solium* cysticercosis and selected neuropsychiatric disorders in Mocuba district, Zambézia province, Mozambique.

Langa, I., Padama, F., Nhancupe, N., Pondja, A., Hlashwayo, D., Gouveia, L., Stelzle, D., da Costa, C., Schmidt, V., Winkler, A., Noormahomed, E.

14-07-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010606>

Background: *Taenia solium* (neuro-)cysticercosis is a neglected tropical disease often associated with epileptic seizures and reportedly with other neuropsychiatric (= neurological and psychiatric) disorders. This study aimed to evaluate the association of the disease with selected neuropsychiatric

Dracunculose

disorders and/or symptoms (chronic headache, epileptic seizures/epilepsy and psychosis) in Mocuba district, Mozambique. **Methodology:** Between March and May 2018, a cross-sectional study was conducted among 1,086 participants aged 2 years or above in Mocuba district, Zambézia province, central Mozambique to assess the seroprevalence of human cysticercosis and risk factors for infection, as well as to explore its relation to selected neuropsychiatric disorders. Socio-demographic and clinical data were collected from each participant using a modified questionnaire designed by the Cysticercosis Working Group for Eastern and Southern Africa. Additionally, neuropsychiatric disorders, such as chronic headache, epileptic seizures/epilepsy and psychosis were assessed using four vignettes. *T. solium* antigen and cysticercosis IgG in serum were detected using both *T. solium* antigen B158/B60 enzyme linked immunosorbent assay (ELISA) and LDBIO Cysticercosis Western Blot, respectively. **Principal findings:** Overall, 112/1,086 participants (10.3%) were sero-positive for *T. solium* antigen or antibodies. Prevalence of antibodies (6.6%; n = 72) was higher than of antigens (4.9%; n = 54). In the questionnaires, 530 (49.5%) of participants reported chronic headache, 293 (27%) had generalized epileptic seizures, 188 (18%) focal seizures and 183 (18.3%) psychosis. We found a statistically significant association between seropositivity for *T. solium* and chronic headache ($p = 0.013$). Additionally, increasing age ($p = 0.03$) was associated with Ag-ELISA seropositivity. **Conclusions:** Our study revealed that in Mocuba, *T. solium* cysticercosis is prevalent and associated with self-reported chronic headache. Additionally, in the study setting, the seroprevalence of cysticercosis increased with age. However, it is not associated with other neuropsychiatric disorders such as epileptic seizures/epilepsy and psychosis. Future studies are needed to confirm the burden of neuropsychiatric disorders and their possible etiology, including neurocysticercosis, with additional serological, molecular biological and radiological diagnostic tools, as well as in-depth clinical examinations.

DRACUNCULOSE

ECHINOCOCCOSE

2-Deoxy-D-glucose and combined 2-Deoxy-D-glucose/albendazole exhibit therapeutic efficacy against *Echinococcus granulosus* protoscoleces and experimental alveolar echinococcosis.

Xin, Q., Lv, W., Xu, Y., Luo, Y., Zhao, C., Wang, B., Yuan, M., Li, H., Song, X., Jing, T.

18-07-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010618>

2-Deoxy-D-glucose (2-DG) is a glucose analog used as a promising anticancer agent. It exerts its effects by inhibiting the glycolytic energy metabolism to deplete cells of energy. The larval stage of *Echinococcus* relies on glycolysis for energy production. Therefore, in this study, we investigated the in vitro and in vivo efficacy of 2-DG against the larval stage of *Echinococcus granulosus* and *E. multilocularis*. 2-DG exhibited significant time- and dose-dependent effects against in vitro cultured *E. granulosus* protoscoleces and *E. multilocularis* metacestodes. A daily oral administration of 500 mg/kg 2-DG in *E. multilocularis*-infected mice effectively reduced the weight of metacestodes. Notably, the combination treatment, either 2-DG (500 mg/kg/day) + albendazole (ABZ) (200 mg/kg/day) or 2-DG (500 mg/kg/day) + half-dose of ABZ (100 mg/kg/day), exhibited a potent therapeutic effect against *E. multilocularis*, significantly promoting the reduction of metacestodes weight compared with the administration of 2-DG or ABZ alone. Furthermore, the combination significantly promoted apoptosis of the cells of metacestodes and inhibited glycolysis in metacestodes, compared with the administration of 2-DG or ABZ alone. In conclusion, 2-DG exerts an effective activity against the larval stage of *Echinococcus*. Thus, it may be a promising anti-*Echinococcus* drug, and its combination with ABZ may provide a new strategy for the treatment of echinococcosis in humans.

Laparoscopic management of a primary gallbladder hydatid cyst with daughter cysts in the common bile duct: Case report.

Kazzaz, R., Nashed, D., Sattout, G., Issa, N., Aldakhil, A., Bitar, O., Danial, A.

12-07-2022

Ann Med Surg (Lond)

<https://doi.org/10.1016/j.amsu.2022.104165>

Introduction and importance: Primary Gallbladder hydatid cysts are a very rare phenomenon caused by *Echinococcus granulosus*. Hydatid cysts usually present as hepatic or pulmonary lesions, but in our case, it presented in the gallbladder with three symptomatic daughter cysts in the CBD. *Echinococcus* caused by *E.granulosus* is the most common parasite causing the disease, accounting for 95% of the cases.

Case presentation: 75 - year - old male presented with colic pain, jaundice, itching, vomiting, nausea, insomnia, Positive murphy's sign, and elevated AST and ALT. Total bilirubin was also elevated with no hepatomegaly or splenomegaly. **Clinical discussion:** This disease is endemic in Mediterranean countries due to high contact with the host of the parasite the lumen or on the external surface of the gallbladder. Which can come from the portal system or the spreading of brood capsules through the biliary tract. **Conclusion:** The method of investigation used was USG, CT, ERCP which are affordable and accessible in low-income countries including Syria. we would like to highlight this rare presentation and the possibility of using laparoscopic surgery.

Trématodes d'origine alimentaire (clonorchiasis, opisthorchiasis, fasciolase et paragonimose)

HIV protease inhibitor nelfinavir is a potent drug candidate against echinococcosis by targeting Ddi1-like protein.

Liu, Z., Guo, X., Guo, A., Zhang, S., Zou, Y., Wang, Y., Li, X., He, W., Pu, L., Zhang, S., Zeng, Q., Cai, X., Wang, S.

14-07-2022

EBioMedicine

<https://pubmed.ncbi.nlm.nih.gov/35843171>

Background: Alveolar echinococcosis (AE), which is caused by larval Echinococcus multilocularis, is one of the world's most dangerous neglected diseases. Currently, no fully effective treatments are available to cure this disease. **Methods:** In vitro protoscolicidal assay along with in vivo murine models was applied in repurposing drugs against AE. Genome-wide identification and homology-based modeling were used for predicting drug targets. RNAi, enzyme assay, and RNA-Seq analyses were utilized for investigating the roles in parasite survival and validations for the drug target. **Findings:** We identified nelfinavir as the most effective HIV protease inhibitor against larval E. multilocularis. Once-daily oral administration of nelfinavir for 28 days resulted in a remarkable reduction in parasite infection in either immune-competent or immunocompromised mice. E. multilocularis DNA damage-inducible 1 protein (EmuDdi1) is predicted as a target candidate for nelfinavir. We proved that EmuDdi1 is essential for parasite survival and protein excretion and acts as a functionally active protease for this helminth. We found nelfinavir is able to inhibit the proteolytic activity of recombinant EmuDdi1 and block the EmuDdi1-related pathways for protein export. With other evidence of drug efficacy comparison, our results suggest that inhibition of EmuDdi1 is a mechanism by which this HIV proteinase inhibitor mediates its antiparasitic action on echinococcosis. **Interpretation:** This study demonstrates that nelfinavir is a promising candidate for treating echinococcosis. This drug repurposing study proves that the widely prescribed drug for AIDS treatment is potent in combating E. multilocularis infection and thus provides valuable insights into the development of single-drug therapy for highly prevalent co-infection between HIV and helminth diseases. **Funding:** This work was supported by the National Natural Science Foundation of China (31802179), the Natural Science Foundation of Gansu Province, China (No. 21JR7RA027), and the State Key Laboratory of Veterinary Etiological Biology (No. SKLVEB2021YQRC01).

Clinical characteristics and antibodies against Echinococcus granulosus recombinant antigen P29 in patients with cystic echinococcosis in China.

Tao, J., Du, X., Liu, K., Wang, C., Lv, Y., Wang, M., Yang, Z., Yang, J., Li, S., Wu, C., Li, M., Zhao, W.

12-07-2022

BMC Infect Dis

<https://doi.org/10.1186/s12879-022-07597-8>

Objectives: Cystic echinococcosis (CE) is a neglected parasitic zoonotic disease caused by the larval stage of the tapeworm

Echinococcus granulosus (E. granulosus). This study aimed to understand the clinical characteristics of human CE in Ningxia Hui Autonomous Region (NHAR) located in northwest China and to investigate the antibody profiles against the recombinant E. granulosus antigen P29 (rEg.P29) in plasma of CE patients. **Methods:** A total of 37 human CE patients, along with 37 healthy donors enrolled in this study and demographic and clinical data were analyzed, including age, gender, laboratory data, symptoms, and cysts description. Plasma levels of cytokines, total IgG, and total IgE were determined by sandwich ELISA kits. Specific antibodies against rEg.P29 and hydatid cyst fluid (HCF) were assessed by indirect ELISA. **Results:** The results revealed that females have a higher percentage of CE patients than males. The incidence of CE reached a peak in the 41-50 years-old group. The liver was the most frequent location, accounting for 91.9%. Based on the CT images, cysts of 34 patients who had liver involvement, were classified as 1 (2.9%) CE1, 12 (35.3%) CE2, 5 (14.7%) CE3a, 1 (2.9%) CE3b, and 15 (44.2%) CE5. Twenty-nine (78.4%) patients had a single cyst and 8 (21.6%) had at least two cysts. The most frequently reported symptom was upper abdominal pain. The plasma level of IL-6 and total IgE were significantly increased in CE patients compared with healthy donors. Additionally, IgG response to rEg.P29 in CE patients was significantly higher than in healthy donors, and the dominant IgG subclass was IgG4. Further analysis of different patient groups revealed that rEg.P29-specific IgG and IgG4 were only elevated in CE patients with CE2 type cysts. **Conclusions:** This study systematically investigated the clinical characteristics of patients with CE and may provide a reference basis for the diagnosis and treatment of CE in NHAR. Furthermore, tests of specific IgG and IgG4 against rEg.P29 can be used as an assisted method for imaging techniques to identify cystic activity and determine the best therapeutic approach for CE.

TREMATODESES D'ORIGINE ALIMENTAIRE (CLONORCHIASIS, OPISTHORCHIASIS, FASCIOLASE ET PARAGONIMOSE)

Fasciola hepatica Cathepsin L Zymogens: Immuno-Proteomic Evidence for Highly Immunogenic Zymogen-Specific Conformational Epitopes to Support Diagnostics Development.

Collett, C., Phillips, H., Fisher, M., Smith, S., Fenn, C., Goodwin, P., Morphew, R., Brophy, P.

18-07-2022

J Proteome Res

<https://doi.org/10.1021/acs.jproteome.2c00299>

Fasciola hepatica, the common liver fluke and causative agent of zoonotic fasciolosis, impacts on food security with global

Filariose lymphatique

economic losses of over \$3.2 BN per annum through deterioration of animal health, productivity losses, and livestock death and is also re-emerging as a foodborne human disease. Cathepsin proteases present a major vaccine and diagnostic target of the *F. hepatica* excretory/secretory (ES) proteome, but utilization in diagnostics of the highly antigenic zymogen stage of these proteins is surprisingly yet to be fully exploited. Following an immuno-proteomic investigation of recombinant and native procathepsins ((r)FhpCL1), including mass spectrometric analyses (DOI: 10.6019/PXD030293), and using counterpart polyclonal antibodies to a recombinant mutant procathepsin L (anti-rFh Δ pCL1), we have confirmed recombinant and native cathepsin L zymogens contain conserved, highly antigenic epitopes that are conformationally dependent. Furthermore, using diagnostic platforms, including pilot serum and fecal antigen capture enzyme-linked immunosorbent assay (ELISA) tests, the diagnostic capacities of cathepsin L zymogens were assessed and validated, offering promising efficacy as markers of infection and for monitoring treatment efficacy.

microsatellite markers may lead to small genotypic differences.

ONCHOCERCOSE

Geospatial modeling of pre-intervention nodule prevalence of *Onchocerca volvulus* in Ethiopia as an aid to onchocerciasis elimination.

Shrestha, H., McCulloch, K., Hedtke, S., Grant, W.

18-07-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010620>

Background: Onchocerciasis is a neglected tropical filarial disease transmitted by the bites of blackflies, causing blindness and severe skin lesions. The change in focus for onchocerciasis management from control to elimination requires thorough mapping of pre-control endemicity to identify areas requiring interventions and to monitor progress. *Onchocerca volvulus* nodule prevalence in sub-Saharan Africa is spatially continuous and heterogeneous, and highly endemic areas may contribute to transmission in areas of low endemicity or vice-versa. Ethiopia is one such onchocerciasis-endemic country with heterogeneous *O. volvulus* nodule prevalence, and many districts are still unmapped despite their potential for onchocerciasis transmission.

Methodology/Principle findings: A Bayesian geostatistical model was fitted for retrospective pre-intervention nodule prevalence data collected from 916 unique sites and 35,077 people across Ethiopia. We used multiple environmental, socio-demographic, and climate variables to estimate the pre-intervention prevalence of *O. volvulus* nodules across Ethiopia and to explore their relationship with prevalence. Prevalence was high in southern and northwestern Ethiopia and low in Ethiopia's central and eastern parts. Distance to the nearest river (RR: 0.9850, 95% BCI: 0.9751-0.995), precipitation seasonality (RR: 0.9837, 95% BCI: 0.9681-0.9995), and flow accumulation (RR: 0.9586, 95% BCI: 0.9321-0.9816) were negatively associated with *O. volvulus* nodule prevalence, while soil moisture (RR: 1.0218, 95% BCI: 1.0135-1.0302) was positively associated. The model estimated the number of pre-intervention cases of *O. volvulus* nodules in Ethiopia to be around 6.48 million (95% BCI: 3.53-13.04 million).

Conclusions/Significance: Nodule prevalence distribution was correlated with habitat suitability for vector breeding and associated biting behavior. The modeled pre-intervention prevalence can be used as a guide for determining priorities for elimination mapping in regions of Ethiopia that are currently unmapped, most of which have comparatively low infection prevalence.

FILARIOSE LYMPHATIQUE

MYCETOME

Madurella mycetomatis grains within a eumycetoma lesion are clonal.

Nyuykonge, B., Siddig, E., Konings, M., Bakhet, S., Verbon, A., Klaassen, C., Fahal, A., van de Sande, W.

14-07-2022

Med Mycol

<https://pubmed.ncbi.nlm.nih.gov/35833294>

Eumycetoma is a neglected tropical infection of the subcutaneous tissue, characterized by tumor-like lesions and most commonly caused by the fungus *Madurella mycetomatis*. In the tissue, *M. mycetomatis* organizes itself in grains, and within a single lesion, thousands of grains can be present. The current hypothesis is that all these grains originate from a single causative agent, however, this hypothesis was never proven. Here we used our recently developed MmySTR assay, a highly discriminative typing method, to determine the genotypes of multiple grains within a single lesion. Multiple grains from surgical lesions obtained from eleven patients were isolated and genotyped using the MmySTR panel. Within a single lesion, all tested grains shared the same genotype. Only in one single grain from one patient, a difference of one repeat unit in one MmySTR marker was noted relative to the other grains from that patient. We conclude that within these lesions the grains originate from a single clone and that the inherent unstable nature of the

SCHISTOSOMIASE

Chromosome-level genome assembly defines female-biased genes associated with sex determination and differentiation in the human blood fluke *Schistosoma japonicum*.

Xu, X., Wang, Y., Wang, C., Guo, G., Yu, X., Dai, Y., Liu, Y., Wei, G., He, X., Ge, J., Zhang, Z., Guan, Q., Pain, A., Wang, S., Zhang, W., Young, N., Gasser, R., McManus, D., Cao, J., Zhou, Q., Zhang, Q.

17-07-2022

Mol Ecol Resour

<https://doi.org/10.1111/1755-0998.13689>

Schistosomiasis is a neglected tropical disease of humans caused by blood flukes of the genus *Schistosoma*, the only dioecious parasitic flatworms. Although aspects of sex determination, differentiation and reproduction have been studied in some *Schistosoma* species, almost nothing is known for *Schistosoma japonicum*, the causative agent of schistosomiasis japonica. This mainly reflects the lack of high-quality genomic and transcriptomic resources for this species. As current genomes for *S. japonicum* are highly fragmented, we assembled and report a chromosome-level reference genome (seven autosomes, the Z-chromosome and partial W-chromosome), achieving a substantially enhanced gene annotation. Utilising this genome, we discovered that the sex chromosomes of *S. japonicum* and its congener *S. mansoni* independently suppressed recombination during evolution, forming five and two evolutionary strata, respectively. By exploring the W-chromosome and sex-specific transcriptomes, we identified 35 W-linked genes and 257 female-preferentially transcribed genes (FTGs) from our chromosomal assembly and uncovered a signature for sex determination and differentiation in *S. japonicum*. These FTGs clustering within autosomes or the Z-chromosome exhibit a highly dynamic transcription profile during the pairing of female and male schistosomula, thereby representing a critical phase for the maturation of the female worms and suggesting distinct layers of regulatory control of gene transcription at this development stage. Collectively, these data provide a valuable resource for further functional genomic characterisation of *S. japonicum*, shed light on the evolution of sex chromosomes in this highly virulent human blood fluke, and provide a pathway to identify novel targets for development of intervention tools against schistosomiasis.

¹⁸F-FDG PET/CT findings in a patient with cerebral schistosomiasis mimicking metastatic tumor.

Sun, R., Liu, L., Zeng, G., Chen, X.

13-07-2022

Asian J Surg

<https://pubmed.ncbi.nlm.nih.gov/35842381>

Schistosomiasis: Basic requirements for the development of a subunit vaccine, using genetic vectors.

Ahmad, G.

13-07-2022

EBioMedicine

<https://pubmed.ncbi.nlm.nih.gov/35841870>

Protein undernutrition reduces the efficacy of praziquantel in a murine model of *Schistosoma mansoni* infection.

Kadjji Fassi, J., Boukeng Jatsa, H., Membe Femoe, U., Greigert, V., Brunet, J., Cannet, C., Kenfack, C., Gipwe Feussom, N., Tienga Nkondo, E., Abou-Bacar, A., Pfaff, A., Kamgang, R., Kamtchouing, P., Tchuem Tchuenté, L.

15-07-2022

PLoS Negl Trop Dis

<https://doi.org/10.1371/journal.pntd.0010249>

Background: Undernutrition and schistosomiasis are public health problems and often occur in low and middle-income countries. Protein undernutrition can alter the host-parasite environment system and aggravate the course of schistosomiasis. This study aimed to assess the impact of a low-protein diet on the efficacy of praziquantel.

Methodology/Principal findings: Thirty-day-old mice were fed with a low-protein diet, and 40 days later, they were individually infected with fifty *Schistosoma mansoni* cercariae. A 28-day-treatment with praziquantel at 100 mg/kg for five consecutive days followed by distilled water begins on the 36th day post-infection. Mice were sacrificed on the 64th day post-infection. We determined the parasitological burden, liver and intestine histomorphometry, liver injury, and immunomodulation parameters. Praziquantel treatment of infected mice fed with a standard diet (IN-PZQ) resulted in a significant reduction of worm and egg burdens and a normalization of iron and calcium levels. The therapy also improved schistosomiasis-induced hepatopathy and oxidative stress. The anti-inflammatory and immunomodulatory activities of praziquantel were also significant in these mice. When infected mice receiving the low-protein diet were treated with praziquantel (ILP-PZQ), the body weight loss and hepatomegaly were not alleviated, and the worm and liver egg burdens were significantly higher than those of IN-PZQ mice ($P < 0.001$). The treatment did not reduce the increased activities of ALT and γ -GGT, the high malondialdehyde concentration, and the liver granuloma volume. The iron and calcium levels were not ameliorated and differed from those of IN-PZQ mice ($P < 0.001$ and $P < 0.05$). Moreover, in these mice, praziquantel treatment did not reverse the high level of IL-5 and the low mRNA expression of CCL3/MIP-1 α and CXCL10/IP-10 induced by *S. mansoni* infection.

Conclusion/Significance: These results demonstrated that a low-protein diet reduced the schistosomicidal, antioxidant, anti-inflammatory, and immunomodulatory activities of praziquantel.

Schistosomiasis related circulating cell-free DNA: A useful biomarker in diagnostics.

Revue de littérature

Ullah, H., Arbab, S., Li, K., Khan, M., Qadeer, A., Muhammad, N.
12-07-2022

Mol Biochem Parasitol

<https://pubmed.ncbi.nlm.nih.gov/35835258>

Schistosoma is a genus of trematodes causing schistosomiasis, a major neglected tropical disease infecting more than 240 million people and with 700 million people at the risk of infection in the tropical and subtropical regions of the world, especially low-income countries. For the elimination of the disease, accurate diagnostic tools are needed. Besides allowing early treatment, early detection prevents environmental contamination and in turn ensures safe water sources in the endemic areas. Cell-free DNA (cfDNA) biomarker detection is a relatively new tool, used for the diagnosis of schistosomiasis in the early stages of infection from non-invasive clinical or experimental samples. cfDNA can be detected in Schistosoma infected host body fluids such as urine, serum, saliva and tissues, mainly in blood offering significant benefits for accurate diagnosis. In the current review, we described different characteristics of cfDNA, evidencing and supporting its potential uses in Schistosoma diagnosis and the improvement of treatment effectiveness.

of an oxyprenylated bioactive secondary metabolite; 2',4'-dihydroxy-4-prenyloxychalcone from the chloroform fraction of the aerial parts of the plant's methanol extract and the *in vivo* evaluation of the compound against *Naja nigricollis* venom. The compound has demonstrated significant ($p < 0.05$) and dose-dependent antivenin activity against LD₉₉ *Naja nigricollis* venom. At a dose of 10mg/kg, the compound protected 60% of the animals tested from death. The observed activity lends credence to the traditional use of the plant in the management of snake bites in northern Nigeria. The compound, 2',4'- dihydroxy-4-prenyloxychalcone, could also serve as a lead in the development of novel antisnake venom agents.

Use of geospatial analyses to address snakebite hotspots in mid-northern Brazil - A direction to health planning in shortfall biodiversity knowledge areas.

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Toxicon

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Knowing the distribution of venomous snakes of medical importance is essential to identify areas at risk for snakebites. Thus, we used an integrative approach based on the application of geographic distribution data of venomous snakes, species distribution modeling (SDM), spatial organization of snakebites, and information on human population density for mapping the potential distribution of snakes and identifying areas at risk of snakebites in the state of Maranhão (mid-northern Brazil). From a compiled database of venomous snake records deposited in biological collections and the literature, we predict the potential distribution of venomous snakes in Maranhão, a state whose diversity and geographic distribution of venomous snake species are poorly known. With this, we constructed potential distribution maps for each venomous snake species with at least one occurrence record within state boundaries, as well as generalized maps by family (Viperidae and Elapidae) and the total number of venomous snakes in Maranhão State. We also obtained data on the number of snakebites recorded in each municipality of Maranhão over a decade (2009-2019) and we ran a Generalized Linear Model to test for relationships between the number of venomous snakebites, the area of occurrence of snakes, and human population density. We obtained 1046 records of venomous snake species for Maranhão, represented by 17 viperid and elapid species. Most of the records were from Viperidae (mostly Bothrops atrox and B. marajoensis) and were concentrated mainly in the Amazon of the northern portion of the state. The models showed accurate predictive performance for all modeled species. The entire area of Maranhão exhibits environmental conditions for the occurrence of venomous snakes, with higher suitability indices in the northern region, in the Amazon rainforest. The number of snakebites was positively correlated with the interaction between high-risk areas (i.e., greater distribution of venomous snakes) and human population density. Our

HELMINTHIASES TRANSMISES PAR LE SOL (ASCARIDIOSE, TRICHURIASE, ANKYLOSTOMIASE)

GALE

MORSURES DE SERPENT

A bioactive chalcone from the aerial parts of *Indigofera conferta* Gillet.

Isah, M., Murtala, S., Abdullahi, S., Hamza, A., Tajuddeen, N., Dauda, M., Mzozoyana, V., Musa, A.

18-07-2022

Nat Prod Res

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Ethnobotanical information indicates that *Indigofera conferta* is used in northern Nigeria for the management of poisonous snakebites and the methanol extract was previously reported to have antivenin activity. In this study, we report the isolation

Morsures de serpent

study is a pioneer in using species distribution modeling in mid-northern Brazil to address the scarcity of data on snakebite-causing species, directly contributing to the theme of neglected tropical diseases of the World Health Organization.