



Veille scientifique

Maladies tropicales négligées

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24 au 30 avril 2023

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Cysticercose

Global research on cysticercosis and neurocysticercosis: A bibliometric analysis.

Gonzalez-Alcaide G, Sosa N, Shevy L, Belinchon-Romero I, Ramos-Rincon JM.

11-04-2023

Front Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37113561/>

Background: Cysticercosis is a parasitic infection caused by the larval stage *Taenia solium*. As a neglected tropical disease that is also difficult to diagnose, cysticercosis constitutes an important public health and research challenge. To characterize the development of research on cysticercosis and neurocysticercosis, considering the level of scientific evidence provided and the contribution of different countries to research, according to their endemic nature and their income level. **Methods:** Indexed publications on cysticercosis and neurocysticercosis were retrieved from the MEDLINE database, and the evolution of scientific production and the topic areas addressed in the body of research were analyzed. **Results:** A total of 7,860 papers published between 1928 and 2021 were analyzed. The volume of annual publications increased over time, standing at over 200 documents/year since 2010. Case studies constitute the main study design (27.4% of the documents with available information, $n = 2,155$), with fewer studies that provide the highest levels of scientific evidence, such as clinical studies (1.9%, $n = 149$) or systematic reviews (0.8%, $n = 63$). The most productive journals belong to the Parasitology and Tropical Medicine categories. Although the USA is the most productive country ($n = 2,292$), countries where *Tenia solium* is endemic, such as India ($n = 1,749$), Brazil ($n = 941$) and Peru ($n = 898$) also stand out, as does Mexico ($n = 1,414$). However, other endemic countries in Latin America and sub-Saharan Africa show little participation in the research. The level of international collaboration by country is very uneven, with some countries presenting very low values, such as India (9.9% of documents in international collaboration) or Brazil (18.7%); while there is evidence of intense international collaboration in countries like Peru (91.3%), Tanzania (88.2%) or Kenya (93.1%). Research output has coalesced in three thematic clusters: basic research in animals; parasitism, animal health, and zoonoses; and the diagnosis and therapeutic approach in diseases associated with cysticercosis and neurocysticercosis. **Conclusions:** The generation of knowledge on cysticercosis presents different features from other areas of research, such as the outstanding contribution of only some endemic countries; and the relevance of comprehensive approaches to research (animal and human health). Studies that provide higher levels of scientific evidence should be promoted, as should research in endemic areas.

Evaluating the Role of Corrals and Insects in the Transmission of Porcine Cysticercosis: A Cohort Study.

Gonzales-Gustavson E, Pray IW, Gamboa R, Muro C, Vilchez P, Gomez-Puerta L, Vargas-Calla A, Bonnet G, Pizzitutti F, Garcia HH, Gonzalez AE, O'Neal SE; Cysticercosis Working Group in Peru.

14-04-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111483/>

Consistent Measurement of Parasite-Specific Antigen Levels in Sera of Patients with Neurocysticercosis Using Two Different Monoclonal Antibody (mAb)-Based Enzyme-Linked Immunosorbent Assays.

Castillo Y, Toribio LM, Guzman C, Arroyo G, Espinoza C, Saavedra H, Bustos JA, Dorny P, O'Neal SE, Garcia HH; Cysticercosis Working Group in Peru.

06-04-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111451/>

Monoclonal antibody (mAb)-based enzyme-linked immunosorbent assay (ELISA) is a complementary diagnosis technique for neurocysticercosis (NCC), which detects circulating parasite antigen (Ag) indicative of viable infection and Ag levels that correlate well with the parasite burden. In this study, we compared the performance of two Ag-ELISA techniques for the detection of NCC. We assessed the agreement between our in-house TsW8/TsW5 Ag-ELISA and the widely used B158/B60 Ag-ELISA for measuring *T. solium* antigen levels in the sera from 113 patients with calcified, parenchymal, and subarachnoid NCC. Concordance was demonstrated evaluating the limits of agreement (LoAs) stratified by the type of NCC. Both ELISA's detected 47/48 (97.8%) subarachnoid NCC cases. In parenchymal and calcified NCC, the B158/B60 Ag-ELISA detected 19/24 (79.2%) and 18/41 (43.9%) cases, while the TsW8/TsW5 Ag-ELISA detected 21/24 (87.5%) and 13/41 (31.7%), respectively. Parenchymal and calcified NCC obtained a perfect agreement (100%), indicating that all sample results were within the predicted LoA, while for subarachnoid NCC, the agreement was 89.6%. The high concordance between the assays was confirmed by Lin's concordance coefficient (LCC = 0.97). Patients with viable parenchymal NCC (LCC = 0.95) obtained the highest concordance between assays, followed by subarachnoid NCC (LCC = 0.93) and calcified NCC (LCC = 0.92). The TsW8/TsW5 Ag-ELISA and B158/B60 Ag-ELISA showed high Ag measurement correlations across diverse types of NCC.

Subcutaneous *Taenia crassiceps* Cysticercosis in a Ring-Tailed Lemur (*Lemur catta*) in a Serbian Zoo.

Šimin S, Vračar V, Kozoderović G, Stevanov S, Alić A, Lalošević D, Lalošević V.

26-04-2023

Acta Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37099074/>

Background: Different rodent species serve as natural intermediate hosts for carnivore tapeworm *Taenia crassiceps*. However, this cestode occasionally infects various dead-end hosts including humans and other primates and may cause serious pathological implications with potentially fatal outcome. In this paper, we present subcutaneous cysticercosis caused by *T. crassiceps*, found in a previously healthy 17-years-old male ring-tailed lemur (*Lemur catta*) in a Serbian Zoo. **Case presentation:** The animal was presented to a veterinarian with a history of periarticular subcutaneous swelling in medial right knee region. After fine needle aspiration revealed cysticerci-like structures, a surgery was performed for complete extraction of the encapsulated multicystic mass containing numerous cysticerci. Collected material was sent for parasitological, histological and molecular analysis. One month after surgery, the lemur died due to respiratory failure unrelated to cysticercosis. Based on morphological features of large and small hooks and characteristic proliferation of cysticerci, a metacestode of *T. crassiceps* was identified, which was confirmed after sequencing of obtained amplicons and comparing them to the GenBank database. **Conclusions:** This is one of the few reported cases of *T. crassiceps* cysticercosis in a ring-tailed lemur, and the first one in Serbia. This endangered species seem to be more sensitive for *T. crassiceps* than other non-human primates, which represents serious conservation challenge for captive animals. Due to zoonotic nature of the parasite, challenging diagnosis, severity of the disease, difficult treatment and possible fatalities, high biosecurity measures are of particular importance, especially in endemic regions.

Solitary cardiac cysticercosis.

Dung LT, Van Sy T, Van NT.

05-04-2023

Radiol Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37089977/>

Dengue, chikungunya et maladie à virus Zika

A dengue vaccine whirlwind update.

Kariyawasam R, Lachman M, Mansuri S, Chakrabarti S, Boggild AK.

20-04-2023

Ther Adv Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37114191/>

Dengue virus (DENV) is a mosquito-borne single-stranded RNA virus of the *Flaviviridae* family with four serotypes (DENV1, DENV2, DENV3, and DENV4) circulating many tropical and subtropical regions of the world. Endemic in more than 100 countries, DENV results in over 400 million cases annually, a subset presenting with severe or life-threatening illnesses such as dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). While no specific treatments outside of supportive management exist, vaccines are an area of major research with two vaccines, Dengvaxia® (CYD-TDV) and Denvax® (TAK003), recently licensed for clinical use. CYD-TDV is highly efficacious in

children 9 years or older who have had prior DENV infection due to the high risk of severe disease in seronegative children aged 2-5 years. Meanwhile, TAK003 has shown efficacy at 97.7% and 73.7% against, DENV2 and DENV1, respectively, in phase 3 clinical trials across Latin America and Asia in healthy children aged 4-16 with virologically confirmed dengue. Other vaccines including TV003 and TV005 continue to be developed across the world, with the hopes of entering clinical trials in the near future. We discuss the current state of vaccine development against dengue, with a focus on CYD-TDV and TAK003 as promising novel vaccines to target this neglected tropical disease (NTD).

Year-round dengue fever in Pakistan, highlighting the surge amidst ongoing flood havoc and the COVID-19 pandemic: a comprehensive review.

Tabassum S, Naeem A, Nazir A, Naeem F, Gill S, Tabassum S.

10-04-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37113909/>

Dengue fever (DF) is an arthropod-borne viral infection caused by four serotypes of dengue virus (DENV 1-4) transmitted to the host by the vector mosquito *Aedes*, which causes fever, vomiting, headache, joint pain, muscle pain, and a distinctive itching and skin rash, ultimately leading to dengue hemorrhagic fever and dengue shock syndrome. The first case of DF in Pakistan was documented in 1994, but outbreak patterns began in 2005. As of 20 August 2022, Pakistan has 875 confirmed cases, raising alarming concerns. Misdiagnosis due to mutual symptoms, lack of an effective vaccine, the weakened and overburdened health system of Pakistan, irrational urbanization, climate change in Pakistan, insufficient waste management system, and a lack of awareness are the significant challenges Pakistan faces and result in recurrent dengue outbreaks every year. The recent flood in Pakistan has caused massive destruction, and stagnant dirty water has facilitated mosquito breeding. Sanitization and spraying, proper waste management, an adequate and advanced diagnostic system, control of population size, public awareness, and promotion of medical research and global collaboration, especially amidst flood devastation, are recommended to combat this deadly infection in Pakistan. This article aims to comprehensively review the year-round DF in Pakistan, highlighting the surge amidst ongoing flood havoc and the coronavirus disease 2019 pandemic.

The recent resurgence of Zika virus: current outbreak, epidemiology, transmission, diagnostic, prevention, treatment and complications - correspondent.

Islam MR, Akash S, Sharma R.

03-04-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37113899/>

Spontaneous splenic hematoma secondary to dengue infection: a rare case report.

Pahari S, Basukala S, Kunwar P, Thapa K, Khand Y, Thapa O.

16-03-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37113826/>

Dengue infection may have various surgical complications. Splenic hematoma is a rare complication of dengue hemorrhagic fever and may be life-threatening. **Case presentation:** A 54-year-old male, diagnosed with dengue infection detected at another hospital, presented on the 10th day of fever with left upper abdominal pain for 7 days without history of trauma. Urgent ultrasonography of the abdomen revealed findings suggestive of a splenic subcapsular hematoma, which was confirmed by computed tomography scan. The grade II splenic hematoma was being managed conservatively. Unfortunately, the patient developed hospital acquired pneumonia and died from septic shock. **Clinical discussion:** Hemorrhagic manifestations are seen in the febrile and critical phase of dengue, but the spleen is infrequently involved. Splenic hematoma can lead to splenic rupture, which can be rapidly fatal. Specific treatment guidelines of such hematomas are needed in the context of dengue infection, as the treatment modality is controversial. **Conclusion:** Patients must be carefully evaluated for the complications and surgical manifestations of dengue as abdominal pain and hypotension from splenic hematoma may be misinterpreted as components of dengue hemorrhagic fever and dengue shock syndrome.

Editorial: Insights in virus and host: 2021.

Hiscott J, Brandt CR.

11-04-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37113129/>

Intrahost Genetic Diversity of Dengue Virus in Human Hosts and Mosquito Vectors under Natural Conditions Which Impact Replicative Fitness In Vitro.

Nonyong P, Ekalaksananan T, Phanthanawiboon S, Overgaard HJ, Alexander N, Thaewongiew K, Sawaswong V, Nimsamer P, Payungporn S, Phadungsombat J, Nakayama EE, Shioda T, Pientong C.

17-04-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112962/>

Dengue virus (DENV) is an arbovirus whose transmission cycle involves disparate hosts: humans and mosquitoes. The error-prone nature of viral RNA replication drives the high mutation rates, and the consequently high genetic diversity affects viral fitness over this transmission cycle. A few studies have been performed to investigate the intrahost genetic diversity between hosts, although their mosquito infections were performed artificially in the laboratory setting. Here, we performed whole-genome

deep sequencing of DENV-1 ($n = 11$) and DENV-4 ($n = 13$) derived from clinical samples and field-caught mosquitoes from the houses of naturally infected patients, in order to analyze the intrahost genetic diversity of DENV between host types. Prominent differences in DENV intrahost diversity were observed in the viral population structure between DENV-1 and DENV-4, which appear to be associated with differing selection pressures. Interestingly, three single amino acid substitutions in the NS2A (K81R), NS3 (K107R), and NS5 (I563V) proteins in DENV-4 appear to be specifically acquired during infection in *Ae. aegypti* mosquitoes. Our *in vitro* study shows that the NS2A (K81R) mutant replicates similarly to the wild-type infectious clone-derived virus, while the NS3 (K107R), and NS5 (I563V) mutants have prolonged replication kinetics in the early phase in both Vero and C6/36 cells. These findings suggest that DENV is subjected to selection pressure in both mosquito and human hosts. The NS3 and NS5 genes may be specific targets of diversifying selection that play essential roles in early processing, RNA replication, and infectious particle production, and they are potentially adaptive at the population level during host switching.

T Cells in Tick-Borne Flavivirus Encephalitis: A Review of Current Paradigms in Protection and Disease Pathology.

Stone ET, Pinto AK.

13-04-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112938/>

Dengue Exposure and Wolbachia wMel Strain Affects the Fertility of Quiescent Eggs of *Aedes aegypti*.

Petersen MT, Couto-Lima D, Garcia GA, Pavan MG, David MR, Maciel-de-Freitas R.

12-04-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112932/>

(1) Background: The deployment of the bacterium *Wolbachia* to reduce arbovirus transmission is ongoing in several countries worldwide. When *Wolbachia*-carrying *Aedes aegypti* are released and established in the field, females may feed on dengue-infected hosts. The effects of simultaneous exposure on life-history traits of *Ae. aegypti* to *Wolbachia* wMel strain and dengue-1 virus DENV-1 remain unclear. (2) Methods: We monitored 4 groups (mosquitoes with either DENV-1 or *Wolbachia*, coinfecting with DENV-1 and *Wolbachia*, as well as negative controls) to estimate *Ae. aegypti* survival, oviposition success, fecundity, collapsing and fertility of quiescent eggs for 12 weeks. (3) Results: Neither DENV-1 nor *Wolbachia* had a significant impact on mosquito survival nor on mosquito fecundity, although the last parameter showed a tendency to decrease with ageing. There was a significant decrease in oviposition success in individuals carrying *Wolbachia*. *Wolbachia* infection and storage time significantly increased egg collapse parameter on the egg viability assay, while DENV-1 had a slight protective effect on the first four weeks of storage. (4) Conclusions: Despite limitations, our results contribute to better understanding

of the tripartite interaction of virus, bacteria and mosquito that may take place in field conditions and aid in guaranteeing the *Wolbachia* strategy success.

Isolation of Flaviviruses and Alphaviruses with Encephalitogenic Potential Diagnosed by Evandro Chagas Institute (Pará, Brazil) in the Period of 1954-2022: Six Decades of Discoveries.

Wanzeller ALM, da Silva FS, Hernández LHA, Barros LJJ, Freitas MNO, Santos MM, Gonçalves EJ, Pantoja JAS, Lima CS, Lima MF, Costa LRO, das Chagas LL, Silva IF, da Cunha TCADS, do Nascimento BLS, Vasconcelos HB, da Rosa EST, Rodrigues SG, Azevedo RDS, Martins LC, Casseb LMN, Chiang JO, Nunes Neto JP, Cruz ACR, Carvalho VL, Vasconcelos PFDC, da Silva EVP.

10-04-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112917>

Viruses with encephalitogenic potential can cause neurological conditions of clinical and epidemiological importance, such as *Saint Louis encephalitis virus*, *Venezuelan equine encephalitis virus*, *Eastern equine encephalitis virus*, *Western equine encephalitis virus*, *Dengue virus*, *Zika virus*, *Chikungunya virus*, *Mayaro virus* and *West Nile virus*. The objective of the present study was to determine the number of arboviruses with neuroinvasive potential isolated in Brazil that corresponds to the collection of viral samples belonging to the Department of Arbovirology and Hemorrhagic Fevers, Evandro Chagas Institute (SAARB/IEC) of the Laboratory Network of National Reference for Arbovirus Diagnosis from 1954 to 2022. In the analyzed period, a total of 1,347 arbovirus samples with encephalitogenic potential were isolated from mice; 5,065 human samples were isolated exclusively by cell culture; and 676 viruses were isolated from mosquitoes. The emergence of new arboviruses may be responsible for diseases still unknown to humans, making the Amazon region a hotspot for infectious diseases due to its fauna and flora species characteristics. The detection of circulating arboviruses with the potential to cause neuroinvasive diseases is constant, which justifies the continuation of active epidemiological surveillance work that offers adequate support to the public health system regarding the virological diagnosis of circulating arboviruses in Brazil.

Laboratory Evaluation and Field Testing of Dengue NS1 and IgM/IgG Rapid Diagnostic Tests in an Epidemic Context in Senegal.

Ndiaye O, Woolston K, Gaye A, Loucoubar C, Coccoza M, Fall C, Dia F, Adams ER, Samb M, Camara D, Sadio BD, Diagne CT, Weidmann M, Faye O, Fitchett JRA, Sall AA, Diagne CT.

31-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112887/>

Grape Seed Proanthocyanidins Inhibit Replication of the Dengue Virus by

Targeting NF- κ B and MAPK-Mediated Cyclooxygenase-2 Expression.

Chen WC, Hossen M, Liu W, Yen CH, Huang CH, Hsu YC, Lee JC.

30-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112864/>

A Perspective on Current Flavivirus Vaccine Development: A Brief Review.

Dutta SK, Langenburg T.

28-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112840/>

The flavivirus genus contains several clinically important pathogens that account for tremendous global suffering. Primarily transmitted by mosquitos or ticks, these viruses can cause severe and potentially fatal diseases ranging from hemorrhagic fevers to encephalitis. The extensive global burden is predominantly caused by six flaviviruses: dengue, Zika, West Nile, yellow fever, Japanese encephalitis and tick-borne encephalitis. Several vaccines have been developed, and many more are currently being tested in clinical trials. However, flavivirus vaccine development is still confronted with many shortcomings and challenges. With the use of the existing literature, we have studied these hurdles as well as the signs of progress made in flavivirus vaccinology in the context of future development strategies. Moreover, all current licensed and phase-trial flavivirus vaccines have been gathered and discussed based on their vaccine type. Furthermore, potentially relevant vaccine types without any candidates in clinical testing are explored in this review as well. Over the past decades, several modern vaccine types have expanded the field of vaccinology, potentially providing alternative solutions for flavivirus vaccines. These vaccine types offer different development strategies as opposed to traditional vaccines. The included vaccine types were live-attenuated, inactivated, subunit, VLPs, viral vector-based, epitope-based, DNA and mRNA vaccines. Each vaccine type offers different advantages, some more suitable for flaviviruses than others. Additional studies are needed to overcome the barriers currently faced by flavivirus vaccine development, but many potential solutions are currently being explored.

Differences in Longevity and Temperature-Driven Extrinsic Incubation Period Correlate with Varying Dengue Risk in the Arizona-Sonora Desert Region.

Ernst KC, Walker KR, Castro-Luque AL, Schmidt C, Joy TK, Brophy M, Reyes-Castro P, Díaz-Caravantes RE, Encinas VO, Aguilera A, Gameros M, Cuevas Ruiz RE, Hayden MH, Alvarez G, Monaghan A, Williamson D, Arnbrister J, Gutiérrez EJ, Carrière Y, Riehle MA.

26-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112832/>

The Others: A Systematic Review of the Lesser-Known Arboviruses of the Insular Caribbean.

Ali I, Alarcón-Elbal PM, Mundle M, Noble SAA, Oura CAL, Anzinger JJ, Sandiford SL.

25-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112824/>

The Caribbean enjoys a long-standing eminence as a popular tourist destination; however, over the years it has also amassed the sobriquet "arbovirus hotspot". As the planet warms and vectors expand their habitats, a cognizant working knowledge of the lesser-known arboviruses and the factors that influence their emergence and resurgence becomes essential. The extant literature on Caribbean arboviruses is spread across decades of published literature and is quite often difficult to access, and, in some cases, is obsolete. Here, we look at the lesser-known arboviruses of the insular Caribbean and examine some of the drivers for their emergence and resurgence. We searched the scientific literature databases PubMed and Google Scholar for peer-reviewed literature as well as scholarly reports. We included articles and reports that describe works resulting in serological evidence of the presence of arboviruses and/or arbovirus isolations in the insular Caribbean. Studies without serological evidence and/or arbovirus isolations as well as those including dengue, chikungunya, Zika, and yellow fever were excluded. Of the 545 articles identified, 122 met the inclusion criteria. A total of 42 arboviruses were identified in the literature. These arboviruses and the drivers that affect their emergence/resurgence are discussed.

The Anti-Dengue Virus Peptide DV2 Inhibits Zika Virus Both In Vitro and In Vivo.

Castro-Amarante MF, Pereira SS, Pereira LR, Santos LS, Venceslau-Carvalho AA, Martins EG, Balan A, Souza Ferreira LC.

25-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112820/>

The C-terminal portion of the E protein, known as stem, is conserved among flaviviruses and is an important target to peptide-based antiviral strategies. Since the dengue (DENV) and Zika (ZIKV) viruses share sequences in the stem region, in this study we evaluated the cross-inhibition of ZIKV by the stem-based DV2 peptide (419-447), which was previously described to inhibit all DENV serotypes. Thus, the anti-ZIKV effects induced by treatments with the DV2 peptide were tested in both in vitro and in vivo conditions. Molecular modeling approaches have demonstrated that the DV2 peptide interacts with amino acid residues exposed on the surface of pre- and postfusion forms of the ZIKA envelope (E) protein. The peptide did not have any significant cytotoxic effects on eukaryotic cells but efficiently inhibited ZIKV infectivity in cultivated Vero cells. In addition, the DV2 peptide reduced morbidity and mortality in mice subjected to lethal challenges with a ZIKV strain isolated in Brazil. Taken together, the present results

support the therapeutic potential of the DV2 peptide against ZIKV infections and open perspectives for the development and clinical testing of anti-flavivirus treatments based on synthetic stem-based peptides.

Alphavirus Evasion of Zinc Finger Antiviral Protein (ZAP) Correlates with CpG Suppression in a Specific Viral nsP2 Gene Sequence.

Nguyen LP, Aldana KS, Yang E, Yao Z, Li MMH.

24-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112813/>

Transient Blockade of Type I Interferon Signalling Promotes Replication of Dengue Virus Strain D2Y98P in Adult Wild-Type Mice.

Wilken L, Stelz S, Prajeeth CK, Rimmelzwaan GF.

24-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112795/>

Dengue virus serotypes 1 to 4 (DENV1-4) place nearly half the global population at risk of infection and the licensed tetravalent dengue vaccine fails to protect individuals who have not previously been exposed to DENV. The development of intervention strategies had long been hampered by the lack of a suitable small animal model. DENV does not replicate in wild-type mice due to its inability to antagonise the mouse type I interferon (IFN) response. Mice deficient in type I IFN signalling (*Ifnar1*^{-/-} mice) are highly susceptible to DENV infection, but their immunocompromised status makes it difficult to interpret immune responses elicited by experimental vaccines. To develop an alternative mouse model for vaccine testing, we treated adult wild-type mice with MAR1-5A3—an IFNAR1-blocking, non-cell-depleting antibody prior to infection with the DENV2 strain D2Y98P. This approach would allow for vaccination of immunocompetent mice and subsequent inhibition of type I IFN signalling prior to challenge infection. While *Ifnar1*^{-/-} mice quickly succumbed to infection, MAR1-5A3-treated mice did not show any signs of illness but eventually seroconverted. Infectious virus was recovered from the sera and visceral organs of *Ifnar1*^{-/-} mice, but not from those of mice treated with MAR1-5A3. However, high levels of viral RNA were detected in the samples of MAR1-5A3-treated mice, indicating productive viral replication and dissemination. This transiently immunocompromised mouse model of DENV2 infection will aid the pre-clinical assessment of next-generation vaccines as well as novel antiviral treatments.

Recent Advancements in Mosquito-Borne Flavivirus Vaccine Development.

Wu B, Qi Z, Qian X.

23-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112794/>

Lately, the global incidence of flavivirus infection has been increasing dramatically and presents formidable challenges for public health systems around the world. Most clinically significant flaviviruses are mosquito-borne, such as the four serotypes of dengue virus, Zika virus, West Nile virus, Japanese encephalitis virus and yellow fever virus. Until now, no effective ant flaviviral drugs are available to fight flaviviral infection; thus, a highly immunogenic vaccine would be the most effective weapon to control the diseases. In recent years, flavivirus vaccine research has made major breakthroughs with several vaccine candidates showing encouraging results in preclinical and clinical trials. This review summarizes the current advancement, safety, efficacy, advantages and disadvantages of vaccines against mosquito-borne flaviviruses posing significant threats to human health.

Development of MVA-d34 Tetravalent Dengue Vaccine: Design and Immunogenicity.

Mintaev RR, Glazkova DV, Orlova OV, Ignatyev GM, Oksanich AS, Shipulin GA, Bogoslovskaya EV.

12-04-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112743/>

A Ferritin Nanoparticle-Based Zika Virus Vaccine Candidate Induces Robust Humoral and Cellular Immune Responses and Protects Mice from Lethal Virus Challenge.

Pattnaik A, Sahoo BR, Struble LR, Borgstahl GEO, Zhou Y, Franco R, Barletta RG, Osorio FA, Petro TM, Pattnaik AK.

10-04-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112733/>

Plant-Produced Anti-Zika Virus Monoclonal Antibody Glycovariant Exhibits Abrogated Antibody-Dependent Enhancement of Infection.

Yang M, Sun H, Lai H, Neupane B, Bai F, Steinkellner H, Chen Q.

29-03-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112665/>

Monoclonal antibodies (mAb) against the envelope (E) protein of Zika virus (ZIKV) have shown great potential as therapeutics against the Zika epidemics. However, their use as a therapy may predispose treated individuals to severe infection by the related dengue virus (DENV) via antibody-dependent enhancement of infection (ADE). Here, we generated a broadly neutralizing flavivirus mAb, ZV1, with an identical protein backbone but different Fc glycosylation profiles. The three glycovariants, produced in wild-type (WT) and glycoengineered Δ XF *Nicotiana benthamiana* plants and in Chinese hamster ovary cells (ZV1^{WT}, ZV1 ^{Δ XF}, and ZV1^{CHO}), respectively, showed equivalent neutralization potency against both ZIKV and DENV. By contrast, the three mAb glycoforms

demonstrated drastically different ADE activity for DENV and ZIKV infection. While ZV1^{CHO} and ZV1 ^{Δ XF} showed ADE activity upon DENV and ZIKV infection, ZV1^{WT} totally forwent its ADE. Importantly, all three glycovariants exhibited antibody-dependent cellular cytotoxicity (ADCC) against virus-infected cells, with increased potency by the fucose-free ZV1 ^{Δ XF} glycoform. Moreover, the in vivo efficacy of the ADE-free ZV1^{WT} was demonstrated in a murine model. Collectively, we demonstrated the feasibility of modulating ADE by Fc glycosylation, thereby establishing a novel approach for improving the safety of flavivirus therapeutics. Our study also underscores the versatile use of plants for the rapid expression of complex human proteins to reveal novel insight into antibody function and viral pathogenesis.

Recombinant Modified Vaccinia Virus Ankara Expressing a Glycosylation Mutant of Dengue Virus NS1 Induces Specific Antibody and T-Cell Responses in Mice.

Wilken L, Stelz S, Agac A, Sutter G, Prajeeth CK, Rimmelzwaan GF.

23-03-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112626/>

Phytochemicals as Invaluable Sources of Potent Antimicrobial Agents to Combat Antibiotic Resistance.

Jadimurthy R, Jagadish S, Nayak SC, Kumar S, Mohan CD, Rangappa KS.

04-04-2023

Life (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37109477/>

Plants have been used for therapeutic purposes against various human ailments for several centuries. Plant-derived natural compounds have been implemented in clinics against microbial diseases. Unfortunately, the emergence of antimicrobial resistance has significantly reduced the efficacy of existing standard antimicrobials. The World Health Organization (WHO) has declared antimicrobial resistance as one of the top 10 global public health threats facing humanity. Therefore, it is the need of the hour to discover new antimicrobial agents against drug-resistant pathogens. In the present article, we have discussed the importance of plant metabolites in the context of their medicinal applications and elaborated on their mechanism of antimicrobial action against human pathogens. The WHO has categorized some drug-resistant bacteria and fungi as critical and high priority based on the need to develop new drugs, and we have considered the plant metabolites that target these bacteria and fungi. We have also emphasized the role of phytochemicals that target deadly viruses such as COVID-19, Ebola, and dengue. Additionally, we have also elaborated on the synergetic effect of plant-derived compounds with standard antimicrobials against clinically important microbes. Overall, this article provides an overview of the importance of considering phytochemicals in the

development of antimicrobial compounds as therapeutic agents against drug-resistant microbes.

Antiviral Activity of Quercetin Hydrate against Zika Virus.

Saivish MV, Menezes GL, da Silva RA, Fontoura MA, Shimizu JF, da Silva GCD, Teixeira IDS, Mistrão NFB, Hernandes VM, Rahal P, Sacchetto L, Pacca CC, Marques RE, Nogueira ML.

19-04-2023

Int J Mol Sci.

<https://pubmed.ncbi.nlm.nih.gov/37108665/>

Physiological and developmental dysfunctions in the dengue vector *Culex pipiens* (Diptera: Culicidae) immature stages following treatment with zinc oxide nanoparticles.

Ibrahim AMA, Thabet MA, Ali AM.

Mai-2023

Pestic Biochem Physiol.

<https://pubmed.ncbi.nlm.nih.gov/37105619/>

The medical value of mosquitoes attracted researchers worldwide to search for a valuable way to control such serious insects. The continuous development of resistance against chemical insecticides pushed toward looking for novel and promising compounds against mosquitoes. In this study, the toxicity and physio-developmental effects of 10-30 nm spherical zinc oxide nanoparticles (ZnONPs) in aqueous suspension was addressed against the first larval instar of *Culex pipiens* mosquito. The calculated value of LC_{50} was about 0.892 g/L while the sub lethal concentration LC_{20} recorded about 0.246 g/L. Larvae treated with ZnONPs suffered reduced growth rate, longer developmental period and malformations in the breathing tube. Furthermore, the treated larvae showed clear abnormal appearance of the gastric caeca and midgut epithelia under transmission electron microscope (TEM). These abnormalities appeared as condensation of the nuclear chromatin, abnormal shape or absence of microvilli, highly increased amount of smooth endoplasmic reticulum in the cytoplasm and appearance of numerous vacuoles. Additionally, ZnONPs interfered with several biochemical pathways such as induction of oxidative stress which appeared in the form of increased levels of hydrogen peroxide and inability to activate the detoxifying enzymes alkaline phosphatase (ALP), catalase and glutathione peroxidase (GPX). On the contrary, the activity of the antioxidant enzyme superoxide dismutase (SOD) increased in treated larvae. Furthermore, LC_{20} and LC_{50} of ZnONPs inhibited the growth rate of the larval gut fauna in vitro. These results clearly show that ZnONPs target several tissues leading to serious alteration in the physiological and developmental processes in *C. pipiens* mosquito larvae.

Potential risk sites and their relationship with dengue cases, Campinas municipality, Southeast Brazil.

Mendes JA, Vanwambeke SO.

27-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104540/>

Background: Among the main activities of dengue and vector control recommended by the Ministry of Health of Brazil is the inspection and monitoring of properties identified as Strategic Points (SPs) and Special Buildings (SBs). SPs are properties associated to hazard, where there is a concentration of suitable egg-laying containers for *Aedes aegypti* mosquitoes, while SBs have greater importance for human exposure to the dengue virus.

Objectives: To investigate the effect of characteristics of the urban landscape on dengue incidence. Specifically, we tested if SPs and SBs affect dengue case distribution in Campinas, and if they do, if they affect the risk differently. We considered the period from 2013 to 2016. **Methods:** We tested whether dengue cases were more numerous than expected in the vicinity of SPs and SBs, putative sources of risk, using the Negative Binomial models. We also tested the existence of a gradient in incidence with increasing distance to SPs and SBs by using Stone's test. **Results:** The Rate Ratios (RR) values were always higher closer to the SPs and SBs, and these values tended to decrease as distance from these sources increased. In general, RR values greater than one, which indicates a higher risk, were associated to the closest buffers from the SPs/SBs properties, until nearly 550 meters for the SPs and 650 meters for the SBs. Stone's test results indicated that for all years considered, there was a correlation between the distance from the SPs/SBs and dengue cases occurrences, except for SBs from 2016. For SPs the relationship is stronger than for SBs. **Discussion:** Results are coherent with other studies which found that these properties contribute to an increased risk of dengue transmission. We emphasize the importance of public agents' survey work and the importance to keep and improve the inspections in SPs/SBs recorded in Campinas.

Self-care practices and health-seeking behaviours in patients with dengue fever: A qualitative study from patients' and physicians' perspectives.

Ng WL, Toh JY, Ng CJ, Teo CH, Lee YK, Loo KK, Abdul Hadi H, Noor Azhar AM.

27-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104529/>

Fusing an agent-based model of mosquito population dynamics with a statistical reconstruction of spatio-temporal abundance patterns.

Cavany SM, España G, Lloyd AL, Vazquez-Prokopec GM, Astete H, Waller LA, Kitron U, Scott TW, Morrison AC, Reiner RC Jr, Perkins TA.

27-04-2023

PLoS Comput Biol.

<https://pubmed.ncbi.nlm.nih.gov/37104528/>

An Integrative Explainable Artificial Intelligence Approach to Analyze Fine-Scale Land-Cover and Land-Use Factors

Associated with Spatial Distributions of Place of Residence of Reported Dengue Cases.

Yang H, Nguyen TN, Chuang TW.

20-04-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104363/>

Dengue fever is a prevalent mosquito-borne disease that burdens communities in subtropical and tropical regions. Dengue transmission is ecologically complex; several environmental conditions are critical for the spatial and temporal distribution of dengue. Interannual variability and spatial distribution of dengue transmission are well-studied; however, the effects of land cover and use are yet to be investigated. Therefore, we applied an explainable artificial intelligence (AI) approach to integrate the EXtreme Gradient Boosting and Shapley Additive Explanation (SHAP) methods to evaluate spatial patterns of the residences of reported dengue cases based on various fine-scale land-cover land-use types, Shannon's diversity index, and household density in Kaohsiung City, Taiwan, between 2014 and 2015. We found that the proportions of general roads and residential areas play essential roles in dengue case residences with nonlinear patterns. Agriculture-related features were negatively associated with dengue incidence. Additionally, Shannon's diversity index showed a U-shaped relationship with dengue infection, and SHAP dependence plots showed different relationships between various land-use types and dengue incidence. Finally, landscape-based prediction maps were generated from the best-fit model and highlighted high-risk zones within the metropolitan region. The explainable AI approach delineated precise associations between spatial patterns of the residences of dengue cases and diverse land-use characteristics. This information is beneficial for resource allocation and control strategy modification.

Assessing the Burden of Dengue during the COVID-19 Pandemic in Mexico.

Lugo-Radillo A, Mendoza-Cano O, Trujillo X, Huerta M, Ríos-Silva M, Guzmán-Esquível J, Benites-Godínez V, Bricio-Barrios JA, Ríos-Bracamontes EF, Cárdenas-Rojas MI, Cárdenas Y, Murillo-Zamora E.

19-04-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104357/>

Proceedings of the 5th Asia Dengue Summit.

Srisawat N, Gubler DJ, Pangestu T, Thisyakorn U, Ismail Z, Goh D, Capeding MR, Bravo L, Yoksan S, Tantawichien T, Hadinegoro SR, Rafiq K, Picot VS, Ooi EE.

19-04-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104356/>

The 5th Asia Dengue Summit, themed "Roll Back Dengue", was held in Singapore from 13 to 15 June 2022. The summit was co-convened by Asia Dengue Voice and Action (ADVA), Global Dengue and Aedes transmitted Diseases

Consortium (GDAC), Southeast Asian Ministers of Education Tropical Medicine and Public Health Network (SEAMEO TROPMED), and the Fondation Mérieux (FMx). Dengue experts from academia and research and representatives from the Ministries of Health, Regional and Global World Health Organization (WHO), and International Vaccine Institute (IVI) participated in the three-day summit. With more than 270 speakers and delegates from over 14 countries, 12 symposiums, and 3 full days, the 5th ADS highlighted the growing threat of dengue, shared innovations and strategies for successful dengue control, and emphasized the need for multi-sectoral collaboration to control dengue.

The Potential of Surveillance Data for Dengue Risk Mapping: An Evaluation of Different Approaches in Cuba.

Baldoquín Rodríguez W, Mirabal M, Van der Stuyft P, Gómez Padrón T, Fonseca V, Castillo RM, Monteagudo Díaz S, Baetens JM, De Baets B, Toledo Romani ME, Vanlerberghe V.

18-04-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104355/>

To better guide dengue prevention and control efforts, the use of routinely collected data to develop risk maps is proposed. For this purpose, dengue experts identified indicators representative of entomological, epidemiological and demographic risks, hereafter called components, by using surveillance data aggregated at the level of Consejos Populares (CPs) in two municipalities of Cuba (Santiago de Cuba and Cienfuegos) in the period of 2010-2015. Two vulnerability models (one with equally weighted components and one with data-derived weights using Principal Component Analysis), and three incidence-based risk models were built to construct risk maps. The correlation between the two vulnerability models was high ($\tau > 0.89$). The single-component and multicomponent incidence-based models were also highly correlated ($\tau \geq 0.9$). However, the agreement between the vulnerability- and the incidence-based risk maps was below 0.6 in the setting with a prolonged history of dengue transmission. This may suggest that an incidence-based approach does not fully reflect the complexity of vulnerability for future transmission. The small difference between single- and multicomponent incidence maps indicates that in a setting with a narrow availability of data, simpler models can be used. Nevertheless, the generalized linear mixed multicomponent model provides information of covariate-adjusted and spatially smoothed relative risks of disease transmission, which can be important for the prospective evaluation of an intervention strategy. In conclusion, caution is needed when interpreting risk maps, as the results vary depending on the importance given to the components involved in disease transmission. The multicomponent vulnerability mapping needs to be prospectively validated based on an intervention trial targeting high-risk areas.

Trends in ELISA-Based Flavivirus IgG Serosurveys: A Systematic Review.

Vista FES, Tantengco OAG, Dispo MD, Opiso DMS, Badua CLDC, Gerardo JPZ, Perez JRM, Baldo KAT, Chao DY, Dalmacio LMM.
13-04-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/37104349/>

Clinical Diagnosis of Chikungunya Infection: An Essential Aid in a Primary Care Setting Where Serological Confirmation Is Not Available.

Rueda JC, Peláez-Ballestas I, Angarita JI, Santos AM, Pinzon C, Saldarriaga EL, Rueda JM, Forero E, Saaibi DL, Pavía PX, Mantilla MJ, Rodríguez-Salas G, Santacruz JC, Rueda I, Cardiel MH, Londono J.
03-04-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/37104340/>

Behavior of Adult *Aedes aegypti* and *Aedes albopictus* in Kinshasa, DRC, and the Implications for Control.

Manzambi EZ, Mbuka GB, Ilombe G, Takasongo RM, Tezzo FW, Del Carmen Marquetti M, Metelo E, Vanlerberghe V, Bortel WV.
30-03-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/37104333/>

Yellow fever and chikungunya outbreaks-and a few dengue cases-have been reported in the Democratic Republic of the Congo (DRC) in recent years. However, little is known about the ecology and behavior of the adult disease vector species, *Aedes aegypti* and *Aedes albopictus*, in DRC. Preliminary studies showed important differences in *Aedes* behavior in DRC and Latin-American sites. Therefore, this study aimed to assess the host-seeking and resting behaviors of female *Ae. aegypti* and *Ae. albopictus*, and their densities in four communes of Kinshasa (Kalamu, Lingwala, Mont Ngafula and Ndjili). Two cross-sectional surveys were carried out, one in the dry season (July 2019) and one in the rainy season (February 2020). We used three different adult vector collection methods: BG-Sentinel 2, BG-GAT, and prokopack. Both *Aedes* species were clearly exophagic, exophilic, and sought breeding sites outdoors. The adult house index for *Ae. aegypti* exceeded 55% in all communes except Lingwala, where it was only 27%. The Adult Breteau Index (ABI) for *Ae. aegypti* was 190.77 mosquitoes per 100 houses inspected in the rainy season and 6.03 in the dry season. For *Ae. albopictus*, the ABI was 11.79 and 3.52 in the rainy and dry seasons, respectively. *Aedes aegypti* showed unimodal host-seeking activity between 6 h and 21 h. The exophagic and exophilic behaviors of both species point to the need to target adult mosquitoes outdoors when implementing vector control.

Development and Utility of Practical Indicators of Critical Outcomes in Dengue Patients Presenting to Hospital: A Retrospective Cross-Sectional Study.

Chi CY, Sung TC, Chang K, Chien YW, Hsu HC, Tu YF, Huang YT, Shih HI.
25-03-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/37104314/>

Long-term projections of the impacts of warming temperatures on Zika and dengue risk in four Brazilian cities using a temperature-dependent basic reproduction number.

Van Wyk H, Eisenberg JNS, Brouwer AF.
27-04-2023
PLoS Negl Trop Dis.
<https://pubmed.ncbi.nlm.nih.gov/37104296/>

For vector-borne diseases the basic reproduction number [Formula: see text], a measure of a disease's epidemic potential, is highly temperature-dependent. Recent work characterizing these temperature dependencies has highlighted how climate change may impact geographic disease spread. We extend this prior work by examining how newly emerging diseases, like Zika, will be impacted by specific future climate change scenarios in four diverse regions of Brazil, a country that has been profoundly impacted by Zika. We estimated a [Formula: see text], derived from a compartmental transmission model, characterizing Zika (and, for comparison, dengue) transmission potential as a function of temperature-dependent biological parameters specific to *Aedes aegypti*. We obtained historical temperature data for the five-year period 2015-2019 and projections for 2045-2049 by fitting cubic spline interpolations to data from simulated atmospheric data provided by the CMIP-6 project (specifically, generated by the GFDL-ESM4 model), which provides projections under four Shared Socioeconomic Pathways (SSP). These four SSP scenarios correspond to varying levels of climate change severity. We applied this approach to four Brazilian cities (Manaus, Recife, Rio de Janeiro, and São Paulo) that represent diverse climatic regions. Our model predicts that the [Formula: see text] for Zika peaks at 2.7 around 30°C, while for dengue it peaks at 6.8 around 31°C. We find that the epidemic potential of Zika will increase beyond current levels in Brazil in all of the climate scenarios. For Manaus, we predict that the annual [Formula: see text] range will increase from 2.1-2.5, to 2.3-2.7, for Recife we project an increase from 0.4-1.9 to 0.6-2.3, for Rio de Janeiro from 0-1.9 to 0-2.3, and for São Paulo from 0-0.3 to 0-0.7. As Zika immunity wanes and temperatures increase, there will be increasing epidemic potential and longer transmission seasons, especially in regions where transmission is currently marginal. Surveillance systems should be implemented and sustained for early detection.

Spatiotemporal and Seasonal Trends of Class A and B Notifiable Infectious Diseases in China: Retrospective Analysis.

Zheng J, Zhang N, Shen G, Liang F, Zhao Y, He X, Wang Y, He R, Chen W, Xue H, Shen Y, Fu Y, Zhang WH, Zhang L, Bhatt S, Mao Y, Zhu B.

27-04-2032

JMIR Public Health Surveill.

<https://pubmed.ncbi.nlm.nih.gov/37103994/>

Background: China is the most populous country globally and has made significant achievements in the control of infectious diseases over the last decades. The 2003 SARS epidemic triggered the initiation of the China Information System for Disease Control and Prevention (CISDCP). Since then, numerous studies have investigated the epidemiological features and trends of individual infectious diseases in China; however, few considered the changing spatiotemporal trends and seasonality of these infectious diseases over time. **Objective:** This study aims to systematically review the spatiotemporal trends and seasonal characteristics of class A and class B notifiable infectious diseases in China during 2005-2020. **Methods:** We extracted the incidence and mortality data of 8 types (27 diseases) of notifiable infectious diseases from the CISDCP. We used the Mann-Kendall and Sen's methods to investigate the diseases' temporal trends, Moran I statistic for their geographical distribution, and circular distribution analysis for their seasonality. **Results:** Between January 2005 and December 2020, 51,028,733 incident cases and 261,851 attributable deaths were recorded. Pertussis ($P=.03$), dengue fever ($P=.01$), brucellosis ($P=.001$), scarlet fever ($P=.02$), AIDS ($P<.001$), syphilis ($P<.001$), hepatitis C ($P<.001$) and hepatitis E ($P=.04$) exhibited significant upward trends. Furthermore, measles ($P<.001$), bacillary and amebic dysentery ($P<.001$), malaria ($P=.04$), dengue fever ($P=.006$), brucellosis ($P=.03$), and tuberculosis ($P=.003$) exhibited significant seasonal patterns. We observed marked disease burden-related geographic disparities and heterogeneities. Notably, high-risk areas for various infectious diseases have remained relatively unchanged since 2005. In particular, hemorrhagic fever and brucellosis were largely concentrated in Northeast China; neonatal tetanus, typhoid and paratyphoid, Japanese encephalitis, leptospirosis, and AIDS in Southwest China; BAD in North China; schistosomiasis in Central China; anthrax, tuberculosis, and hepatitis A in Northwest China; rabies in South China; and gonorrhea in East China. However, the geographical distribution of syphilis, scarlet fever, and hepatitis E drifted from coastal to inland provinces during 2005-2020. **Conclusions:** The overall infectious disease burden in China is declining; however, hepatitis C and E, bacterial infections, and sexually transmitted infections continue to multiply, many of which have spread from coastal to inland provinces.

Soluble NS1 antagonizes IgG- and IgA-mediated monocytic phagocytosis of DENV infected cells.

Waldran MJ, Wegman AD, Bahr LE, Roy NH, Currier JR, Waickman AT.

26-04-2032

J Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37103221/>

Spatial Distribution and Long-Term Persistence of Wolbachia-Infected Aedes aegypti in the Mentari Court, Malaysia.

Cheong YL, Nazni WA, Lee HL, NoorAfizah A, MohdKhairuddin IC, Kamarul GMR, Nizam NMN, Arif MAK, NurZatilAqmar ZM, Irwan SM, Khadijah K, Paid YM, Topek O, Hasnor AH, AbuBakar R, Singh Gill B, Fadzilah K, Tahir A, Sinkins SP, Hoffmann AA.

11-04-2023

Insects.

<https://pubmed.ncbi.nlm.nih.gov/37103189/>

Placental and Doppler ultrasound findings in pregnant women with SARS-CoV-2 infection.

Soto-Sánchez EM, López-Gorosabel C, Ibáñez-Santamaría AB, Sánchez-Estévez B, De la Fuente-Valero J, Hernández-Aguado JJ.

Mai-2023

AJOG Glob Rep.

<https://pubmed.ncbi.nlm.nih.gov/37102135/>

Background: Several viral infections cause changes in the placenta. Cytomegalovirus, herpes viruses, and HIV cause increased placental thickness; Zika virus induces focal regions of necrosis; parvovirus B19 causes a structural injury. Umbilical flow can be considered a direct measurement of vascular placental function. **Objective:** This study aimed to compare placental ultrasound and umbilical Doppler findings in pregnant women who tested positive or negative for SARS-CoV-2. Our work aimed to confirm the suspicion of placental infection and the consequence in fetal physiopathology. **Study design:** Fifty-seven pregnant women who tested positive for SARS-CoV-2 at the time of or 1 month before the ultrasound scan were evaluated. Cases included 9 first trimester, 16 second trimester, and 32 third trimester ultrasound scans. For comparison, 110 pregnant women (controls) were evaluated. They included 19 women in their first trimester, 43 in their second trimester, and 48 in the third trimester. Controls were asymptomatic and tested negative for SARS-CoV-2 infection in the last 72 hours before the ultrasound scan. Fetal biometry, placental thickness, placental lakes and Doppler umbilical vein parameters, including venous cross-sectional area (mean transverse diameter and radius of umbilical vein, mean velocity of umbilical vein), and umbilical vein blood flow were evaluated. **Results:** Placental thickness (in millimeter) was significantly higher in the group of pregnant women with SARS-CoV-2 infection (53.82 [10-115]) than in the control group (33.82 [12-66]; $P<.001$) in their second and third trimesters. The frequency of >4 placental lakes was significantly higher in the group of pregnant women with SARS-CoV-2 infection (28/57 [50.91%]) than in the control (7/110 [6.36]; $P<.001$) in all 3 trimesters. The mean velocity of umbilical vein was significantly higher in the group of pregnant women with SARS-CoV-2 infection (12.45 [5.73-21]) than in the control group (10.81 [6.31-18.80]; $P=.001$) in all 3 trimesters. Umbilical vein blood flow (in milliliter per minute) was significantly higher in the group of pregnant women with SARS-CoV-2 infection (389.9 [6.52-1496.1]) than in the control group (305.05 [3.11-1441]; $P=.05$) in all 3 trimesters. **Conclusion:** Significant differences in placental and venous Doppler ultrasound were documented. Placental thickness, placental venous lakes, mean velocity of umbilical vein,

and umbilical vein flow were significantly higher in the group of pregnant women with SARS-CoV-2 infection in all 3 trimesters.

Inhibition of 3-Hydroxykynurenine Transaminase from *Aedes aegypti* and *Anopheles gambiae*: A Mosquito-Specific Target to Combat the Transmission of Arboviruses.

Maciel LG, Ferraz MVF, Oliveira AA, Lins RD, Dos Anjos JV, Guido RVC, Soares TA.

16-02-2023

ACS Bio Med Chem Au.

<https://pubmed.ncbi.nlm.nih.gov/37101811/>

Future perspectives of emerging novel drug targets and immunotherapies to control drug addiction.

Malik JA, Agrewala JN.

24-03-2023

Int Immunopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37099943/>

Substance Use Disorder (SUD) is one of the major mental illnesses that is terrifically intensifying worldwide. It is becoming overwhelming due to limited options for treatment. The complexity of addiction disorders is the main impediment to understanding the pathophysiology of the illness. Hence, unveiling the complexity of the brain through basic research, identification of novel signaling pathways, the discovery of new drug targets, and advancement in cutting-edge technologies will help control this disorder. Additionally, there is a great hope of controlling the SUDs through immunotherapeutic measures like therapeutic antibodies and vaccines. Vaccines have played a cardinal role in eliminating many diseases like polio, measles, and smallpox. Further, vaccines have controlled many diseases like cholera, dengue, diphtheria, Haemophilus influenza type b (Hib), human papillomavirus, influenza, Japanese encephalitis, etc. Recently, COVID-19 was controlled in many countries by vaccination. Currently, continuous effort is done to develop vaccines against nicotine, cocaine, morphine, methamphetamine, and heroin. Antibody therapy against SUDs is another important area where serious attention is required. Antibodies have contributed substantially against many serious diseases like diphtheria, rabies, Crohn's disease, asthma, rheumatoid arthritis, and bladder cancer. Antibody therapy is gaining immense momentum due to its success rate in cancer treatment. Furthermore, enormous advancement has been made in antibody therapy due to the generation of high-efficiency humanized antibodies with a long half-life. The advantage of antibody therapy is its instant outcome. This article's main highlight is discussing the drug targets of SUDs and their associated mechanisms. Importantly, we have also discussed the scope of prophylactic measures to eliminate drug dependence.

Where boundaries become bridges: Mosquito community composition, key vectors, and environmental associations

at forest edges in the central Brazilian Amazon.

Hendy A, Hernandez-Acosta E, Valério D, Fé NF, Mendonça CR, Costa ER, Andrade ES, Andes Júnior JT, Assunção FP, Scarpassa VM, Lacerda MVG, Buenemann M, Vasilakis N, Hanley KA.

26-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37099599/>

Molecular Characterization and Phylogenetic Analysis of Dengue Fever Viruses in Three Outbreaks in Tanzania Between 2017 and 2019.

Kelly ME, Msafiri F, Affara M, Gehre F, Moremi N, Mghamba J, Misinzio G, Thye T, Gatei W, Whistler T, Joachim A, Lema N, Santiago GA.

26-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37099594/>

Prevalence and Risk Factors of Acute Kidney Injury in Hospitalized Children with Dengue Infection Using Kidney Disease Improving Global Outcomes Criteria: Correspondence.

Sookaromdee P, Wiwanitkit V.

25-04-2022

Indian J Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/37097535/>

Screening for Zika Virus in U.S. Armed Services Blood Program Donors: An Opportunity to Compare Emerging Infectious Disease Risk between the General U.S. Population and Military Donors.

Fedyk CG, Shahin GM, Hill R, Cap AP; DoD Zika IND Investigators.

25-04-2022

Transfusion.

<https://pubmed.ncbi.nlm.nih.gov/37097201/>

Background: The U.S. Department of Defense (DoD) collects blood from volunteer DoD donors in U.S. Food and Drug Administration (FDA)-regulated centers, and from emergency donor panels in overseas operations. Emerging infectious diseases could reduce DoD access to blood products. In August 2016, FDA determined that Zika virus was transfusion-transmitted and advised that donated blood should be screened for Zika utilizing one of two investigational new drug (IND) applications. The Armed Services Blood Program (ASBP) tested blood using its own protocol concurrently with the IND study sponsored by Roche Molecular Systems, Inc., titled "A Prospective Study to Evaluate the Specificity of the cobas Zika test for use on the cobas 6800/8800 System for Screening of Blood Donations for the Presence of Zika virus RNA." **Study design and methods:** This prospective clinical trial (September 2016 to August 2017) evaluated the specificity of the cobas Zika 6800/8800 System. Consenting

volunteers were screened for Zika by participating reference labs. Participants with positive screens were offered a follow-up study using alternative PCR and serology assays. **Results:** 92,618 DoD donors enrolled; four tested positive on screening (0.0043%; CI 0.001176896%, 0.01105894%). Three enrolled in follow-up testing and none were positive. These results were comparable to all U.S. donors: 3,858,114 enrolled (excluding Puerto Rico) with 459 positive screens (0.0119%; I 0.01083582%, 0.01303962%). **Conclusion:** The study demonstrated the effectiveness of the cobas Zika test. DoD donors, who are included in emergency donor panels during military operations, were at no higher risk for Zika than the overall U.S. donor population. This article is protected by copyright. All rights reserved.

An Observational Study on Pattern of Empirical Acyclovir Therapy in Children With Acute Encephalitis From Northern India.

Adarsha N, Samprathi M, Sankhyan N, Singh MP, Bansal A, Jayashree M, Angurana SK, Nallasamy K.

25-04-2023

Pediatr Crit Care Med.

<https://pubmed.ncbi.nlm.nih.gov/37097038/>

Incidence, causes, and risk factors of stillbirth in an Amazonian context: Saint Laurent du Maroni maternity ward 2016-2021.

Mathieu M, Lambert V, Carles G, Picone O, Carod JF, Pomar L, Nacher M, Hcini N.

30-03-2023

Eur J Obstet Gynecol Reprod Biol X.

<https://pubmed.ncbi.nlm.nih.gov/37095766/>

Interval February 2023 Updates of the Advisory Committee on Immunization Practices.

Gaviria-Agudelo C, Yonts AB, Kimberlin DW, O'Leary ST, Paulsen G.

24-04-2023

J Pediatric Infect Dis Soc.

<https://pubmed.ncbi.nlm.nih.gov/37094832/>

The Advisory Committee on Immunization Practices (ACIP), a group of medical and public health experts that provides expert advice to the Centers for Disease Control and Prevention (CDC), normally meets three times per year to develop US vaccine recommendations. The ACIP met on 22-24 February 2023 to discuss mpox vaccine, influenza vaccines, pneumococcus vaccines, meningococci vaccines, polio vaccines, RSV vaccine, chikungunya vaccines, dengue vaccines, and COVID-19 vaccines.

Dengue and COVID-19 Co-circulation in the Peruvian Amazon: A Population-Based Study.

Pons MJ, Mayanga-Herrera A, Ulloa GM, Ymaña B, Medina S, Alava F, Álvarez-Antonio C, Meza-Sánchez G,

Calampa C, Casanova W, Carey C, Rodríguez-Ferrucci H, Morrison AC, Quispe AM.

24-04-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37094790/>

House Condition Scoring Scale as a Risk Indicator of Infestation by Aedes in Two Mexican Localities.

Monroy-Díaz ÁL, Ramos-Castañeda J, Amaya-Larios IY, Diaz-Quijano FA, Martínez-Vega RA.

24-04-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37094787/>

Mexico has shown an increase in dengue incidence rates. There are factors related to the location that determine housing infestation by Aedes. This study aimed to determine factors associated with housing infestation by immature forms of Aedes spp. in the dengue endemic localities of Axochiapan and Tepalcingo, Mexico, from 2014 to 2016. A cohort study was carried out. Surveys and inspections of front- and backyards were conducted every 6 months, looking for immature forms of Aedes spp. A house condition scoring scale was developed using three variables (house maintenance, tidiness of the front- and backyards, and shading of the front- and backyards). Multiple and multilevel regression logistic analysis were conducted considering the housing infestation as the outcome and the household characteristics observed 6 months before the outcome as factors; this was adjusted by time (seasonal and cyclical variations of the vector). The infestation oscillated between 5.8% of the houses in the second semester of 2015 and 29.3% in the second semester of 2016. The factors directly associated with housing infestation by Aedes were the house condition score (adjusted odds ratio [aOR]: 1.64; 95% CI: 1.40-1.91) and the previous record of housing infestation (aOR: 2.99; 95% CI: 2.00-4.48). Moreover, the breeding-site elimination done by house residents reduced the housing infestation odds by 81% (95% CI: 25-95%). These factors were independent of the seasonal and cyclical variations of the vector. In conclusion, our findings could help to focalize antivectorial interventions in dengue-endemic regions with similar demographic and socioeconomic characteristics.

Structure-Activity Relationships Reveal Beneficial Selectivity Profiles of Inhibitors Targeting Acetylcholinesterase of Disease-Transmitting Mosquitoes.

Vidal-Albalat A, Kindahl T, Rajeshwari R, Lindgren C, Forsgren N, Kitur S, Tengo LS, Ekström F, Kamau L, Linusson A.

24-04-2023

J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37094110/>

CSNK2B modulates IRF1 binding to functional DNA elements and promotes

basal and agonist-induced antiviral signaling.

Matsumoto M, Modliszewski JL, Shinozaki K, Maezawa R, Perez VM, Ishikawa Y, Suzuki R, McKnight KL, Masaki T, Hirai-Yuki A, Kohara M, Lemon SM, Selitsky SR, Yamane D.

24-04-2023

Nucleic Acids Res.

<https://pubmed.ncbi.nlm.nih.gov/37094077/>

Zika virus-induces metabolic alterations in fetal neuronal progenitors that could influence in neurodevelopment during early pregnancy.

Gilbert-Jaramillo J, Purnama U, Molnár Z, James WS.

15-04-2023

Biol Open.

<https://pubmed.ncbi.nlm.nih.gov/37093064/>

Cortical development consists of an orchestrated process in which progenitor cells exhibit distinct fate restrictions regulated by time-dependent activation of energetic pathways. Thus, the hijacking of cellular metabolism by Zika virus (ZIKV) to support its replication may contribute to damage in the developing fetal brain. Here, we showed that ZIKV replicates differently in two glycolytically distinct pools of cortical progenitors derived from human induced pluripotent stem cells (hiPSCs), which resemble the metabolic patterns of quiescence (early hi-NPCs) and immature brain cells (late hi-NPCs) in the forebrain. This differential replication alters the transcription of metabolic genes in both pools of cortical progenitors but solely upregulates the glycolytic capacity of early hi-NPCs. Analysis using Imagestream® revealed that, during early stages of ZIKV replication, in early hi-NPCs there is an increase in lipid droplet abundance and size. This stage of ZIKV replication significantly reduced the mitochondrial distribution in both early and late hi-NPCs. During later stages of ZIKV replication, late hi-NPCs show reduced mitochondrial size and abundance. The finding that there are alterations of cellular metabolism during ZIKV infection which are specific to pools of cortical progenitors at different stages of maturation may help to explain the differences in brain damage over each trimester.

Viral meningitis and encephalitis: an update.

Gundamraj V, Hasbun R.

01-06-2023

Curr Opin Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37093042/>

Virus Propagation and Cell-Based Colorimetric Quantification.

Tan JY, Wong JE, Zainal N, AbuBakar S, Tan KK.

07-04-2023

J Vis Exp.

<https://pubmed.ncbi.nlm.nih.gov/37092849/>

Effect of temperature on mosquito olfaction.

Lahondère C, Vinauger C, Liaw JE, Tobin KKS, Joiner JM, Riffell JA.

10-04-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37090630/>

Mosquitoes use a wide range of cues to find a host to feed on, eventually leading to the transmission of pathogens. Among them, olfactory cues (e.g., host emitted odors, including CO₂, and skin volatiles) play a central role in mediating host seeking behaviors. While mosquito olfaction can be impacted by many factors, such as the physiological state of the insect (e.g., age, reproductive state), the impact of environmental temperature on the olfactory system remains unknown. In this study, we quantified the behavioral responses of *Aedes aegypti* mosquitoes, vectors of dengue, yellow fever and Zika viruses, to host and plant related odors under different environmental temperatures.

Role of MXRA8 in Ross River Virus Disease Pathogenesis.

Ng WH, Ling ZL, Kueh AJ, Herold MJ, West NP, King NJC, Mahalingam S, Liu X.

25-04-2023

mBio.

<https://pubmed.ncbi.nlm.nih.gov/37036079/>

Arthritogenic alphaviruses such as Ross River virus (RRV) and Chikungunya virus (CHIKV) are responsible for large-scale epidemics that cause debilitating acute and chronic musculoskeletal diseases. MXRA8 was recently discovered as an entry receptor for multiple alphaviruses including CHIKV, RRV, Mayaro virus (MAYV), and O'nyong-nyong virus (ONNV). However, the role of MXRA8 in the development of alphavirus-induced musculoskeletal inflammation has not yet been fully studied. Here, we attempt to fully characterize the contribution of MXRA8 to RRV disease in an established mouse model. MXRA8 knockout (MXRA8^{-/-}) mice generated on a C57BL/6J background, showed abrogated disease signs and reduced viral replication, which correlated with lower viral load, diminished proinflammatory cytokines, and limited cell infiltrates in inflamed tissues. Immunomodulation genes were upregulated to higher levels in RRV-infected wild-type (WT) mice than in MXRA8^{-/-} mice. Intriguingly, *Cdkn1a* and *Ifi44* genes in blood and CD127/IL7RA, CD45, BatF3, IFNGR, Ly6G/Ly6C, CD40, CD127, F4/80, and MHC-II genes in quadriceps were found to be upregulated in RRV-infected MXRA8^{-/-} mice compared to WT mice. Our results showed an essential role of MXRA8 in the immune response of mice infected with RRV and, more importantly, demonstrated novel changes in immunomodulation genes, which shed light on the immunopathogenesis of alphavirus-induced disease. **IMPORTANCE** Previous studies have shown the importance of the cell surface protein MXRA8 as an entry receptor for several different prominent alphaviruses such as CHIKV, RRV, MAYV, and ONNV. In particular, the role of MXRA8 in the tissue tropism, viral pathogenesis, and immune response of a CHIKV mouse model have already been briefly characterized. However, the role of MXRA8 warrants further characterization in RRV disease background, since there are noticeable differences in the

disease profile between CHIKV and RRV. For example, patients infected with CHIKV are usually affected by sudden onset of severe arthritis and fever, whereas RRV-infected patients generally only have minor joint pain and mild fever. Here, we characterized the role of MXRA8 in RRV disease and assessed several key mechanisms of MXRA8 that may contribute to the disease progression.

WHO: Concerning Spread of Dengue, Chikungunya in Latin America.

Harris E.

25-04-2023

JAMA.

<https://pubmed.ncbi.nlm.nih.gov/37017997/>

Chromobacterium Biopesticide Exposure Does Not Select for Resistance in Aedes Mosquitoes.

Engdahl CS, Caragata EP, Tavadia M, Dimopoulos G.

25-04-2023

mBio.

<https://pubmed.ncbi.nlm.nih.gov/37017525/>

Developing effective tools to control mosquito populations is essential for reducing the incidence of diseases like malaria and dengue. Biopesticides of microbial origin are a rich, underexplored source of mosquitocidal compounds. We previously developed a biopesticide from the bacterium *Chromobacterium* sp. Panama that rapidly kills vector mosquito larvae, including *Aedes aegypti* and *Anopheles gambiae*. Here, we demonstrate that two independent *Ae. aegypti* colonies exposed to a sublethal dose of that biopesticide over consecutive generations persistently exhibited high mortality and developmental delays, indicating that resistance did not develop during the study period. Critically, the descendants of biopesticide-exposed mosquitoes experienced decreased longevity and did not display increased susceptibility to dengue virus or decreased susceptibility to common chemical insecticides. Through RNA sequencing, we observed no link between biopesticide exposure and the increased activity of xenobiotic metabolism and detoxification genes typically associated with insecticide resistance. These findings indicate that the *Chromobacterium* biopesticide is an exciting, emerging mosquito control tool. **IMPORTANCE** Vector control is an essential part of mitigating diseases caused by pathogens that mosquitoes spread. Modern vector control is highly reliant on using synthetic insecticides to eliminate mosquito populations before they can cause disease. However, many of these populations have become resistant to commonly used insecticides. There is a strong need to explore alternative vector control strategies that aim to mitigate disease burden. Biopesticides, insecticides of biological origin, can have unique mosquitocidal activities, meaning they can effectively kill mosquitoes that are already resistant to other insecticides. We previously developed a highly effective mosquito biopesticide from the bacterium *Chromobacterium* sp. Csp_P. Here, we investigate whether exposure to a sublethal dose of this Csp_P biopesticide over 9 to 10 generations causes resistance to

arise in *Aedes aegypti* mosquitoes. We find no evidence of resistance at the physiological or molecular levels, confirming that the Csp_P biopesticide is a highly promising new tool for controlling mosquito populations.

Zika virus replication on endothelial cells and invasion into the central nervous system by inhibiting interferon β translation.

Wang K, Zou S, Chen H, Higazy D, Gao X, Zhang Y, Cao S, Cui M.

Mai-2023

Virology.

<https://pubmed.ncbi.nlm.nih.gov/36996689/>

An untargeted metabolomics investigation in liver of flaviviruses-infected mice.

Zheng X, Wang R, Yin C.

Mai-2023

Virology.

<https://pubmed.ncbi.nlm.nih.gov/36989936/>

Strong Positive Selection in *Aedes aegypti* and the Rapid Evolution of Insecticide Resistance.

Love RR, Sikder JR, Vivero RJ, Matute DR, Schrider DR.

04-04-2023

Mol Biol Evol.

<https://pubmed.ncbi.nlm.nih.gov/36971242/>

Aedes aegypti vectors the pathogens that cause dengue, yellow fever, Zika virus, and chikungunya and is a serious threat to public health in tropical regions. Decades of work has illuminated many aspects of *Ae. aegypti*'s biology and global population structure and has identified insecticide resistance genes; however, the size and repetitive nature of the *Ae. aegypti* genome have limited our ability to detect positive selection in this mosquito. Combining new whole genome sequences from Colombia with publicly available data from Africa and the Americas, we identify multiple strong candidate selective sweeps in *Ae. aegypti*, many of which overlap genes linked to or implicated in insecticide resistance. We examine the voltage-gated sodium channel gene in three American cohorts and find evidence for successive selective sweeps in Colombia. The most recent sweep encompasses an intermediate-frequency haplotype containing four candidate insecticide resistance mutations that are in near-perfect linkage disequilibrium with one another in the Colombian sample. We hypothesize that this haplotype may continue to rapidly increase in frequency and perhaps spread geographically in the coming years. These results extend our knowledge of how insecticide resistance has evolved in this species and add to a growing body of evidence suggesting that *Ae. aegypti* has an extensive genomic capacity to rapidly adapt to insecticide-based vector control.

Prevalence and Risk Factors of Acute Kidney Injury in Hospitalized Children

with Dengue Infection Using Kidney Disease Improving Global Outcomes Criteria.

Mekangkul E, Siripen N, Rianthavorn P.

Mai-2023

Indian J Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/36943633/>

SOCS2 regulates alveolar bone loss in *Aggregatibacter actinomycetemcomitans*-induced periodontal disease.

Santos MRG, Chaves IM, Queiroz-Junior CM, Cramer AT, Anestino TA, Dos Santos ACPM, Leite PG, Macari S, Barrioni BR, Pereira MM, Teixeira MM, de Souza DDG, Madeira MFM, Machado FS.

Avr-2023

Inflamm Res.

<https://pubmed.ncbi.nlm.nih.gov/36912916/>

Introduction: The role of suppressor of cytokine signaling 2 (SOCS2) in *Aggregatibacter actinomycetemcomitans* (Aa)-induced alveolar bone loss is unknown; thus, it was investigated in this study. **Methods:** Alveolar bone loss was induced by infecting C57BL/6 wild-type (WT) and *Socs2*-knockout (*Socs2*^{-/-}) mice with Aa. Bone parameters, bone loss, bone cell counts, the expression of bone remodeling markers, and cytokine profile were evaluated by microtomography, histology, qPCR, and/or ELISA. Bone marrow cells (BMC) from WT and *Socs2*^{-/-} mice were differentiated in osteoblasts or osteoclasts for analysis of the expression of specific markers. **Results:** *Socs2*^{-/-} mice intrinsically exhibited irregular phenotypes in the maxillary bone and an increased number of osteoclasts. Upon Aa infection, SOCS2 deficiency resulted in the increased alveolar bone loss, despite decreased proinflammatory cytokine production, in comparison to the WT mice. In vitro, SOCS2 deficiency resulted in the increased osteoclasts formation, decreased expression of bone remodeling markers, and proinflammatory cytokines after Aa-LPS stimulus. **Conclusions:** Collectively, data suggest that SOCS2 is a regulator of Aa-induced alveolar bone loss by controlling the differentiation and activity of bone cells, and proinflammatory cytokines availability in the periodontal microenvironment and an important target for new therapeutic strategies. Thus, it can be helpful in preventing alveolar bone loss in periodontal inflammatory conditions.

Tackling chikungunya and dengue crisis in Paraguay amidst COVID-19: an epidemiological alert - a correspondence.

Sadiq SUR, Eneh SC, Nazir A, Mustapha MJ, Saleem F, Nazir A, Uwishema O.

01-03-2023

Int J Surg.

<https://pubmed.ncbi.nlm.nih.gov/36912892/>

Recent outbreak of zika virus in India amid ongoing COVID-19 and monkeypox outbreak: A call for action.

Sah R, Mohanty A, Paul D, Padhi BK.

01-03-2023

Int J Surg.

<https://pubmed.ncbi.nlm.nih.gov/36912540/>

Impact of regional climate change on the mosquito vector *Aedes albopictus* in a tropical island environment: La Réunion.

Lamy K, Tran A, Portafaix T, Leroux MD, Baldet T.

01-06-2023

Sci Total Environ.

<https://pubmed.ncbi.nlm.nih.gov/36889019/>

The recent expansion of *Aedes albopictus* across continents in both tropical and temperate regions and the exponential growth of dengue cases over the past 50 years represent a significant risk to human health. Although climate change is not the only factor responsible for the increase and spread of dengue cases worldwide, it might increase the risk of disease transmission at global and regional scale. Here we show that regional and local variations in climate can induce differential impacts on the abundance of *Ae. albopictus*. We use the instructive example of Réunion Island with its varied climatic and environmental conditions and benefiting from the availability of meteorological, climatic, entomological and epidemiological data. Temperature and precipitation data based on regional climate model simulations (3 km × 3 km) are used as inputs to a mosquito population model for three different climate emission scenarios. Our objective is to study the impact of climate change on the life cycle dynamics of *Ae. albopictus* in the 2070-2100 time horizon. Our results show the joint influence of temperature and precipitation on *Ae. albopictus* abundance as a function of elevation and geographical subregion. At low-elevations areas, decreasing precipitation is expected to have a negative impact on environmental carrying capacity and, consequently, on *Ae. albopictus* abundance. At mid- and high-elevations, decreasing precipitation is expected to be counterbalanced by a significant warming, leading to faster development rates at all life stages, and consequently increasing the abundance of this important dengue vector in 2070-2100.

IL-6 Levels in Prediction of Severity of Dengue Fever.

Vachher H, Metgud T, Srikanth B.

Mai-2023

Indian J Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/36848012/>

Evaluation of an Engineered Zika Virus-Like Particle Vaccine Candidate in a Mosquito-Mouse Transmission Model.

Mancini MV, Tandavanitj R, Ant TH, Murdochy SM, Gingell DD, Setthapramote C, Natsrita P, Kohl A, Sinkins SP, Patel AH, De Lorenzo G.

20-04-2023

mSphere.

<https://pubmed.ncbi.nlm.nih.gov/36840596/>

The primary route of Zika virus (ZIKV) transmission is through the bite of an infected *Aedes* mosquito, when it probes the skin of a vertebrate host during a blood meal. Viral particles are injected into the bite site together with mosquito saliva and a complex mixture of other components. Some of them are known to play a key role in the augmentation of the arbovirus infection in the host, with increased viremia and/or morbidity. This vector-derived contribution to the infection is not usually considered when vaccine candidates are tested in preclinical animal models. In this study, we performed a preclinical validation of a promising ZIKV vaccine candidate in a mosquito-mouse transmission model using both Asian and African ZIKV lineages. Mice were immunized with engineered ZIKV virus-like particles and subsequently infected through the bite of ZIKV-infected *Aedes aegypti* mosquitoes. Despite a mild increase in viremia in mosquito-infected mice compared to those infected through traditional needle injection, the vaccine protected the animals from developing the disease and strongly reduced viremia. In addition, during peak viremia, naive mosquitoes were allowed to feed on infected vaccinated and nonvaccinated mice. Our analysis of viral titers in mosquitoes showed that the vaccine was able to inhibit virus transmission from the host to the vector.

IMPORTANCE Zika is a mosquito-borne viral disease, causing acute debilitating symptoms and complications in infected individuals and irreversible neuronal abnormalities in newborn children. The primary vectors of ZIKV are *Aedes aegypti* mosquitoes. Despite representing a significant public health burden with a widespread transmission in many regions of the world, Zika remains a neglected disease with no effective antiviral therapies or approved vaccines. It is known that components of the mosquito bite lead to an enhancement of viral infection and spread, but this aspect is often overlooked when vaccine candidates undergo preclinical validation. In this study, we included mosquitoes as viral vectors, demonstrating the ability of a promising vaccine candidate to protect animals against ZIKV infections after the bite of an infected mosquito and to also prevent its further transmission. These findings represent an additional crucial step for the development of an effective prevention tool for clinical use.

The Incompetence of Mosquitoes-Can Zika Virus Be Adapted To Infect *Culex tarsalis* Cells?

Gallichotte EN, Samaras D, Murrieta RA, Sexton NR, Robison A, Young MC, Byas AD, Ebel GD, Rückert C.

20-04-2023

mSphere.

<https://pubmed.ncbi.nlm.nih.gov/36794947/>

Promising efforts to develop an mRNA vaccine against Zika.

Wilder-Smith A, Durbin A.

Mai-2023

Lancet Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36682366/>

The safety and immunogenicity of two Zika virus mRNA vaccine candidates in healthy flavivirus baseline seropositive and seronegative adults: the results of two randomised, placebo-controlled, dose-ranging, phase 1 clinical trials.

Essink B, Chu L, Seger W, Barranco E, Le Cam N, Bennett H, Faughnan V, Pajon R, Paila YD, Bollman B, Wang S, Dooley J, Kalidindi S, Leav B.

Mai-2023

Lancet Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36682364/>

Background: Developing a safe and immunogenic vaccine against Zika virus remains an unmet medical need. We did two phase 1 studies that evaluated the safety and immunogenicity of two mRNA-based Zika virus vaccines (mRNA-1325 and mRNA-1893) in adults. **Methods:** Two randomised, placebo-controlled, dose-ranging, multicentre, phase 1 trials, one of mRNA-1325 (mRNA-1325 trial) and one of mRNA-1893 (mRNA-1893 trial), were done. For both studies, eligible participants were healthy adults (aged 18-49 years) who were flavivirus seronegative or flavivirus seropositive at baseline. Participants in the mRNA-1325 trial, which was done at three centres in the USA, were randomly assigned centrally (1:4), using a randomisation table, to the placebo group or one of three mRNA-1325 dose groups (10, 25, or 100 µg). All participants received two doses. The mRNA-1325 vaccine encoded the premembrane and envelope E structural proteins (prME) from a Micronesia 2007 Zika virus isolate. Participants in the mRNA-1893 trial, which was done at three centres in the USA and one centre in Puerto Rico, were randomly assigned (1:4) to the placebo group or one of four mRNA-1893 dose groups (10, 30, 100, or 250 µg) using centralised interactive response technology. All participants in the mRNA-1893 trial received dose one on day 1 and then dose two on day 29. The mRNA-1893 vaccine encoded the prME from the RIO-U1 Zika virus isolate. Safety was the primary outcome of each study, which was evaluated in the respective safety populations (mRNA-1325 trial: participants who received at least one dose and provided safety data; mRNA-1893 trial: participants who received at least one dose) and the solicited safety population (mRNA-1893 trial only: received at least 1 dose and contributed solicited adverse reaction data). Endpoints in both trials included solicited adverse reactions within 7 days after vaccination and unsolicited adverse events within 28 days after vaccination. The secondary outcome of both trials was immunogenicity assessed by Zika virus-specific neutralising antibodies (nAbs) in the per-protocol populations in either trial (participants with no major protocol deviations received full dose[s] of assigned dose level within the acceptable time window, had samples drawn within acceptable time window, and had prevaccination and corresponding post-vaccination serum samples for testing). These were descriptive studies, with no formal hypothesis testing in either trial. Both trials are registered with ClinicalTrials.gov, NCT03014089 (mRNA-

1325 trial) and NCT04064905 (mRNA-1893 trial). **Findings:** The mRNA-1325 trial was done from Dec 14, 2016, to Aug 16, 2018. 90 participants were enrolled: 53 (59%) participants were women and 37 (41%) were men; 84 (93%) were White; and 74 (82%) were not Hispanic or Latino. All three dose levels of mRNA-1325 (10, 25, and 100 µg) were generally well tolerated, but the vaccine elicited poor Zika virus-specific nAb responses. At 28 days after dose two, geometric mean titres (GMTs) were highest for mRNA-1325 10 µg (10·3 [95% CI 5·9-18·2]). The mRNA-1893 trial was done from July 23, 2019, to March 22, 2021. 120 participants (70 [58%] women and 50 [42%] men) were enrolled, most participants were White (89 [74%]), and not Hispanic or Latino (91 [76%]). In the mRNA-1893 trial, solicited adverse reactions in participants who received a vaccine were mostly grade 1 or 2 and occurred more frequently at higher dose levels and after dose two. No participants withdrew due to an unsolicited treatment-emergent adverse event and most of these events were not treatment related. On day 57, all evaluated mRNA-1893 dose levels induced robust Zika virus-specific nAb responses, independent of flavivirus serostatus, that persisted until month 13. At day 57 in participants who were flavivirus seronegative, plaque reduction neutralisation titre test nAb GMTs were highest for mRNA-1893 100 µg (454·2 [330·0-619·6]); in participants who were flavivirus seropositive, GMTs were highest for mRNA-1893 10 µg (224·1 [43·5-1153·5]) and mRNA-1893 100 µg (190·5 [19·2-1887·2]). **Interpretation:** These findings support the continued development of mRNA-1893 against Zika virus, which was well tolerated at all evaluated dose levels and induced strong Zika virus-specific serum nAb responses after two doses, regardless of baseline flavivirus serostatus.

"Glass Eel" Sign in Chikungunya Myelopathy.

Nobrega PR, Junior PH, Galdino GS, Dias DA, Castro JDV.
25-04-2023
Neurology.
<https://pubmed.ncbi.nlm.nih.gov/36549908/>

Single B cell transcriptomics identifies multiple isotypes of broadly neutralizing antibodies against flaviviruses.

Lubow J, Levoir LM, Ralph DK, Belmont L, Contreras M, Cartwright-Acar CH, Kikawa C, Kannan S, Davidson E, Doranz BJ, Duran V, Sanchez DE, Sanz AM, Rosso F, Einav S, Matsen FA, Goo L.
10-04-2023
bioRxiv.
<https://pubmed.ncbi.nlm.nih.gov/37090561/>

Oligodendrocyte-derived IL-33 functions as a microglial survival factor during neuroinvasive flavivirus infection.

Norris GT, Ames JM, Ziegler SF, Oberst A.
12-04-2023
bioRxiv.
<https://pubmed.ncbi.nlm.nih.gov/37090518/>

In order to recover from infection, organisms must balance robust immune responses to pathogens with the tolerance of immune-mediated pathology. This balance is particularly critical within the central nervous system, whose complex architecture, essential function, and limited capacity for self-renewal render it susceptible to both pathogen-and immune-mediated pathology. Here, we identify the alarmin IL-33 and its receptor ST2 as critical for host survival to neuroinvasive flavivirus infection. We identify oligodendrocytes as the critical source of IL-33, and microglia as the key cellular responders. Notably, we find that the IL-33/ST2 axis does not impact viral control or adaptive immune responses; rather, it is required to promote the activation and survival of microglia. In the absence of intact IL-33/ST2 signaling in the brain, neuroinvasive flavivirus infection triggered aberrant recruitment of monocyte-derived peripheral immune cells, increased neuronal stress, and neuronal cell death, effects that compromised organismal survival. These findings identify IL-33 as a critical mediator of CNS tolerance to pathogen-initiated immunity and inflammation. **Author summary:** The central nervous system (CNS) is an extraordinarily complex organ system with limited capacity for repair and renewal. When infectious pathogens invade the CNS, resulting immune responses must clear the pathogen while limiting immune-mediated tissue pathology. IL-33 is an "alarmin" cytokine, whose release from dying cells can promote a variety of immune responses. IL-33 is expressed at high levels in the brain, and previous work has implicated signaling by IL-33 in CNS development as well as in the response to parasitic infection of the CNS. Here, we identify IL-33 as a key mediator of disease tolerance in the context of neuroinvasive infection with the flaviviruses West Nile virus and Zika virus. Notably, we find that IL-33 signaling is not involved in the clearance of virus from the brain; rather, IL-33 is required to promote the survival and reprogramming brain-resident immune cells (microglia). When IL-33 signaling is disrupted in mice, flavivirus infection results in defective microglial activation, increased death of both microglia and neurons, increased invasion of the brain by peripheral immune cells, and increased host death. This work suggests that IL-33 is a key mediator of host tolerance upon neuroinvasive flavivirus infection.

Dengue Hemorrhagic Encephalitis in Dengue Epidemic.

Singh PK, Sheoran A, Tatarwal P, Singh P, Singh P.
15-11-2022
J Glob Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/37090143/>

Effects of public health emergencies of international concern on disease control: a systematic review.

de Araújo GR, de Castro PASV, Ávila IR, Bezerra JMT, Barbosa DS.
21-04-2023
Rev Panam Salud Publica.
<https://pubmed.ncbi.nlm.nih.gov/37089787/>

Identification of novel Zika virus NS3 protease inhibitors with different inhibition modes by integrative experimental and computational approaches.

Andrade MA, Mottin M, Sousa BKP, Barbosa JARG, Dos Santos Azevedo C, Lasse Silva C, Gonçalves de Andrade M, Motta FN, Maulay-Bailly C, Amand S, Santana JM, Horta Andrade C, Grellier P, M D Bastos I.

21-04-2023

Biochimie.

<https://pubmed.ncbi.nlm.nih.gov/37088408/>

Zika virus (ZIKV) infection is associated with severe neurological disorders and congenital malformation. Despite efforts to eradicate the disease, there is still neither vaccine nor approved drugs to treat ZIKV infection. The NS2B-NS3 protease is a validated drug target since it is essential to polyprotein virus maturation. In the present study, we describe an experimental screening of 2,320 compounds from the chemical library of the Muséum National d'Histoire Naturelle of Paris on ZIKV NS2B-NS3 protease. A total of 96 hits were identified with 90% or more of inhibitory activity at 10 μ M. Amongst the most active compounds, five were analyzed for their inhibitory mechanisms by kinetics assays and computational approaches such as molecular docking. 2-(3-methoxyphenoxy) benzoic acid (compound 945) show characteristics of a competitive inhibition (K_i = 0.49 μ M) that was corroborated by its molecular docking at the active site of the NS2B-NS3 protease. Taxifolin (compound 2292) behaves as an allosteric inhibitor whereas 3,8,9-trihydroxy-2-methyl-1H-phenalen-1-one (compound 128), harmol (compound 368) and anthrapurpurin (compound 1499) show uncompetitive inhibitions. These new NS2B-NS3 protease inhibitors are valuable hits to further hit-to-lead optimization.

Phylogeographic analysis of dengue virus serotype 1 and Cosmopolitan serotype 2 in Africa.

Philippe S, Sebastian L, Gytis D, Sam P, Pascal L, Freddy K, Kadrie R, Isabel M, Steve AM, Veerle V, Marjan VE, Kevin AK.

21-04-2023

Int J Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37088357/>

Background: The origin and spread of dengue virus (DENV) circulating in Africa remain poorly characterized, with African sequences representing <1% of global sequence data. **Methods:** Whole genome sequencing was performed on serum samples (n=29) from an undifferentiated fever study in 2016 in the Democratic Republic of Congo (DRC), and from febrile travelers returning from Africa. The evolutionary history of the newly acquired African DENV-1 (n=1) and Cosmopolitan genotype DENV-2 (n=18) genomes, was reconstructed using a phylogeographic, time-scaled Bayesian analysis on a curated DENV panel including all known African sequences. **Results:** A minimum of 10 and 8 introductions could be identified into Africa for respectively DENV-1 and Cosmopolitan DENV-2, almost all originating from Asia. Three

introductions were previously unknown. The currently circulating virus comprises mainly recently introduced clades and one long-established, African clade. Robust geographical clustering suggests limited spread of DENV after each introduction. Our data identified the DRC as the source of the 2018 Angolan DENV-2 epidemic, and similarly, the 2013 Angolan DENV-1 outbreak as the origin of our DRC study. **Conclusion:** Active genomic surveillance of DENV in Africa at the portals of entry might help early outbreak response, and limit sero- and genotype spread and human disease burden.

Discovery of ZFD-10 of a pyridazino[4,5-b]indol-4(5H)-one derivative as an anti-ZIKV agent and a ZIKV NS5 RdRp inhibitor.

Zhou GF, Qian W, Li F, Yang RH, Wang N, Zheng CB, Li CY, Gu XR, Yang LM, Liu J, Xiong SD, Zhou GC, Zheng YT.

21-04-2023

Antiviral Res.

<https://pubmed.ncbi.nlm.nih.gov/37088168/>

Effects of high temperatures and heatwaves on dengue fever: a systematic review and meta-analysis.

Damtew YT, Tong M, Varghese BM, Anikeeva O, Hansen A, Dear K, Zhang Y, Morgan G, Driscoll T, Capon T, Bi P.

21-04-2023

EBioMedicine.

<https://pubmed.ncbi.nlm.nih.gov/37088034/>

The patterns and driving forces of dengue invasions in China.

Zhao Z, Yue Y, Liu X, Li C, Ma W, Liu Q.

21-04-2023

Infect Dis Poverty.

<https://pubmed.ncbi.nlm.nih.gov/37085941/>

Background: Global connectivity and environmental change pose continuous threats to dengue invasions from worldwide to China. However, the intrinsic relationship on introduction and outbreak risks of dengue driven by the landscape features are still unknown. This study aimed to map the patterns on source-sink relation of dengue cases and assess the driving forces for dengue invasions in China. **Methods:** We identified the local and imported cases (2006-2020) and assembled the datasets on environmental conditions. The vector auto-regression model was applied to detect the cross-relations of source-sink patterns. We selected the major environmental drivers via the Boruta algorithm to assess the driving forces in dengue outbreak dynamics by applying generalized additive models. We reconstructed the internal connections among imported cases, local cases, and external environmental drivers using the structural equation modeling. **Results:** From 2006 to 2020, 81,652 local dengue cases and 12,701 imported dengue cases in China were reported. The hotspots of dengue introductions and outbreaks were in southeast and southwest China, originating from South and Southeast Asia. Oversea-imported dengue cases, as the Granger-cause, were the initial driver of the dengue dynamic; the

suitable local bio-socioecological environment is the fundamental factor for dengue epidemics. The Bio8 [odds ratio (OR) = 2.11, 95% confidence interval (CI): 1.67-2.68], Bio9 (OR = 291.62, 95% CI: 125.63-676.89), Bio15 (OR = 4.15, 95% CI: 3.30-5.24), normalized difference vegetation index in March (OR = 1.27, 95% CI: 1.06-1.51) and July (OR = 1.04, 95% CI: 1.00-1.07), and the imported cases are the major drivers of dengue local transmissions (OR = 4.79, 95% CI: 4.34-5.28). The intermediary effect of an index on population and economic development to local cases via the path of imported cases was detected in the dengue dynamic system. **Conclusions:** Dengue outbreaks in China are triggered by introductions of imported cases and boosted by landscape features and connectivity. Our research will contribute to developing nature-based solutions for dengue surveillance, mitigation, and control from a socio-ecological perspective based on invasion ecology theories to control and prevent future dengue invasion and localization.

Conjugates of ibuprofen inhibit CHIKV infection and inflammation.

Dash RN, Prabhudutta M, De S, Swain RP, Moharana AK, Subudhi BB, Chattopadhyay S.

21-04-2023

Mol Divers.

<https://pubmed.ncbi.nlm.nih.gov/37085737/>

Species-specific MARCO-alphavirus interactions dictate chikungunya virus viremia.

Li FS, Carpentier KS, Hawman DW, Lucas CJ, Ander SE, Feldmann H, Morrison TE.

20-04-2023

Cell Rep.

<https://pubmed.ncbi.nlm.nih.gov/37083332/>

Arboviruses are public health threats that cause explosive outbreaks. Major determinants of arbovirus transmission, geographic spread, and pathogenesis are the magnitude and duration of viremia in vertebrate hosts. Previously, we determined that multiple alphaviruses are cleared efficiently from murine circulation by the scavenger receptor MARCO (Macrophage receptor with collagenous structure). Here, we define biochemical features on chikungunya (CHIKV), o'nyong 'nyong (ONNV), and Ross River (RRV) viruses required for MARCO-dependent clearance in vivo. In vitro, MARCO expression promotes binding and internalization of CHIKV, ONNV, and RRV via the scavenger receptor cysteine-rich (SRCR) domain. Furthermore, we observe species-specific effects of the MARCO SRCR domain on CHIKV internalization, where those from known amplification hosts fail to promote CHIKV internalization. Consistent with this observation, CHIKV is inefficiently cleared from the circulation of rhesus macaques in contrast with mice. These findings suggest a role for MARCO in determining whether a vertebrate serves as an amplification or dead-end host following CHIKV infection.

Effect of remdesivir post-exposure prophylaxis and treatment on pathogenesis of measles in rhesus macaques.

Peart Akindele NA, Katamoni LD, Brockhurst J, Ghimire S, Suwanmanee S, Pieterse L, Metcalf Pate KA, Bunyan E, Bannister R, Cihlar T, Porter DP, Griffin DE.

20-04-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37081035/>

Measles is a systemic disease initiated in the respiratory tract with widespread measles virus (MeV) infection of lymphoid tissue. Mortality can be substantial, but no licensed antiviral therapy is available. We evaluated both post-exposure prophylaxis and treatment with remdesivir, a broad-spectrum antiviral, using a well-characterized rhesus macaque model of measles. Animals were treated with intravenous remdesivir for 12 days beginning either 3 days after intratracheal infection (post-exposure prophylaxis, PEP) or 11 days after infection at the onset of disease (late treatment, LT). As PEP, remdesivir lowered levels of viral RNA in peripheral blood mononuclear cells, but RNA rebounded at the end of the treatment period and infectious virus was continuously recoverable. MeV RNA was cleared more rapidly from lymphoid tissue, was variably detected in the respiratory tract, and not detected in urine. PEP did not improve clinical disease nor lymphopenia and reduced the antibody response to infection. In contrast, LT had little effect on levels of viral RNA or the antibody response but also did not decrease clinical disease. Therefore, remdesivir transiently suppressed expression of viral RNA and limited dissemination when provided as PEP, but virus was not cleared and resumed replication without improvement in the clinical disease parameters evaluated.

Discovery and structural characterization of monkeypox virus methyltransferase VP39 inhibitors reveal similarities to SARS-CoV-2 nsp14 methyltransferase.

Silhan J, Klima M, Otava T, Skvara P, Chalupska D, Chalupsky K, Kozic J, Nencka R, Boura E.

20-04-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37080993/>

Phylogenetic Analysis of Transmission Dynamics of Dengue in Large and Small Population Centers, Northern Ecuador.

Márquez S, Lee G, Gutiérrez B, Bennett S, Coloma J, Eisenberg JNS, Trueba G.

Mai-2023

Emerg Infect Dis.

Although dengue is typically considered an urban disease, rural communities are also at high risk. To clarify dynamics of dengue virus (DENV) transmission in settings with characteristics generally considered rural (e.g., lower population density, remoteness), we conducted a phylogenetic analysis in 6 communities in northwestern

Ecuador. DENV RNA was detected by PCR in 121/488 serum samples collected from febrile case-patients during 2019-2021. Phylogenetic analysis of 27 samples from Ecuador and other countries in South America confirmed that DENV-1 circulated during May 2019-March 2020 and DENV-2 circulated during December 2020-July 2021. Combining locality and isolation dates, we found strong evidence that DENV entered Ecuador through the northern province of Esmeraldas. Phylogenetic patterns suggest that, within this province, communities with larger populations and commercial centers were more often the source of DENV but that smaller, remote communities also play a role in regional transmission dynamics.

Deforestation impacts on dengue incidence in the Brazilian Amazon.

da Silva CFA, Dos Santos AM, do Bonfim CV, da Silva Melo JL, Sato SS, Barreto EP.

20-04-2023

Environ Monit Assess.

<https://pubmed.ncbi.nlm.nih.gov/37079116/>

Massive mosquito factory in Brazil aims to halt dengue.

Lenharo M.

Avr-2023

Nature.

<https://pubmed.ncbi.nlm.nih.gov/37059855/>

The relative importance of key meteorological factors affecting numbers of mosquito vectors of dengue fever.

Liu Y, Wang X, Tang S, Cheke RA.

13-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37053307/>

Dengue and chikungunya virus loads in the mosquito *Aedes aegypti* are determined by distinct genetic architectures.

Novelo M, Dutra HL, Metz HC, Jones MJ, Sigle LT, Frentiu FD, Allen SL, Chenoweth SF, McGraw EA.

12-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37043515/>

Aedes aegypti is the primary vector of the arboviruses dengue (DENV) and chikungunya (CHIKV). These viruses exhibit key differences in their vector interactions, the latter moving more quickly through the mosquito and triggering fewer standard antiviral pathways. As the global footprint of CHIKV continues to expand, we seek to better understand the mosquito's natural response to CHIKV- both to compare it to DENV:vector coevolutionary history and to identify potential targets in the mosquito for genetic modification. We used a modified full-sibling design to estimate the contribution of mosquito genetic variation to viral loads of both DENV and CHIKV. Heritabilities were significant, but higher for DENV (40%)

than CHIKV (18%). Interestingly, there was no genetic correlation between DENV and CHIKV loads between siblings. These data suggest *Ae. aegypti* mosquitoes respond to the two viruses using distinct genetic mechanisms. We also examined genome-wide patterns of gene expression between High and Low CHIKV families representing the phenotypic extremes of viral load. Using RNAseq, we identified only two loci that consistently differentiated High and Low families: a long non-coding RNA that has been identified in mosquito screens post-infection and a distant member of a family of Salivary Gland Specific (SGS) genes. Interestingly, the latter gene is also associated with horizontal gene transfer between mosquitoes and the endosymbiotic bacterium *Wolbachia*. This work is the first to link the SGS gene to a mosquito phenotype. Understanding the molecular details of how this gene contributes to viral control in mosquitoes may, therefore, also shed light on its role in *Wolbachia*.

Chimeric flavivirus causes vascular leakage and bone marrow suppression in a mouse model.

Kurosu T, Hanabara K, Asai A, Pambudi S, Phanthanawiboon S, Omokoko MD, Sakai Y, Suzuki T, Ikuta K.

04-06-2023

Biochem Biophys Res Commun.

<https://pubmed.ncbi.nlm.nih.gov/37037066/>

Previously, we demonstrated the utility of a recombinant chimeric flavivirus (DV2ChimV), which carries the premembrane (prM) and envelope (E) genes of a type 2 DENV clinical (Thai) isolate on a backbone of Japanese encephalitis virus, for evaluating the protective efficacy of antidengue envelope antibodies both in vitro and in vivo. Here, to assess the potential use of this model for pathological studies, we aimed to characterize interferon- $\alpha/\beta/\gamma$ -receptor double-knockout mice (IFN- $\alpha/\beta/\gamma$ R dKO mice) infected with DV2ChimV. Vascular leakage and bone marrow suppression are unique features of severe dengue. In the current model, DV2ChimV caused vascular leakage in the liver and intestine at the moribund stage. High levels of virus were detected in the bone marrow, and strong bone marrow suppression (i.e., disappearance of megakaryocytes and erythroblastic islets) was observed. These observations suggest that the DV2ChimV-infected mouse model mimics the vascular leakage and bone marrow suppression observed in human cases.

Dracunculose

Studies of the Tarragon Essential Oil Effects on the Characteristics of Doped Hydroxyapatite/Chitosan Biocomposites.

Predoi D, Iconaru SL, Ciobanu CS, Raita MS, Ghegoiu L, Trusca R, Badea ML, Cimpeanu C.

16-04-2023

Polymers (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112055/>

Due to the emergence of antibiotic-resistant pathogens, the need to find new, efficient antimicrobial agents is rapidly increasing. Therefore, in this study, we report the development of new biocomposites based on zinc-doped hydroxyapatite/chitosan enriched with essential oil of *Artemisia dracunculus* L. with good antimicrobial activity. Techniques such as scanning electron microscopy (SEM), X-ray diffraction (XRD), energy dispersive X-ray spectroscopy (EDX) and Fourier transform infrared spectroscopy (FTIR) were used in order to evaluate their physico-chemical properties. Our studies revealed that biocomposite materials with nanometric dimension and homogeneous composition could be obtained through an economic and cost-effective synthesis method. The biological assays demonstrated that ZnHA (zinc-doped hydroxyapatite), ZnHACH (zinc-doped hydroxyapatite/chitosan) and ZnHACHT (zinc-doped hydroxyapatite/chitosan enriched with essential oil of *Artemisia dracunculus* L.) did not exhibit a toxic effect on the cell viability and proliferation of the primary osteoblast culture (hFOB 1.19). Moreover, the cytotoxic assay also highlighted that the cell morphology of the hFOB 1.19 was not altered in the presence of ZnHA, ZnHACH or ZnHACHT. Furthermore, the in vitro antimicrobial studies emphasized that the samples exhibited strong antimicrobial properties against *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923 and *Candida albicans* ATCC 10231 microbial strains. These results are encouraging for the following development of new composite materials with enhanced biological properties that could promote the osteogenic process of bone healing and also exhibit good antimicrobial properties.

Does *A. Velamen Radicum* Effectively Protect Epiphyte Roots against Excessive Infrared Radiation?

Rodríguez Quiel C, Einzmann HJR, Zotz G.

18-04-2023

Plants (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37111916/>

Empirical and Mechanistic Modeling of Release Kinetics of Heavy Metals and Their Chemical Distribution in the Rhizosphere and Non-rhizosphere Soils Under Vegetable Cultivation.

Fakhri R, Jalali M, Ranjbar F.

21-04-2023

Arch Environ Contam Toxicol.

<https://pubmed.ncbi.nlm.nih.gov/37084006/>

Optimization of starch extraction from *Amorphophallus paeoniifolius* corms using response surface methodology (RSM) and artificial neural network (ANN) for improving yield with tenable chemical attributes.

Karmakar B, Saha SP, Chakraborty R, Roy S.

15-05-2023

Int J Biol Macromol.

<https://pubmed.ncbi.nlm.nih.gov/36972818/>

The development of the extraction process for improving the starch yield from unconventional plants is emerging as a topic of interest. In this respect, the present work aimed to optimize the starch extraction from the corms of elephant foot yam (*Amorphophallus paeoniifolius*) with the help of response surface methodology (RSM) and artificial neural network (ANN). The RSM model performed better than the ANN in predicting the starch yield with higher precision. In this connection, this study for the first time reports the significant improvement of starch yield from *A. paeoniifolius* (51.76 g/100 g of the corm dry weight). The extracted starch samples based on yield - high (APHS), medium (APMS), and low (APLS) exhibited a variable granule size (7.17-14.14 μ m) along with low ash content, moisture content, protein, and free amino acid indicating purity and desirability. The FTIR analysis also confirmed the chemical composition and purity of the starch samples. Moreover, the XRD analysis showed the prevalence of C-type starch ($2\theta = 14.303^\circ$). Based on other physicochemical, biochemical, functional, and pasting properties, the three starch samples showed more or less similar characteristics thereby indicating the sustenance of beneficial attributes of starch molecules irrespective of the variation in extraction parameters.

Comparative study on the effect of inhibitory methods on the color and gelation properties of alkali induced heat-set konjac gel from *Amorphophallus bulbifer*.

Zhang M, Chang C, Li J, Sun Y, Cai Y, Gu L, Xiong W, Yang Y, Su Y.

15-05-2023

Int J Biol Macromol.

<https://pubmed.ncbi.nlm.nih.gov/36907300/>

As a newly superior konjac variety, the *Amorphophallus bulbifer* (*A. bulbifer*) was easily browning during the alkali-induced process. In this study, five different inhibitory methods, such as citric-acid heat pretreatment (CAT), mixed with citric acid (CA), mixed with ascorbic acid (AA), mixed with L-cysteine (CYS), and mixed with potato starch (PS, containing TiO_2), were separately used to inhibit the browning of alkali-induced heat-set *A. bulbifer* gel (ABG). The color and gelation properties were then investigated and compared. Results showed that the inhibitory methods had significant influences on the appearance, color, physicochemical properties, rheological properties, and microstructures of ABG. Among them, the CAT method not only significantly inhibited the browning of ABG (ΔE value dropped from 25.74 to 14.68) but also improved the water-holding capacity, moisture distribution, and thermal stability without damaging the textural properties of ABG. Moreover, SEM revealed that both CAT and adding PS methods could exhibit the more dense gel network structures of ABG than other methods. It was reasonable to conclude that ABG-CAT offered a superior method to prevent browning compared to the other methods based on the texture, microstructure, color, appearance, and thermal stability of the product.

Chemical Characterization and Multidirectional Biological Effects of Different Solvent Extracts of *Arum elongatum*: in Vitro and in Silico Approaches.

Fawzi Mahomoodally M, Zengin G, Roumita SS, Caprioli G, Mustafa AM, Piatti D, Yildiztugay E, Ak G, Esra Karadağ A, Khalid A, Abdalla AN, Ibrahim Uba A, Demirci F.

Avr-2023

Chem Biodivers.

<https://pubmed.ncbi.nlm.nih.gov/36891864/>

Integrated analysis of metabolome and transcriptome reveals key candidate genes involved in flavonoid biosynthesis in *Pinellia ternata* under heat stress.

Guo L, Tan J, Deng X, Mo R, Pan Y, Cao Y, Chen D.

Mai-2023

J Plant Res.

<https://pubmed.ncbi.nlm.nih.gov/36881276/>

Echinococcosis

Acute abdomen due to rupture of a hydatid cyst of the liver: a rare complication - a case report.

Adhikari S, Bhattarai M, Gyawali S, Subedi S, Bhattarai A, Awale L, Kansakar PBS.

27-03-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37113932/>

Hydatid cyst is a parasitic disease that is transmitted from animals to humans caused by the larval stage *Echinococcus*, especially *Echinococcus granulosus*. A complication of a hydatid cyst of the liver is its rupture, either traumatic or spontaneously. **Case presentation:** A 19-year-old male presented with an acute abdomen for 12 h. After clinical assessment, contrast-enhanced computed tomography showed a rupture of the anterior wall of the hepatic hydatid cyst with intra-abdominal and pelvic dissemination. Exploratory laparotomy was performed with the evacuation of the daughter cyst and peritoneal lavage. The patient recovered well and was discharged with albendazole therapy. **Clinical discussion:** Hydatid cyst rupture is a rare but serious complication. Computed tomography has high sensitivity in demonstrating cyst rupture. The patient underwent laparotomy, where disseminated cysts were evacuated, and the anterior wall of the cyst was deroofed, along with the removal of a ruptured laminated membrane. Emergency surgery plus albendazole therapy are recommended protocols for cases like ours. **Conclusions:** A patient from an endemic region with acute presentation of right upper quadrant pain can have spontaneously ruptured hydatidosis as a differential diagnosis. Intraperitoneal rupture and dissemination of hydatid cysts of the liver can be life-

threatening if intervention is delayed. Immediate surgery is life-saving and prevents complications.

Retrovesical hydatid cyst: an unusual location of hydatid disease about a case series.

Hermi A, Saadi A, Mokadem S, Boussaffa H, Zaghib S, Haroun A, Bouzouita A, Derouiche A, Chakroun M, Ben Slama MR.

27-03-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37113869/>

A rare location of cardio hydatid cyst with multiple organ involvement: a case report.

Ahmad Y, Maree G, Omar S, Alkhalaf H.

12-04-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37113847/>

Cardiac cysts in hydatid cysts, a parasitic disease, are extremely rare, and left-atrial hydatid cysts are even more unusual. Therefore, the authors report herein a rare case of a hydatid cyst in the left atrium. According to them, this is the third documented case of left-atrial hydatid cysts.

Presentation of case: A 25-year-old male presented at the outpatient clinic with atypical chest pain, hacking cough, dyspnoea, nausea, and vomiting for 2 months. Echocardiography showed a left-atrial unilocular, well-delineated mass. The authors also found multiple liver cysts and spleen cysts. **Discussion:** The widespread distribution of the disease in our regions, the dog contact story of the patient, and the appearance on echocardiograms were strong reasons to diagnose a hydatid cyst in the left atrium, which may cause many symptoms (bundle branch conduction, arrhythmias, myocardial infarction) or unexpected death. **Conclusions:** The authors aimed to report this case due to the disease's high probability of death, even asymptomatic patients with cardiac hydatid disease should all be referred for early surgery.

Seroprevalence of Anti-*Echinococcus granulosus* Antibodies and Risk Factors for Infection in Blood Donors from Western Romania.

Paduraru AA, Lupu MA, Lighezan R, Pavel R, Cretu OM, Olariu TR.

24-03-2023

Life (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37109399/>

Cystic echinococcosis is a worldwide-distributed zoonotic parasitic disease. This cross-sectional study aimed to assess the seroprevalence and risk factors potentially associated with *Echinococcus granulosus* in healthy blood donors from Timis County, an endemic region in Western Romania. Serum samples were collected from 1347 Romanian blood donors. Serologic tests to determine the presence of anti-*Echinococcus* antibodies were performed using an anti-*Echinococcus*-ELISA immunoassay. Anti-

Echinococcus antibodies were detected in 38 blood donors, indicating an overall seroprevalence of 2.8%. The seropositivity rate was 3.7% in females and 3.1% in blood donors residing in urban areas. The highest seropositivity was found in the age group of 31-40 years (3.6%). There were no significant differences between *Echinococcus* seropositivity and gender, area of residence, age, contact with dogs, or raising sheep. This serologic survey evaluated for the first time the presence of *Echinococcus* antibodies in healthy blood donors from Western Romania and the potential risk factors associated with echinococcosis. Our results suggest that this zoonotic infection might evolve asymptotically in apparently healthy individuals. Further studies should be conducted in the general population to estimate the true extent of human echinococcosis and its risk factors.

Giant hydatid cyst of the brain: Intact cyst removal in 8-year-old child.

Ghasemi AA, Mohammadzade H, Mohammadi R.

11-04-2023

Int J Surg Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37086506/>

Alveolar echinococcosis in immunocompromised hosts.

Autier B, Gottstein B, Millon L, Ramharter M, Gruener B, Bresson-Hadni S, Dion S, Robert-Gangneux F.

Mai-2023

Clin Microbiol Infect.

<https://pubmed.ncbi.nlm.nih.gov/36528295/>

[Spread and Development of Alveolar Echinococcosis in Germany, 1992-2018].

Kwiedor I, Kratzer W, Schlingeloff P, Schmidberger J.

Avr-2023

Gesundheitswesen.

<https://pubmed.ncbi.nlm.nih.gov/34872118/>

Goal of the study: Alveolar echinococcosis (AE) is a rare parasitosis caused by the pathogen *Echinococcus multilocularis*. There is an increase in the number of cases in many countries. The aim of the study was to investigate the current prevalence and the change in the geographical distribution pattern. **Methodology:** Data were collected retrospectively for the period 1992-2018 using the registered cases in the national disease register for AE in Germany. Statistical analysis was performed using the SAS statistical analysis system version 9.4 (SAS Institute, Cary, N.C., USA). **Results:** The study population of n=569 patients included n=322 (56,59%) women and n=247 (43,40%) men. The mean average age of patients with alveolar echinococcosis at first presentation was 53,90±17,54 years (median: 56,00 years). The Moran's I test statistic showed a positive spatial autocorrelation for the period 1992-2018 corresponding to a heterogeneous distribution of disease cases in Germany (I=0,4165; Z=10,9591, p=0,001). An increase in age- and sex-specific prevalence could be determined for the entire study period (1992-2018). The overall prevalence in the period 1992-2018 was 0,71 cases per 100,000 population. The determination of the prevalence for the period 1992-2018 resulted in 0,31

cases for men and 0,40 cases for women per 100,000 population. In the period 1992-1996, no AE cases had been registered in 11/16 (68,8%) federal states (Berlin, Brandenburg, Bremen, Hamburg, Mecklenburg-Vorpommern, Rheinland-Pfalz, Saarland, Sachsen, Sachsen-Anhalt, Schleswig-Holstein und Thüringen). The evaluation recently shows an increased occurrence of cases in the federal states of Hessen, Rheinland-Pfalz and Nordrhein-Westfalen.

Filariose lymphatique

Assessing Geographic Overlap between Zero-Dose Diphtheria-Tetanus-Pertussis Vaccination Prevalence and Other Health Indicators.

Haeuser E, Nguyen JQ, Rolfe S, Nesbit O, Fullman N, Mosser JF.

05-04-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112714/>

The integration of immunization with other essential health services is among the strategic priorities of the Immunization Agenda 2030 and has the potential to improve the effectiveness, efficiency, and equity of health service delivery. This study aims to evaluate the degree of spatial overlap between the prevalence of children who have never received a dose of the diphtheria-tetanus-pertussis-containing vaccine (no-DTP) and other health-related indicators, to provide insight into the potential for joint geographic targeting of integrated service delivery efforts. Using geospatially modeled estimates of vaccine coverage and comparator indicators, we develop a framework to delineate and compare areas of high overlap across indicators, both within and between countries, and based upon both counts and prevalence. We derive summary metrics of spatial overlap to facilitate comparison between countries and indicators and over time. As an example, we apply this suite of analyses to five countries-Nigeria, Democratic Republic of the Congo (DRC), Indonesia, Ethiopia, and Angola-and five comparator indicators-children with stunting, under-5 mortality, children missing doses of oral rehydration therapy, prevalence of lymphatic filariasis, and insecticide-treated bed net coverage. Our results demonstrate substantial heterogeneity in the geographic overlap both within and between countries. These results provide a framework to assess the potential for joint geographic targeting of interventions, supporting efforts to ensure that all people, regardless of location, can benefit from vaccines and other essential health services.

Crystal structure of dihydrofolate reductase from the filarial nematode *W. bancrofti* in complex with NADPH and folate.

Lange K, Frey KM, Eck T, Janson CA, Gubler U, Goodey NM.

27-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104530/>

Geospatial modelling of lymphatic filariasis and malaria co-endemicity in Nigeria.

Eneanya OA, Reimer LJ, Fischer PU, Weil GJ.

24-04-2023

Int Health.

<https://pubmed.ncbi.nlm.nih.gov/37096453/>

Diethylcarbamazine elicits Ca²⁺ signals through TRP-2 channels that are potentiated by emodepside in *Brugia malayi* muscles.

Williams PDE, Kashyap SS, Robertson AP, Martin RJ.

11-04-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37090573/>

Filarial nematode infections are a major health concern in several countries. Lymphatic filariasis is caused by *Wucheria bancrofti* and *Brugia spp.* affecting over 120 million people. Heavy infections can lead to elephantiasis having serious effects on individuals' lives. Although current anthelmintics are effective at killing the microfilariae in the bloodstream, they have little to no effect against adult parasites found in the lymphatic system. The anthelmintic diethylcarbamazine is one of the central pillars of lymphatic filariasis control. Recent studies have reported that diethylcarbamazine can open Transient Receptor Potential (TRP) channels on the muscles of adult female *Brugia malayi* leading to contraction and paralysis. Diethylcarbamazine has synergistic effects in combination with emodepside on *Brugia* inhibiting motility: emodepside is an anthelmintic that has effects on filarial nematodes and is under trials for treatment of river blindness. Here we have studied the effects of diethylcarbamazine on single *Brugia* muscle cells by measuring the change in Ca²⁺ fluorescence in the muscle using Ca²⁺-imaging techniques. Diethylcarbamazine interacts with the TRPC orthologue receptor TRP-2 to promote Ca²⁺ entry into the *Brugia* muscle cells which can activate SLO-1 Ca²⁺ activated K⁺ channels, the putative target of emodepside. A combination of diethylcarbamazine and emodepside leads to a bigger Ca²⁺ signal than when either compound is applied alone. Our study shows that diethylcarbamazine targets TRP channels to promote Ca²⁺ entry that is increased by emodepside activation of SLO-1 channels.

Human immune response against filarial HSP70 and its role in the diagnosis of lymphatic filariasis.

Ahmad F, Liebau E, Rathaur S.

Mai-2023

Parasite Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37073092/>

Gale

Breaking the Bubble: Bullous scabies - A case report.

Daim SUR, Ashraf MF, Ashraf A, Zubair R, Ahmed RU.

12-04-2023

IDCases.

<https://pubmed.ncbi.nlm.nih.gov/37114209/>

In Vitro Efficacy of Terpenes from Essential Oils against *Sarcoptes scabiei*.

Li M, Feng S, Huang S, Guillot J, Fang F.

11-04-2023

Molecules.

<https://pubmed.ncbi.nlm.nih.gov/37110595/>

Community-Led Data Collection: Enhancing Local-Level Scabies Surveillance in Remote Aboriginal Communities in Australia.

Glennie M, Dowden M, Scolyer M, O'Meara I, Angeles G, Woerle H, Campbell PT, Gardner K.

29-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104325/>

Novel approaches to geohealth data analysis offer major benefits to neglected tropical disease control by identifying how social, economic and environmental elements of place interact to influence disease outcomes. However, a lack of timely and accurate geohealth data poses substantial risks to the accuracy of risk identification and challenges to the development of suitably targeted disease control programs. Scabies is one of many skin-related NTDs that is nominated as a priority for global disease control by the World Health Organization, but for which there remains a lack of baseline geospatial data on disease distribution. In this opinion paper, we consider lessons on impediments to geohealth data availability for other skin-related NTDs before outlining challenges specific to the collection of scabies-related geohealth data. We illustrate the importance of a community-centred approach in this context using a recent initiative to develop a community-led model of scabies surveillance in remote Aboriginal communities in Australia.

Study of the Use of Permethrin 5% Cream in Galicia (Spain) between 2018 and 2021.

Vázquez-Prieto S, Vaamonde A, Paniagua E.

19-04-2023

Infect Dis Rep.

<https://pubmed.ncbi.nlm.nih.gov/37102983/>

Drug utilization studies can provide direct insights into how a drug is used in real-world conditions and can give a rough estimate of the proportion of the study population treated with it. In the present work, we examined the consumption of permethrin 5% cream in the four provinces of Galicia (a Spanish autonomous community) and described the seasonal variability and the annual

evolution of its consumption between 2018 and 2021. A descriptive, cross-sectional, and retrospective study of the consumption of this drug, expressed in defined daily dose per 1000 inhabitants per day (DID), was carried out. The results obtained revealed differences between the amounts consumed in the four Galician provinces ($p < 0.001$). No specific geographical pattern was observed; however, the results suggested a marked seasonality and a slightly increasing global trend in the consumption of permethrin 5% cream throughout the study period. Since the only authorized indication of this drug in the study area is the treatment of scabies, this work may give an idea of the epidemiological situation of the disease in Galicia and serve to establish public health strategies against this parasitosis.

Dermoscopy of Crusted Scabies: Revisiting the New and Old Signs.

Mundhra R, Rambhia K, Makhecha MB, Gera RG.

14-12-2022

Indian Dermatol Online J.

<https://pubmed.ncbi.nlm.nih.gov/37089854/>

Answer to April 2023 Photo Quiz.

Feng Y, Feng J, Qin B.

20-04-2023

J Clin Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37078716/>

Helminthiases transmissibles par le sol (ascaridiose, trichuriase, ankylostomiase)

Establishment of a Simple and Rapid Nucleic Acid Detection Method for Hookworm Identification.

Ding X, Yang Y, Zhang Y, Zhang Q, Mao F, Dai Y.

21-04-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111516/>

Hookworm infection is one of the most common neglected tropical diseases and is mainly found in tropical and subtropical areas. Two species of human hookworm are distributed in China, i.e., *Ancylostoma duodenale* (AD) and *Necator americanus* (NA). **Background:** Traditional microscopic technology such as the Kato-Katz method is not suitable for hookworm diagnosis due to the rapid degeneration of fragile hookworm eggs or for species identification of hookworm infection. The aim of the present study was to establish and evaluate a novel nucleic acid detection method based on recombinase-aided isothermal amplification (RAA) for the detection of hookworm infections and species identification. **Methods:** Based on the specific target gene sequences of hookworms (5.8S rRNA for AD and ITS2 for NA, respectively), we designed and synthesized amplification primers and fluorescence probes referring to the principle

of the fluorescence recombinase-aided amplification (RAA) technique. **Results:** Each assay provided specific amplification of larval DNA from AD and NA by fluorescence RAA, and the detection limits in plasmids reached 10^2 copies and 10 copies, respectively. Genomic DNA of two hookworm species was successfully detected at a concentration of 0.1 pg/ μ L, revealing a high detection sensitivity. No positive amplification occurred for genomic DNA from crossed hookworm species and genomic DNA from *Cryptosporidium*, *Giardia lamblia*, *Strongyloides stercoralis*, *Schistosoma japonicum*, *Ascaris lumbricoides*, and *Clonorchis sinensis*, revealing a satisfactory specificity. Fecal sample detection results demonstrated a similar efficacy to the Kato-Katz method; however, it had a greater sensitivity than the larvae culture method. **Conclusion:** A simple and rapid nucleic acid method was successfully established based on RAA, which improved the detection efficacy and species identification for human hookworm infections.

First Study of *Ascaris lumbricoides* from the Semiwild Population of the Sumatran Orangutan *Pongo abelii* in the Context of Morphological Description and Molecular Phylogeny.

Civáňová Křížová K, Seifertová M, Baruš V, Hodová I, Mašková Š, Nurcahyo W, Foitová I.

14-04-2023

Life (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37109546/>

There is little evidence that the already described and accepted taxa of ascarids (*Ascaris lumbricoides*, *A. suum*, and *A. ovis*) infecting individuals of taxonomically distant groups (hominids, pigs, sheep, goats, and dogs) can be genetically or morphologically distinguished. However, despite described morphological differences, e.g., due to intraspecific variation, these are insufficient for species determination and may indicate differences amongst ascarids because of cross infections, hybrid production, and specific adaptations to hosts. Herein, the results of a molecular and morphological analysis of ascarids parasitising Sumatran orangutans (*Pongo abelii* Lesson, 1827) in native populations are presented. The research took place in the Bukit Lawang area, Indonesia, in 2009. Throughout the year, fresh faecal samples were collected regularly from 24 orangutans, and all were examined for the presence of nematode adults. Only five adult worms from two orangutan females were found during regular collection. Using the integrative taxonomic approach, the nematodes found were identified as *A. lumbricoides*. The significance of the find and its rarity is documented by the fact that this is the first confirmed finding of adult ascarids from an original orangutan site (not from a zoo) in more than 130 years (including the long-term study spanning the last 20 years focusing on orangutan parasites and natural antiparasitic drugs). More accurate morphometric parameters and genetic differences for the identification of ascarids were established. These parameters will be helpful for other findings in great apes and will also be suitable for further and precise determination of this parasite. The details distinguishing between male and female specimens are also stated and well defined. A

comprehensive evaluation of the situation of *Ascaris* species parasitising orangutans, including a comparison with previously described orangutan parasite (i.e., *A. satyri*-species inquirenda), is discussed.

A case report and literature review of an aortoduodenal fistula complicated with intestinal *Ascaris lumbricoides*.

Hou XF, Liu LX, Zhao ZX, Yang JY.

25-04-2023

Asian J Surg.

<https://pubmed.ncbi.nlm.nih.gov/37105813/>

Assessment of an Immuno-Diagnostic Method for Hookworm-Related Cutaneous Larva Migrans Using Crude Extracts of *Ancylostoma caninum*.

Adam S, Dekumyoy P, Nacapunchai D, Ketboonlue T, Charunwatthana P, Dhitavat J, Koompapong K, Chonsawat P, Watthanakulpanich D.

30-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104335/>

People can become infected with cutaneous larva migrans (CLM) through skin penetration by the infective zoonotic larvae of hookworms. Few studies have investigated CLM's immunodiagnosis, and the existing studies were limited to crude somatic or excretory/secretory antigens (Ags) from adult worms. Here, we aimed to develop an indirect enzyme-linked immunosorbent assay (ELISA) to differentiate and diagnose hwCLM by detecting immunoglobulin (Ig)E, IgG, and IgG subclasses 1-4 (IgG₁₋₄) against the somatic Ag of adult *Ancylostoma caninum* checkerboard titrations of adult *A. caninum* worm extract. Pooled serum controls were immunocharacterized using an indirect ELISA. The IgG₁₋₄ and IgE results were unsatisfactory; however, the use of total IgG achieved results comparable to those of immunoblotting. Thus, we continued to analyze the IgG-ELISA using serum samples from patients with hwCLM and heterologous infections as well as from healthy controls. The sensitivity and excellent specificity of the total IgG-ELISA were 93.75% and 98.37%, respectively, and its positive and negative predictive values were 75% and 99.67%, respectively. Antibodies from five cases of angiostrongyliasis, gnathostomiasis, and dirofilariasis cross-reacted with the somatic Ag of adult *A. caninum*. This new assay can adequately serodiagnose hwCLM when combined with clinical features and/or histological examination.

Leishmaniose

Role of Natural plant extracts for potential Antileishmanial targets-In-depth review of the molecular mechanism.

Naik N, Kaushal RS, Upadhyay TKU, Kahrizi D, Al-Najjar MAA, Khan MS, Siddiqui S.

30-09-2023

Cell Mol Biol (Noisy-le-grand).

<https://pubmed.ncbi.nlm.nih.gov/37114261/>

A group of protozoan parasites known as *Leishmania* species can cause a variety of chronic illnesses, ranging from self-healing lesions to fatal outcomes. Drug-resistant pathogens have become common due to the lack of safe and effective medications, which has sparked the development of new therapeutic interventions, particularly plant-based natural extracts. As a way to avoid chemotherapy's side effects, natural herbal remedies have drawn more attention. In addition to having anti-inflammatory, anticancer, and cosmetic properties, the secondary metabolites of plants, such as phenolic compounds, flavonoids, alkaloids, and terpenes, have a number of positive effects on our health. Natural metabolites such as naphthoquinone, alkaloids, benzophenones, etc. that have antileishmanial and antiprotozoal activity have been the subject of extensive research. In this review paper, it can be concluded that these natural extracts can be developed into excellent therapeutic agents against Leishmaniasis.

The Role of the *Leishmania infantum* Infected Dogs as a Potential Reservoir Host for Toscana Virus in a Zoonotic Visceral Leishmaniasis Focus of Northern Tunisia.

Dachraoui K, Chelbi I, Labidi I, Ben Osman R, Sayadi A, Ben Said M, Cherni S, Abbas MAS, Charrel R, Zhioua E.

20-04-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112992/>

In Vitro Evaluation of Aerosol Therapy with Pentamidine-Loaded Liposomes Coated with Chondroitin Sulfate or Heparin for the Treatment of Leishmaniasis.

Román-Álamo L, Allaw M, Avalos-Padilla Y, Manca ML, Manconi M, Fulgheri F, Fernández-Lajo J, Rivas L, Vázquez JA, Peris JE, Roca-Geronès X, Poonlapdecha S, Alcover MM, Fisa R, Riera C, Fernández-Busquets X.

06-04-2023

Pharmaceutics.

<https://pubmed.ncbi.nlm.nih.gov/37111648/>

The second-line antileishmanial compound pentamidine is administered intramuscularly or, preferably, by intravenous infusion, with its use limited by severe adverse effects, including diabetes, severe hypoglycemia, myocarditis and renal toxicity. We sought to test the potential of phospholipid vesicles to improve the patient compliance and efficacy of this drug for the treatment of leishmaniasis by means of aerosol therapy. The targeting to macrophages of pentamidine-loaded liposomes coated with chondroitin sulfate or heparin increased about twofold (up to ca. 90%) relative to noncoated liposomes. The encapsulation of pentamidine in liposomes ameliorated its activity on the amastigote and promastigote forms of *Leishmania infantum* and *Leishmania pifanoi*, and it significantly reduced cytotoxicity on human umbilical endothelial cells, for

which the concentration inhibiting 50% of cell viability was $144.2 \pm 12.7 \mu\text{M}$ for pentamidine-containing heparin-coated liposomes vs. $59.3 \pm 4.9 \mu\text{M}$ for free pentamidine. The deposition of liposome dispersions after nebulization was evaluated with the Next Generation Impactor, which mimics human airways. Approximately 53% of total initial pentamidine in solution reached the deeper stages of the impactor, with a median aerodynamic diameter of $\sim 2.8 \mu\text{m}$, supporting a partial deposition on the lung alveoli. Upon loading pentamidine in phospholipid vesicles, its deposition in the deeper stages significantly increased up to $\sim 68\%$, and the median aerodynamic diameter decreased to a range between 1.4 and $1.8 \mu\text{m}$, suggesting a better aptitude to reach the deeper lung airways in higher amounts. In all, nebulization of liposome-encapsulated pentamidine improved the bioavailability of this neglected drug by a patient-friendly delivery route amenable to self-administration, paving the way for the treatment of leishmaniasis and other infections where pentamidine is active.

Zinc(II)-Sterol Hydrazone Complex as a Potent Anti-Leishmania Agent: Synthesis, Characterization, and Insight into Its Mechanism of Antiparasitic Action.

Visbal G, Justo RMS, Dos Santos da Silva E Miranda G, Teixeira de Macedo Silva S, de Souza W, Rodrigues JCF, Navarro M.

31-03-2023

Pharmaceutics.

<https://pubmed.ncbi.nlm.nih.gov/37111599/>

Searching for new alternatives for treating leishmaniasis, we present the synthesis, characterization, and biological evaluation against *Leishmania amazonensis* of the new $\text{ZnCl}_2(\text{H3})_2$ complex. **H3** is 22-hydrazone-imidazoline-2-yl-chole-5-ene-3 β -ol, a well-known bioactive molecule functioning as a sterol Δ^{24} -sterol methyl transferase (24-SMT) inhibitor. The $\text{ZnCl}_2(\text{H3})_2$ complex was characterized by infrared, UV-vis, molar conductance measurements, elemental analysis, mass spectrometry, and NMR experiments. The biological results showed that the free ligand **H3** and $\text{ZnCl}_2(\text{H3})_2$ significantly inhibited the growth of promastigotes and intracellular amastigotes. The IC_{50} values found for **H3** and $\text{ZnCl}_2(\text{H3})_2$ were $5.2 \mu\text{M}$ and $2.5 \mu\text{M}$ for promastigotes, and 543 nM and 32 nM for intracellular amastigotes, respectively. Thus, the $\text{ZnCl}_2(\text{H3})_2$ complex proved to be seventeen times more potent than the free ligand **H3** against the intracellular amastigote, the clinically relevant stage. Furthermore, cytotoxicity assays and determination of selectivity index (SI) revealed that $\text{ZnCl}_2(\text{H3})_2$ ($\text{CC}_{50} = 5 \mu\text{M}$, $\text{SI} = 156$) is more selective than **H3** ($\text{CC}_{50} = 10 \mu\text{M}$, $\text{SI} = 20$). Furthermore, as **H3** is a specific inhibitor of the 24-SMT, free sterol analysis was performed. The results showed that **H3** was not only able to induce depletion of endogenous parasite sterols (episterol and 5-dehydroepisterol) and their replacement by 24-desalkyl sterols (cholesta-5,7,24-trien-3 β -ol and cholesta-7,24-dien-3 β -ol) but also its zinc derivative resulting in a loss of cell viability. Using electron microscopy, studies on the fine ultrastructure of the parasites showed significant differences between the

control cells and parasites treated with **H3** and $\text{ZnCl}_2(\text{H3})_2$. The inhibitors induced membrane wrinkle, mitochondrial injury, and abnormal chromatin condensation changes that are more intense in the cells treated with $\text{ZnCl}_2(\text{H3})_2$.

Infectiousness of Asymptomatic Meriones shawi, Reservoir Host of Leishmania major.

Sadlova J, Vojtkova B, Lestinova T, Becvar T, Frynta D, Benallal KE, Mekarnia N, Harrat Z, Volf P.

18-0-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111500/>

Leishmania Infection-Induced Proteolytic Processing of SIRP α in Macrophages.

Hirai H, Hong J, Fujii W, Sanjoba C, Goto Y.

13-04-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111479/>

Toll-like Receptor-9 (TLR-9) Signaling Is Crucial for Inducing Protective Immunity following Immunization with Genetically Modified Live Attenuated Leishmania Parasites.

Bhattacharya P, Gannavaram S, Ismail N, Saxena A, Dagur PK, Akue A, KuKuruga M, Nakhasi HL.

29-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111420/>

No human vaccine is available for visceral leishmaniasis (VL). Live attenuated centrin gene-deleted *L. donovani* (*LdCen*^{-/-}) parasite vaccine has been shown to induce robust innate immunity and provide protection in animal models. Toll-like receptors (TLRs) are expressed in innate immune cells and are essential for the early stages of *Leishmania* infection. Among TLRs, TLR-9 signaling has been reported to induce host protection during *Leishmania* infection. Importantly, TLR-9 ligands have been used as immune enhancers for non-live vaccination strategies against leishmaniasis. However, the function of TLR-9 in the generation of a protective immune response in live attenuated *Leishmania* vaccines remains unknown. In this study, we investigated the function of TLR-9 during *LdCen*^{-/-} infection and found that it increased the expression of TLR-9 on DCs and macrophages from ear-draining lymph nodes and spleen. The increase in TLR-9 expression resulted in changes in downstream signaling in DCs mediated through signaling protein myeloid differentiation primary response 88 (MyD88), resulting in activation and nuclear translocation of nuclear factor- κB (NF- κB). This process resulted in an increase in the DC's proinflammatory response, activation, and DC-mediated CD4⁺T cell proliferation. Further, *LdCen*^{-/-} immunization in TLR-9^{-/-} mice resulted in a significant loss of protective immunity. Thus, *LdCen*^{-/-} vaccine naturally activates the TLR-9 signaling pathway to elicit protective immunity against virulent *L. donovani* challenge.

Evaluation of Molecular Methods to Identify Chagas Disease and Leishmaniasis in Blood Donation Candidates in Two Brazilian Centers.

Ferreira JJG, Costa SCB, Addas-Carvalho M, Pereira MB, França AO, de Lima RG, Andrade PD, Wanderley JDS, Martins LC, de Almeida EA, Marcon GEB.

24-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111394/>

Meroterpenoids from *Gongolaria abies-marina* against Kinetoplastids: In Vitro Activity and Programmed Cell Death Study.

Nicolás-Hernández DS, Rodríguez-Expósito RL, López-Arencibia A, Bethencourt-Estrella CJ, Sifaoui I, Salazar-Villatoro L, Omaña-Molina M, Fernández JJ, Díaz-Marrero AR, Piñero JE, Lorenzo-Morales J.

23-03-2023

Pharmaceuticals (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37111233/>

Leishmaniasis and Chagas disease affect millions of people worldwide. The available treatments against these parasitic diseases are limited and display multiple undesired effects. The brown alga belonging to the genus *Gongolaria* has been previously reported as a source of compounds with different biological activities. In a recent study from our group, *Gongolaria abies-marina* was proven to present antiamebic activity. Hence, this brown alga could be a promising source of interesting molecules for the development of new antiprotozoal drugs. In this study, four meroterpenoids were isolated and purified from a dichloromethane/ethyl acetate crude extract through a bioguided fractionation process targeting kinetoplastids. Moreover, the in vitro activity and toxicity were evaluated, and the induction of programmed cell death was checked in the most active and less toxic compounds, namely gongolarone B (2), 6Z-1'-methoxyamentadione (3) and 1'-methoxyamentadione (4). These meroterpenoids triggered mitochondrial malfunction, oxidative stress, chromatin condensation and alterations of the tubulin network. Furthermore, a transmission electron microscopy (TEM) image analysis showed that meroterpenoids (2-4) induced the formation of autophagy vacuoles and ER and Golgi complex disorganization. The obtained results demonstrated that the mechanisms of action at the cellular level of these compounds were able to induce autophagy as well as an apoptosis-like process in the treated parasites.

A QSAR Study for Antileishmanial 2-Phenyl-2,3-dihydrobenzofurans[†].

Bernal FA, Schmidt TJ.

12-04-2023

Molecules.

<https://pubmed.ncbi.nlm.nih.gov/37110632/> s

Leishmaniasis, a parasitic disease that represents a threat to the life of millions of people around the globe, is currently lacking effective treatments. We have previously

reported on the antileishmanial activity of a series of synthetic 2-phenyl-2,3-dihydrobenzofurans and some qualitative structure-activity relationships within this set of neolignan analogues. Therefore, in the present study, various quantitative structure-activity relationship (QSAR) models were created to explain and predict the antileishmanial activity of these compounds. Comparing the performance of QSAR models based on molecular descriptors and multiple linear regression, random forest, and support vector regression with models based on 3D molecular structures and their interaction fields (MIFs) with partial least squares regression, it turned out that the latter (i.e., 3D-QSAR models) were clearly superior to the former. MIF analysis for the best-performing and statistically most robust 3D-QSAR model revealed the most important structural features required for antileishmanial activity. Thus, this model can guide decision-making during further development by predicting the activity of potentially new leishmanicidal dihydrobenzofurans before synthesis.

Next-Generation Leishmanization: Revisiting Molecular Targets for Selecting Genetically Engineered Live-Attenuated *Leishmania*.

Moreira POL, Nogueira PM, Monte-Neto RL.

16-04-2023

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/37110466/>

Leishmania infantum (JPCM5) Transcriptome, Gene Models and Resources for an Active Curation of Gene Annotations.

Camacho E, González-de la Fuente S, Solana JC, Tabera L, Carrasco-Ramiro F, Aguado B, Requena JM.

04-04-2023

Genes (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37107624/>

Kaurane-Type Diterpenoids as Potential Inhibitors of Dihydrofolate Reductase-Thymidylate Synthase in New World *Leishmania* Species.

Herrera-Acevedo C, de Menezes RPB, de Sousa NF, Scotti L, Scotti MT, Coy-Barrera E.

28-03-2023

Antibiotics (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37107025/>

Cultivation of Protozoa Parasites In Vitro: Growth Potential in Conventional Culture Media versus RPMI-PY Medium.

Castelli G, Oliveri E, Valenza V, Giardina S, Facciponte F, La Russa F, Vitale F, Bruno F.

27-03-2023

Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37104407/>

The in vitro cultivation of *Leishmania* and *Trypanosoma* parasites plays an important role in the diagnosis and

treatment of parasitic diseases. Although Evans's modified Tobie and Novy-MacNeal-Nicolle media, for *Leishmania* spp. and *Trypanosoma cruzi*, respectively, are the two commonly used media for both isolation and maintenance of strains in vitro, their preparation is expensive and laborious and requires fresh rabbit blood from housed animals. The purpose of this study was to evaluate the in vitro growth of both parasites with an alternative monophasic, blood-free, easy, and affordable medium called RPMI-PY, which was previously demonstrated suitable for the in vitro growth of *Leishmania infantum*. The potential growth of different *Leishmania* species and *Trypanosoma cruzi* was evaluated in traditional culture media versus RPMI-PY medium, and we recorded the protozoa parasites' morphology via orange acridine-ethidium bromide staining. The results of our study show that RPMI-PY medium can be used for *Trypanosoma cruzi*, *Leishmania amazonensis*, *Leishmania major*, and *Leishmania tropica* species since in all the species except *Leishmania braziliensis*, the exponential growth of the parasite was observed, in many cases higher than conventional media. The staining confirmed not only their growth during the 72 h investigation but also the optimal morphology and viability of the protozoa in the RPMI-PY medium.

A Rare Case of Imported Cutaneous Leishmaniasis Caused by *Leishmania infantum* in the Republic of Korea, 2021.

Kim HJ, Kim EJ, Choi JW, Kim YC, Lee HI, Shin HI.

12-04-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104348/>

In Vivo Antileishmanial Effect of 3,5-Diaryl-isoxazole Analogues Based on Veraguensin, Grandisin, and Machilin G: A Glance at a Preclinical Study.

das Neves AR, Carvalho DB, Silva F, Rosalem RF, Pelizaro BI, Castilho PF, Oliveira KMP, Cassemiro NS, Pessatto LR, Paredes-Gamero EJ, Piranda EM, Silva DB, Arruda CCP, Baroni ACM.

27-04-2023

ACS Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37103973/>

New treatment approaches targeting cutaneous leishmaniasis (CL) are required since conventional drugs exhibit limitations due to their several adverse effects and toxicity. In this study, we aimed to evaluate the in vivo intralésional treatment efficacy of five isoxazole derivatives previously synthesized and effective in vitro against intracellular amastigote forms of *Leishmania* (*L.*) *amazonensis*. Among the tested analogues, **7** exhibited relevant in vivo therapeutic effects. The in silico predictions provided interesting information about the toxicity, suggesting the safety of analogue **7**. Experiments performed with *Salmonella typhimurium* strains (TA98, TA100, and TA102) showed a non-mutagenicity profile of **7**. The treatment of *Leishmania*-infected BALB/c mice with isoxazole **7** showed remarkably smaller CL lesions and decreased the parasitism (by 98.4%) compared to the

control group. Hence, analogue **7** is a promising drug candidate and alternative treatment for CL caused by *L. amazonensis*.

A neglected among the neglected: a review of cutaneous leishmaniasis in Guatemala.

Lopez Y, Arana B, Rizzo N, Duran E, Acosta-Serrano Á, Mendizabal-Cabrera R.

27-04-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37103337/>

Cutaneous leishmaniasis (CL) is a parasitic vector-borne disease affecting mostly low- and middle-income countries. CL is endemic in Guatemala, where an increase in the number of cases and incidence and a changing disease distribution in the past decade have been reported. Important research was conducted in Guatemala in the 1980s and 1990s to understand the epidemiology of CL and two *Leishmania* species were identified as the aetiologic agents. Several species of sand flies have been reported, five of which are naturally infected with *Leishmania*. Clinical trials conducted in the country evaluated different treatments against the disease and provided solid evidence for CL control strategies that are applicable worldwide. More recently, in the 2000s and 2010s, qualitative surveys were conducted to understand community perceptions of the disease and to highlight the challenges and enablers for disease control. However, limited recent data have been generated regarding the current CL situation in Guatemala, and key information necessary for effective disease control, such as incrimination of vectors and reservoirs, is still lacking. This review describes the current state of knowledge of CL in Guatemala, including the main parasite and sand fly species, disease reservoirs, diagnosis and control, as well as the perceptions of communities in endemic regions.

Evaluation of the susceptibility of *Tritrichomonas foetus* to extracts of *Lantana camara* (Verbenaceae) by flow cytometry.

López LA, Luque ME, Rivero MB, Abdala ME, Carranza PG, Luna BE, Di Lullo D, Volta BJ, Rodríguez SA, Rivero FD.

27-04-2032

Vet Res Commun.

<https://pubmed.ncbi.nlm.nih.gov/37100969/>

Pharmacophore-guided drug design using LdNMT as a model drug target for leishmaniasis.

Sooram B, Mallikarjunachari U, Uddavesh S, Saudagar P.

25-04-2023

J Biomol Struct Dyn.

<https://pubmed.ncbi.nlm.nih.gov/37096664/>

Synthesis and physicochemical characterization of Zn-Al layered double

hydroxides (LDHs) as a delivery system for amphotericin B: In vitro and in silico antileishmanial study.

Bahraminejad S, Pardakhty A, Sharifi I, Keyhani A, Salarkia E, Ranjbar M.

08-04-2023

Heliyon.

<https://pubmed.ncbi.nlm.nih.gov/37096004/>

Leishmaniasis as a widespread neglected vector-borne protozoan disease is a major public health concern in endemic areas due to 12 million people affected worldwide and 60,000 deaths annually. Several problems and side effects in using current chemotherapies leads to progression of new drug delivery systems against leishmaniasis. For instance, layered double hydroxides (LDHs) so-called anionic clays due to their proper characteristics, have been considered recently. In the present study, LDH nanocarriers were prepared using co-precipitation method. Then, the intercalation reactions with amphotericin B were conducted via indirect ion exchange assay. Finally, after characterization of prepared LDHs, the anti-leishmanial effects of Amp-Zn/Al-LDH nanocomposites against *Leishmania major* were evaluated using an *in vitro* and *in silico* model. According to results, current study demonstrated that Zn/Al-NO₃ LDH nanocarriers can be used as a new promising delivery system by intercalating amphotericin B into its interlayer space for leishmaniasis treatment by eliminating the *L. major* parasites by remarkable immunomodulatory, antioxidant and apoptotic effects.

The sphingolipids ceramide and inositol phosphorylceramide protect the *Leishmania major* membrane from sterol-specific toxins.

Haram CS, Moitra S, Keane R, Kuhlmann FM, Frankfater C, Hsu FF, Beverley SM, Zhang K, Keyel PA.

22-04-2023

J Biol Chem.

<https://pubmed.ncbi.nlm.nih.gov/37094699/>

Drug repositioning to discover novel Ornithine Decarboxylase inhibitors against Visceral Leishmaniasis.

Sheikh SY, Ansari WA, Hassan F, Faruqui T, Khan MF, Akhter Y, Khan AR, Siddiqui MA, Al-Khedhairi AA, Nasibullah M.

24-04-2023

J Mol Recognit.

<https://pubmed.ncbi.nlm.nih.gov/37092713/>

Visceral leishmaniasis (VL) is caused by *Leishmania donovani* (Ld), and most cases occur in Brazil, East Africa, and India. The treatment for VL is limited and has many adverse effects. The development of safer and more efficacious drugs is urgently needed. Drug repurposing is one of the best processes to repurpose existing drugs. Ornithine decarboxylase (ODC) is an important target against *L. donovani* in the polyamine biosynthesis pathway. In this study, we have modeled the 3D structure of ODC and performed high-throughput virtual screening (HTVS) of 8630 ZINC database ligands against *Leishmania*

donovani ornithine decarboxylase (Ld ODC), selecting 45 ligands based on their high binding score. It is further validated through molecular docking simulation and the selection of the top two lead molecules (ceftaroline fosamil and rimegepant) for Molecular Dynamics (MD) simulation, DFT, and MMGBSA analysis. The results showed that the binding affinities of ceftaroline fosamil, and rimegepant are, respectively, -10.719 and 10.159 kcal/mol. The docking complexes of the two lead compounds, ceftaroline fosamil, and rimegepant, with the target ODC, were found stable during molecular dynamics simulations. Furthermore, the analysis of molecular mechanics generalized Born surface area (MMGBSA) revealed that these compounds had a high binding free energy. The DFT analysis showed that the top lead molecules were more reactive than the standard drug (pentamidine). In-silico findings demonstrated that ceftaroline fosamil, and rimegepant might be recognized as potent antagonists against ODC for the treatment of VL. This article is protected by copyright. All rights reserved.

Apigenin is a promising molecule for treatment of visceral leishmaniasis.

Emiliano YSS, Almeida-Amaral EE.

05-04-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37091674/>

Omics data integration facilitates target selection for new antiparasitic drugs against *TriTryp* infections.

Rivara-Espasandín M, Palumbo MC, Sosa EJ, Radío S, Turjanski AG, Sotelo-Silveira J, Fernandez Do Porto D, Smircich P.

06-04-2023

Front Pharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37089958/>

Amphotericin B resistance correlates with increased fitness in vitro and in vivo in *Leishmania* (*Mundinia*) *martiniquensis*.

Mano C, Kongkaew A, Tippawangkosol P, Somboon P, Roytrakul S, Pescher P, Späth GF, Uthapibull C, Tantiworawit A, Siriyasatien P, Jariyapan N.

06-04-2023

Front Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37089544/>

Amphotericin B (AmpB) deoxycholate is the available first-line drug used to treat visceral leishmaniasis caused by *Leishmania* (*Mundinia*) *martiniquensis*, however, some cases of AmpB treatment failure have been reported in Thailand. Resistance to drugs is known to affect parasite fitness with a potential impact on parasite transmission but still little is known about the effect of resistance to drugs on *L. martiniquensis*. Here we aimed to gain insight into the fitness changes occurring after treatment failure or *in vitro*-induced resistance to AmpB. *L. martiniquensis* parasites isolated from a patient before (LSCM1) and after relapse (LSCM1-6) were compared for *in vitro* and *in vivo* fitness changes together with an *in vitro* induced AmpB-

resistant parasite generated from LSCM1 parasites (AmpBRP2i). Results revealed increased metacyclogenesis of the AmpBRP2i and LSCM1-6 strains (AmpB-resistant strains) compared to the LSCM1 strain and increased fitness with respect to growth and infectivity. The LSCM1-6 and AmpBRP2i strains were present in mice for longer periods compared to the LSCM1 strain, but no clinical signs of the disease were observed. These results suggest that the AmpB-resistant parasites could be more efficiently transmitted to humans and maintained in asymptomatic hosts longer than the susceptible strain. The asymptomatic hosts therefore may represent "reservoirs" for the resistant parasites enhancing transmission. The results in this study advocate an urgent need to search and monitor for AmpB-resistant *L. martiniquensis* in patients with relapsing leishmaniasis and in asymptomatic patients, especially, in HIV/*Leishmania* coinfecting patients.

Swarna Bhasma Induces Antigen-Presenting Abilities of Macrophages and Helps Antigen Experienced CD4⁺ T Cells to Acquire Th1 Phenotypes Against *Leishmania donovani* Antigens.

Saini S, Anand A, Singh A, Mahapatra B, Sirohi S, Singh S, Singh RK.

24-04-2023

Biol Trace Elem Res.

<https://pubmed.ncbi.nlm.nih.gov/37088826/>

In leishmaniasis, the protective immunity is largely mediated by proinflammatory cytokine producing abilities of T cells and an efficient parasite killing by phagocytic cells. Notwithstanding a substantial progress that has been made during last decades, the mechanisms or factors involved in establishing protective immunity against *Leishmania* are not identified. In ancient Indian literature, metallic "bhasma," particularly that of "swarna" or gold (fine gold particles), is indicated as one of the most prominent metal-based therapeutic medicine, which is known to impart protective and curative properties in various health issues. In this work, we elucidated the potential of swarna bhasma (SB) on the effector properties of phagocytes and antigen-activated CD4⁺ T cells in augmenting the immunogenicity of *L. donovani* antigens. The characterization of SB revealing its shape, size, composition, and measurement of cytotoxicity established the physiochemical potential for its utilization as an immunomodulator. The activation of macrophages with SB enhanced their capacity to produce nitric oxide and proinflammatory cytokines, which eventually resulted in reduced uptake of parasites and their proliferation in infected cells. Further, in *Leishmania*-infected animals, SB administration reduced the generation of IL-10, an anti-inflammatory cytokine, and enhanced pro-inflammatory cytokine generation by antigen activated CD4⁺ T cells with increased frequency of double (IFN γ ⁺/TNF α ⁺) and triple (IFN γ ⁺/TNF α ⁺/IL-2⁺) positive cells and abrogated disease pathogenesis at the early days of infection. Our results also suggested that cow-ghee (A2) emulsified preparation of SB, either alone or with yashtimadhu, a known natural immune modulator which enhances the SB's potential in enhancing the immunogenicity of parasitic antigens. These findings suggested a definite potential of SB in

enhancing the effector functions of phagocytes and CD4⁺ T cells against *L. donovani* antigens. Therefore, more studies are needed to elucidate the mechanistic details of SB and its potential in enhancing vaccine-induced immunity.

MiniPCR as a portable equipment for the molecular diagnosis of american cutaneous leishmaniasis.

Castellanos-Gonzalez A, Cossio A, Jojoa J, Moen S, Travi BL.

23-04-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37088354/>

Identification and analysis of the DNA content of small extracellular vesicles isolated from *Leishmania* parasites.

Ibarra-Meneses AV, Amin A, Dong G, Olivier M, Langlais D, Fernandez-Prada C.

21-04-2023

STAR Protoc.

<https://pubmed.ncbi.nlm.nih.gov/37087735/>

Asymptomatic *Leishmania donovani* infection and associated factors among blood donors attending at Metema district Blood Bank, Northwest Ethiopia: a cross-sectional study.

Melkie I, Yimer M, Alemu G, Tegegne B.

21-04-2023

Arch Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37085820/>

In vitro and in vivo evaluation of efficacy of berberine chloride: Phyto-alternative approach against *Trypanosoma evansi* infection.

Gupta S, Vohra S, Sethi K, Rani R, Gupta S, Kumar S, Kumar R.

20-04-2023

Mol Biochem Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37084956/>

Current chemotherapy against the Surra organism, *Trypanosoma evansi* has several limitations in terms of efficacy, toxicity, availability and emerging resistance. These reasons make the search of new chemo-preventive and chemo-therapeutic agent with high potency and low toxicity. Alkaloid phyto-molecules, berberine has shown promising anti-kinetoplastid activity against *T. cruzi*, *T. congolense*, *T. brucei*, *Leishmania donovani* and *L. tropica*. However, till date, there is no investigation of therapeutic efficacy of berberine chloride (BC) against *T. evansi*. The IC₅₀ value of BC for growth inhibition of *T. evansi* at 24 h of culture was calculated as 12.15 μ M. The specific selectivity index (SSI) of BC was calculated as 19.01 and 10.43 against Vero cell line and Equine PBMC's, respectively. Thirteen drug target genes affecting various metabolic pathways were studied to investigate the mode of trypanocidal action of BC. In transcript analysis, the mRNA expression

of arginine kinase 1 remained refractory to exposure with BC, which provides metabolic plasticity in adverse environmental conditions. In contrary, rest all the drug target gene were down-regulated, which indicates that drug severely affect DNA replication, cell proliferation, energy homeostasis, redox homeostasis and calcium homeostasis of *T. evansi*, leading to the death of parasite in low concentrations. It is the first attempt to investigate in vitro anti-trypansomal activity of BC against *T. evansi*. These data imply that phytochemicals as alternative strategies can be explored in the future as an alternative treatment for Surra in animal.

Systematic study of 1,2,3-triazolyl sterols for the development of new drugs against parasitic Neglected Tropical Diseases.

Porta EOJ, Ballari MS, Carlucci R, Wilkinson S, Ma G, Tekwani BL, Labadie GR.

13-04-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37084599/>

Genome Analysis of Triploid Hybrid Leishmania Parasite from the Neotropics.

Van den Broeck F, Heeren S, Maes I, Sanders M, Cotton JA, Cupolillo E, Alvarez E, Garcia L, Tasia M, Marneffe A, Dujardin JC, Van der Auwera G.

Mai-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37081624/>

Cutaneous Leishmaniasis Caused by Leishmania infantum, Israel, 2018-2021.

Solomon M, Astman N, Warshavsky K, Barzilai A, Meninger T, Avni D, Schwartz E.

Mai-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37081590/>

Cutaneous leishmaniasis (CL) is endemic to Israel. Previously, CL caused by *Leishmania infantum* had been reported in Israel only once (in 2016). We report 8 *L. infantum* CL cases; 7 occurred during 2020-2021. None of the patients had systemic disease. *L. infantum* CL may be an emerging infection in Israel.

Leishmania donovani Transmission Cycle Associated with Human Infection, Phlebotomus alexandri Sand Flies, and Hare Blood Meals, Israel¹.

Studentsky L, Orshan L, Akad F, Ben Avi I, Diaz D, Elbaz S, Sagi O, Zagron G, Valinsky L, Davidovich-Cohen M, Baneth G.

Mai-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37080961/>

Cutaneous leishmaniasis caused by *Leishmania major* or *L. tropica* and visceral leishmaniasis caused by *L. infantum* have been reported in Israel. We collected *Phlebotomus* spp. sand flies in the Negev desert of southern Israel to

identify circulating *Leishmania* spp. Of 22,636 trapped sand flies, 80% were *P. alexandri*. We sequenced *Leishmania*-specific internal transcribed spacer 1 fragments and K26 genes. Of 5,019 *Phlebotomus* female sand flies, 2.5% were *Leishmania* DNA-positive; 92% of infections were *L. donovani*. Phylogenetic analyses showed separate clustering of *L. donovani* and *L. infantum*. *P. alexandri* flies positive for *L. donovani* harbored blood meals from European hares. *Leishmania* DNA isolated from a patient with cutaneous leishmaniasis who lived in the survey area was identical to *L. donovani* from *P. alexandri* flies. We report circulation of *L. donovani*, a cause of visceral leishmaniasis, in southern Israel. Prompt diagnosis and *Leishmania* spp. identification are critical to prevent leishmaniasis progression.

Modulating leishmanial pteridine metabolism machinery via some new coumarin-1,2,3-triazoles: Design, synthesis and computational studies.

Hassan NW, Sabt A, El-Attar MAZ, Ora M, Bekhit AEA, Amagase K, Bekhit AA, Belal ASF, Elzahhar PA.

05-05-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37031526/>

Exploration of seryl tRNA synthetase to identify potent inhibitors against leishmanial parasites.

Narsimulu B, Qureshi R, Jakkula P, Singh P, Arifuddin M, Qureshi IA.

15-03-023

Int J Biol Macromol.

<https://pubmed.ncbi.nlm.nih.gov/36963547/>

Aminoacyl-tRNA synthetases are crucial enzymes for cellular protein metabolism and have been considered as an attractive target for development of new antimicrobials. In the current study, seryl tRNA synthetase of *Leishmania donovani* (LdSerRS) and its mutants were purified and characterized through biochemical and structural methods. Purified LdSerRS was found to be enzymatically active and exhibited more alpha helices in secondary structure. The enzymatic activity of purified protein was observed as highest near physiological temperature and pH. Mutation in ATP binding residues (R295 and E297) demonstrated reduction in the affinity for cofactor with no significant deviation in secondary structure. In vitro inhibition studies with ureidosulfocoumarin derivatives helped to identify Comp 5I as a specific inhibitor for leishmanial SerRS that showed lesser potency towards purified HsSerRS. The identified compound presented competitive mode of inhibition for LdSerRS and also revealed druglikeness along with very low toxicity for human macrophages. Structural analysis of protein and ligand complex depicted the binding of Comp 5I into the cofactor binding site of LdSerRS with high affinity succeeded by validation employing molecular dynamics simulations. Altogether, our study presents a promising scaffold to explore small molecules to target the enzymatic activity of leishmanial SerRS to develop the specific therapeutics.

Detection of asymptomatic *Leishmania donovani* in healthy voluntary blood donors.

Abdul Naeem M, Aamir M, Ijaz F, Amin N, Khurram Aftab R.

Mai-2023

Transfus Clin Biol.

<https://pubmed.ncbi.nlm.nih.gov/36634863/>

Krebs cycle enzymes for targeted therapeutics and immunotherapy for anti-leishmanial drug development using: Pathways, potential targets, and future perspectives.

Ranjan P, Dubey VK.

01-06-2023

<https://pubmed.ncbi.nlm.nih.gov/36566880/> Life Sci.

Lèpre

Dual insulin resistance causes: how frequently type 2 diabetes mellitus and COVID-19 infection caused diabetic ketoacidosis? a case report.

Bereda G.

27-03-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37113916/>

Infection with coronavirus disease 2019 (COVID-19) worsens insulin resistance and causes diabetic ketoacidosis (DKA). Patients with COVID-19 infection who develop DKA run the risk of worse outcomes. In both diabetic and nondiabetic patients, the COVID-19 infection may hasten the development of ketoacidosis, which could have negative effects on the fetus. **Case presentation:** A 61-year-old retired Black African female was taken into the emergency room on 22 April 2022, with significant complaints of frequent midnight urination, shortness of breath, blurry vision, and tingling in her hands and feet. On a chest radiography, bilateral diffuse, patchy airspace opacities that might be due to multifocal pneumonia or viral pneumonia were seen. The severe acute respiratory syndrome infection was confirmed by real-time reverse transcription-PCR testing from nasopharyngeal swabs. She received intravenous fluids and an intravenous insulin infusion and monitored her blood electrolyte levels as part of her treatment. She received subcutaneous enoxaparin 80 mg every 12 h a day for prophylaxis of deep venous thrombosis due to her confirmed COVID-19. **Clinical discussion:** In a large number of patients, COVID-19 has the ability to trigger DKA, and type 2 diabetes mellitus amplifies the underlying COVID-19 infection. Diabetes mellitus and COVID-19 are noted to have a reciprocal relationship in this regard. **Conclusions:** By making the body resistant to insulin and raising blood sugar levels, a COVID-19 infection can cause DKA. It is probable that her severe acute respiratory syndrome coronavirus 2 infection has a detrimental effect on the pancreatic beta cells,

which are responsible for her body producing insufficient levels of insulin.

Acute pancreatitis in pregnancy: how was it determined whether it was caused by pregnancy or by COVID-19? A case report.

Bereda G.

27-03-2023

Ann Med Surg (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37113884/>

Mind Mapping as a Novel Method in Teaching the Morphology of Skin Lesions: A Quasi-Experimental Study.

Palaniappan V, Karthikeyan K, Mohan R.

Avr-2023

J Adv Med Educ Prof.

<https://pubmed.ncbi.nlm.nih.gov/37113684/>

Introduction: Mind mapping is a visual mapping technique used in a few disciplines of medical education to represent ideas linked to and arranged around a central core idea or topic through different subtopics/categories. We aimed to utilize this technique to teach the undergraduate medical students the morphology of skin lesions and assess its effectiveness. **Methods:** This pre- and post-test quasi-experimental study was done among 144 undergraduate medical students. A total of 144 students were selected, and odd and even roll numbers were categorized into two groups using simple random sampling. Group 1 (intervention group) students were taught using mind mapping technique and Group 2 (control group) with traditional lecture-based teaching. A Computer-Assisted pre-test and post-test were carried out. A feedback questionnaire was administered to the intervention group to explore the students' perceptions regarding mind mapping as a learning tool. The data were analysed using SPSS software (version 16), and the difference in the mean pre- and post-test scores was found using independent sampled-t-test. **Results:** Pre and post-test score distribution was 5.04 ± 1.27 and 11.44 ± 2.52 (p -value= ≤ 0.001), respectively, in the intervention group. In the control group, the pre and post-test score distributions were 4.83 ± 1.39 and 8.04 ± 1.63 , respectively. The mean rank of the mind mapping group was higher (76.43) than the lecture group (67.5). Among the students, 97.2% agreed on the fact that mind mapping enhanced their interest in learning, and 91.7% of the students were satisfied with mind mapping as the learning method. **Conclusion:** To kindle the interest and develop critical thinking skills in students, faculty members should continue to explore and evaluate the efficacy of various learning and teaching strategies. Mind mapping could be a novel and integral part of conventional teaching techniques in medical education as evidenced by our student's performances.

Hypertensive emergency occurred due to forgetting to take antihypertensive medication: A case study.

Bereda G.

20-04-2023

SAGE Open Med Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37113389/>

A life-threatening condition known as a "hypertensive emergency" is marked by a severe increase in blood pressure together with acute or significant target-organ damage. On 1 June 2022, a 67-year-old black male farmer was admitted to the emergency department with a major chief complaint of breathing difficulty. The patient was traveling to the village for work and forgetting his medication at home, and he was losing consciousness and motor activity at his workplace. He presented with symptoms of shortness of breath, confusion, dizziness, nausea, vomiting, blurred vision, and faintness. An abnormal cardiac region was visible on chest X-rays, and there were no changes to the pulmonary parenchyma or fluid overload. Upon admission, hydralazine (5 mg) intravenously was administered immediately, and he was reassessed after 20 min and kept at the emergency department. The next day, sustained-release nifedipine (20 mg) was initiated orally twice a day for the patient, and he was transferred to the medical ward. In the medical ward, the patient was assessed for 4 days, and in those 4 days, he showed marked improvement. Hypertensive emergency treatment intends to reverse target-organ damage, readily lowering blood pressure, decreasing adverse clinical complications, and enhancing the quality of life.

Bohn's Nodules.

Yumnam D, Moirangthem A.

27-04-2023

J Cutan Med Surg.

<https://pubmed.ncbi.nlm.nih.gov/37113022/>

A comparison of the quality of images of chest X-ray between handheld portable digital X-ray & routinely used digital X-ray machine.

Kamal R, Singh M, Roy S, Adhikari T, Gupta AK, Singh H, Rao VV, Panda S, Khan AM, Bhargava B.

27-04-2023

Indian J Med Res.

<https://pubmed.ncbi.nlm.nih.gov/37102518/>

Analysis of intronic SNP (rs4147358) and expression of SMAD3 gene in Atopic Dermatitis: A case-control study.

Shafi T, Rasool R, Ayub S, Bhat IA, Gull A, Hussain S, Hassan Shah I, Shah ZA.

23-04-2023

Immunobiology.

<https://pubmed.ncbi.nlm.nih.gov/37100019/>

Blue light and skin: what is the intriguing link?

Das A, Sil A, Kumar P, Khan I.

25-04-2023

Clin Exp Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/37097168/>

Clofazimine pKa Determination by Potentiometry and Spectrophotometry: Reverse Cosolvent Dependence as an Indicator of the Presence of Dimers in Aqueous Solutions.

Verbić TŽ, Tam KY, Veljković DŽ, Serajuddin ATM, Avdeef A.

25-04-2023

Mol Pharm.

<https://pubmed.ncbi.nlm.nih.gov/37096898/>

The weakly basic antibiotic and anti-inflammatory drug, clofazimine (CFZ), was first described in 1957. It has been used therapeutically, most notably in the treatment of leprosy. However, the compound is extremely insoluble in aqueous media, and, indeed, there is poor consensus about what its intrinsic solubility is since the reported values range from 0.04 to 11 ng/mL. To understand the speciation and solubilization of CFZ as a function of pH, it is of paramount importance to know the true aqueous pK_a . However, there is also poor consensus about the value of the pK_a (reported measured values range from 6.08 to 9.11). In the present study, we report the determination of the CFZ ionization constant using two independent techniques. A state-of-the-art potentiometric analysis was performed, drawing on titration data in methanol-water solutions (46-75 wt % MeOH) of CFZ, using the bias-reducing consensus of two different procedures of extrapolating the apparent pK_a values to zero cosolvent to approximate the true aqueous pK_a as 9.43 ± 0.12 (25 °C, $I = 0.15$ M reference ionic strength). In parallel, spectrophotometric UV/vis titration data were acquired (250-600 nm at different pH) in 10 mM HEPES buffer solutions containing up to 54 wt % MeOH. The alternating least squares (ALS) method was used in the analysis of the absorbance-pH spectra. Uncharacteristically, the cosolvent UV/vis data in our study showed reverse cosolvent dependence (apparent pK_a values increased with increasing cosolvent) which could be explained by a dimerization of the free base. The analysis of UV/vis data obtained from 54 wt % MeOH-water solution containing 20 μ M CFZ yielded the apparent pK_a 9.51 ± 0.17 ($I \approx 0.005$ M). To assess whether self-assembly of CFZ was energetically feasible, density functional theory (DFT) calculations were used to study the putative CFZ dimers in aqueous and methanol media. The DFT-optimized geometries and infrared spectra of CFZ dimers using water and methanol as solvents were calculated and analyzed. Based on the lack of negative frequencies in calculated infrared spectra, it was confirmed that optimized geometries correspond to the true energetic minima. Visual analysis of optimized structures indicates the presence of stacking interactions between two CFZ molecules. The protonation site (the imine nitrogen atom) was determined by 1 H NMR spectroscopy.

The application of digital health as a nursing solution for leprosy patients during the COVID-19 pandemic: A systematic review.

Dahoklory DF, Haryanto J, Indarwati R.

Fév-2023

IADVL SIG Pediatric Dermatology (Academy) Recommendations on Hemangioma of Infancy (HOI).

Katakam BK, Chiramel MJ, Gulati R, Gupta M, Munisamy M, Ranugha PSS, Seetharam KA.

03-03-2023

Indian Dermatol Online J.

<https://pubmed.ncbi.nlm.nih.gov/37089858/>

Hair Shaft Disorders in Children - An Update.

Bhat YJ, Trumboo T, Krishan K.

23-02-2023

Indian Dermatol Online J.

<https://pubmed.ncbi.nlm.nih.gov/37089857/>

Disorders of hair shaft are a diverse group of congenital and acquired abnormalities of the hair that can pose a diagnostic and therapeutic challenge to the dermatologists. Hair shaft abnormalities can occur as an isolated phenomenon or can be associated with an underlying genetic syndrome. Any change in the texture, appearance, and growth of the hair should prompt evaluation of the patient for the presence of any hair shaft anomaly. The diagnosis can be suggested by a complete history and physical examination of the hair-bearing areas as well as other ectodermal structures (nails and teeth). A key feature in the evaluation of hair shaft defects is to determine the fragility of the hair shaft that can be elucidated by performing the "tug test." Trichoscopy and light microscopy serve as valuable tools in establishing the specific type of hair shaft disorder. An update of the approach for the diagnosis and management is included in this review.

Diagnostic Utility of Nailfold Capillaroscopy using Hand-held Dermoscope in Systemic Sclerosis.

Jeelani S, Bali SK, Hassan I, Bashir Y.

03-03-2023

Indian Dermatol Online J.

<https://pubmed.ncbi.nlm.nih.gov/37089847/>

Introduction: The pathogenesis in systemic sclerosis (SSc) mainly involves vascular injury, fibrosis, and immune activation. Visualization of these microvascular changes by nailfold capillaroscopy (NFC) can help in the early diagnosis of the disease. Even though the gold standard for NFC is a videodermoscope, the ease, practicality, and accessibility make the hand-held dermoscope a more versatile and suitable device in the hands of the dermatologists in the busy outpatient department. **Aim:** To study the pattern of nail fold capillaries using hand-held dermoscope in the patients of SSc and correlate the findings with disease severity. **Materials and methods:** An observational, cross-sectional hospital-based study was carried out over a span of 2 years, from January 2020 till December 2021, in 50 patients of SSc. NFC using DermLite DL4 was performed in all the patients and distribution, morphology, density of

capillaries, and nail fold capillary pattern were observed.

Results: Out of 50 patients, 38 patients had diffuse type of disease, and 12 had limited type of disease. The mean capillary density in our patients was $4.7 \pm 0.81/\text{mm}$. Dilated capillaries was the most common NFC finding (80%), whereas active scleroderma pattern was the most common pattern (56%). A significant association was found between the type of capillary pattern and duration of disease, type of disease, and cutaneous manifestations.

Conclusion: Hand-held dermoscope is reliable, practical, and assessable tool that aids in early diagnosis of the disease and also helps in assessing the severity and prognosis of SSc.

Bimatoprost versus Clobetasol Propionate in Scalp Alopecia Areata: A Prospective Non-Randomized Open-Label Clinical Trial.

Bhusal M, Bhattarai S, Thapa B, Shrestha PR, Sagar GC.

03-03-2023

Indian Dermatol Online J.

<https://pubmed.ncbi.nlm.nih.gov/37089845/>

Dermoscopy of Cyndroma in Fitzpatrick Type IV Skin: A Case Report and Review of Literature.

Adya KA, Inamadar AC, Palit A.

12-10-2022

Indian Dermatol Online J.

<https://pubmed.ncbi.nlm.nih.gov/37089843/>

Squamous Cell Carcinoma Arising in Lesions of Discoid Lupus Erythematosus in a Patient with Overlap Syndrome: A Chronic Rare Complication.

Saxena S, Arora P, Misra S, Bhattacharya S.

12-10-2022

Indian Dermatol Online J.

<https://pubmed.ncbi.nlm.nih.gov/37089836/>

Salt-and-Pepper Dyspigmentation with Groove Sign in Erasmus Syndrome: A Double Jeopardy.

Mohta A, Jain SK, Shyam R.

21-09-2022

Indian Dermatol Online J.

<https://pubmed.ncbi.nlm.nih.gov/37089834/>

Unveiling the TGF- β 1 paradox: Significant implication of TGF- β 1 promoter variants and its mRNA and protein expression in atopic dermatitis.

Shafi T, Rasool R, Ayub S, Bhat IA, Shah IH, Hussain S, Shah ZA, Baba SM, Makhdoomi R, Bashir SA.

19-04-2023

Mol Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37084506/>

Background: Atopic Dermatitis (AD) is a chronic inflammatory skin disorder with evidence of lichenification

in later stages. There is mounting evidence supporting the role of TGF- β 1 in mediating inflammation as well as subsequent tissue remodeling, often resulting in fibrosis. Given the role of genetic variants in the differential expression of TGF- β 1 in various diseases, this study seeks to ascertain the role of TGF- β 1 promoter variants (rs1800469 and rs1800468) in AD susceptibility, as well as their association with TGF- β 1 mRNA expression, TGF- β 1 serum levels and skin prick test positivity in Atopic Dermatitis patients. **Methods:** An aggregate of 246 subjects including 134 AD cases and 112 matched healthy controls were genotyped for TGF- β 1 promoter polymorphisms by PCR-RFLP. TGF- β 1 mRNA was quantified by quantitative Real-Time PCR (qRT-PCR), Vitamin-D levels by chemiluminescence, and serum TGF- β 1, and total IgE levels were determined by ELISA. In-vivo allergy testing was performed for the evaluation of allergic reactions to house dust mites and food allergens. **Results:** A higher frequency of TT genotypes of rs1800469 (OR = 7.7, $p = 0.0001$) and GA+AA genotypes of rs1800468 (OR = 4.4, $p < 0.0001$) were observed in AD cases than those in controls. Haplotype analysis demonstrated that TG haplotype carriers had an increased risk of AD ($p = 0.013$). Quantitative analysis revealed a significant upregulation of both mRNA ($p = 0.0002$) and serum levels ($p < 0.0001$) of TGF- β 1 with a substantial positive correlation between them (Correlation coefficient=0.504; $p = 0.01$). Moreover, serum TGF- β 1 levels were associated with quality of life ($p = 0.03$), the severity of the disease ($p = 0.03$), and House dust mite allergy ($p = 0.01$) whereas TGF- β 1 mRNA levels positively correlated with disease severity ($p = 0.02$). Stratification analysis revealed that the TT genotype of rs1800469 was associated with higher IgE levels ($p = 0.01$) and eosinophil percentage ($p = 0.007$) whereas the AA genotype of rs1800468 correlated with elevated serum IgE levels ($p = 0.01$). Besides, no significant association of genotypes with mRNA and serum expression of TGF- β 1 was observed. **Conclusion:** Our study indicates that TGF- β 1 promoter SNPs bear a significant risk of AD development. Moreover, upregulation of TGF- β 1 mRNA and serum levels and their association with disease severity, quality of life, and HDM allergy suggests its role as a diagnostic/prognostic biomarker that could help in the development of new therapeutic and prevention strategies.

Hansen's disease presenting as polyneuropathy: an unusual presentation.

Baskar D, Menon D, Rao S, Pal PK.

Avr-2023

Acta Neurol Belg.

<https://pubmed.ncbi.nlm.nih.gov/35157243/>

Morsures de serpent

Changes in Serum Enzymes and Related Mechanisms of Respiratory Dysfunction in Patients after Venomous Snake Bite and Analysis of Anti-Venomous Snake Serum Treatment.

Nong J, Huang Z, Huang Z, Yang J, Li J, Huang D, Wang W. 30-09-2032

Cell Mol Biol (Noisy-le-grand).

<https://pubmed.ncbi.nlm.nih.gov/37114264/>

To explore the changes in serum enzymes in patients with a snake bite, the treatment of respiratory dysfunction, and the clinical effect of anti-snake serum treatment. Fifty snake bite patients admitted to the emergency medicine department were selected and rolled into a light group ($n=27$), heavy group ($n=15$), and critical group ($n=8$). Anti-venomous snake serum was injected intravenously. Patients with severe respiratory dysfunction were treated with mechanical ventilation. The white blood cell (WBC), C-reactive protein (CRP), interleukin-6 (IL-6), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), and creatinine (Cr) counts of the heavy group and the critical group were higher versus light group ($P<0.05$). The WBC, CRP, IL-6, ALT, AST, BUN, and Cr of the critical group were higher versus the heavy group ($P<0.05$). The prothrombin time (PT), activated partial thrombin time (APTT), and thrombin time (TT) of the heavy group and critical group were longer versus the light group ($P<0.05$). The PT, APTT, and TT of the critical group were longer than the heavy group ($P<0.05$). The fibrinogen (FIB) of the light group was higher in contrast to that in the other two groups ($P<0.05$), while the critical group was the lowest ($P<0.05$). In summary, the severity of snakebites in patients can be evaluated according to the indexes of WBC, IL-6, coagulation function, and liver and kidney function.

Clinical aspects of snakebite envenoming and its treatment in low-resource settings.

Warrell DA, Williams DJ.

22-04-2032

Lancet.

<https://pubmed.ncbi.nlm.nih.gov/36931290/>

Rage

Editorial: Zoonotic emerging viral infectious diseases.

Chen JM, Ji YF, Duan ZJ, Wei B.

11-04-2023

Front Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37113559/>

Development and Evaluation of an Enzyme-Linked Immunosorbent Assay Targeting Rabies-Specific IgM and IgG in Human Sera.

Zajac MD, Ortega MT, Moore SM.

29-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112853/>

Orthopoxvirus Circulation in an Endemic Area in Brazil: Investigation of

Infections in Small Mammals during an Absence of Outbreaks.

Domingos IJS, Rocha KLS, Graciano JM, Almeida LR, Doty JB, Paglia AP, Oliveira DB, Nakazawa YJ, Trindade GS.
25-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/37112823/>

Vaccinia virus (VACV) is the causative agent of an emerging viral zoonosis called bovine vaccinia (BV). Several studies have documented characteristics of VACV infections in Brazil; however, the manner in which this virus is maintained in wildlife remains unknown. This work investigated the presence of viral DNA and anti-orthopoxvirus (OPXV) antibodies in samples collected from small mammals in a VACV-endemic area in Minas Gerais, Brazil, in the absence of current outbreaks. Samples did not show amplification of OPXV DNA in molecular tests. However, 5/142 serum samples demonstrated the presence of anti-OPXV neutralizing antibodies in serological tests. These data reinforce the involvement of small mammals in the natural cycle of VACV, highlighting the need for further ecological studies to better understand how this virus is maintained in nature and to develop measures to prevent BV outbreaks.

Reply to Kapur, V. Is Pre-Exposure Prophylaxis a Cost-Effective Intervention to Avert Rabies Deaths among School-Aged Children in India? Comment on "Royal et al. A Cost-Effectiveness Analysis of Pre-Exposure Prophylaxis to Avert Rabies Deaths in School-Aged Children in India. *Vaccines* 2023, 11, 88".

Royal A, John D, Bharti O, Tanwar R, Bhagat DK, Padmawati RS, Chaudhary V, Umapathi R, Bhadola P, Utarini A.

06-04-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112719/>

Developments in Rabies Vaccines: The Path Traversed from Pasteur to the Modern Era of Immunization.

Natesan K, Isloor S, Vinayagamurthy B, Ramakrishnaiah S, Doddamane R, Fooks AR.

29-03-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112668/>

One Health Approach on Dog Bites: Demographic and Associated Socioeconomic Factors in Southern Brazil.

Constantino C, Da Silva EC, Dos Santos DM, Paploski IAD, Lopes MO, Morikawa VM, Biondo AW.

25-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104315/>

A Case Report on a Human Bite Contact with a Rabid Honey Badger *Mellivora capensis* (Kromdraai Area, Cradle of Humankind, South Africa).

Mohale DK, Ngoepe E, Mparamoto M, Blumberg L, Sabeta CT.

24-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104312/>

Spatiotemporal and Seasonal Trends of Class A and B Notifiable Infectious Diseases in China: Retrospective Analysis.

Zheng J, Zhang N, Shen G, Liang F, Zhao Y, He X, Wang Y, He R, Chen W, Xue H, Shen Y, Fu Y, Zhang WH, Zhang L, Bhatt S, Mao Y, Zhu B.

27-04-2023

JMIR Public Health Surveill.

<https://pubmed.ncbi.nlm.nih.gov/37103994/>

Future perspectives of emerging novel drug targets and immunotherapies to control drug addiction.

Malik JA, Agrewala JN.

24-04-2023

Int Immunopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37099943/>

Background: China is the most populous country globally and has made significant achievements in the control of infectious diseases over the last decades. The 2003 SARS epidemic triggered the initiation of the China Information System for Disease Control and Prevention (CISDCP). Since then, numerous studies have investigated the epidemiological features and trends of individual infectious diseases in China; however, few considered the changing spatiotemporal trends and seasonality of these infectious diseases over time. **Objective:** This study aims to systematically review the spatiotemporal trends and seasonal characteristics of class A and class B notifiable infectious diseases in China during 2005-2020. **Methods:** We extracted the incidence and mortality data of 8 types (27 diseases) of notifiable infectious diseases from the CISDCP. We used the Mann-Kendall and Sen's methods to investigate the diseases' temporal trends, Moran I statistic for their geographical distribution, and circular distribution analysis for their seasonality. **Results:** Between January 2005 and December 2020, 51,028,733 incident cases and 261,851 attributable deaths were recorded. Pertussis ($P=.03$), dengue fever ($P=.01$), brucellosis ($P=.001$), scarlet fever ($P=.02$), AIDS ($P<.001$), syphilis ($P<.001$), hepatitis C ($P<.001$) and hepatitis E ($P=.04$) exhibited significant upward trends. Furthermore, measles ($P<.001$), bacillary and amebic dysentery ($P<.001$), malaria ($P=.04$), dengue fever ($P=.006$), brucellosis ($P=.03$), and tuberculosis ($P=.003$) exhibited significant seasonal patterns. We observed marked disease burden-related geographic disparities and heterogeneities. Notably, high-risk areas for various infectious diseases have remained relatively unchanged since 2005. In particular, hemorrhagic fever and brucellosis were largely

concentrated in Northeast China; neonatal tetanus, typhoid and paratyphoid, Japanese encephalitis, leptospirosis, and AIDS in Southwest China; BAD in North China; schistosomiasis in Central China; anthrax, tuberculosis, and hepatitis A in Northwest China; rabies in South China; and gonorrhea in East China. However, the geographical distribution of syphilis, scarlet fever, and hepatitis E drifted from coastal to inland provinces during 2005-2020. **Conclusions:** The overall infectious disease burden in China is declining; however, hepatitis C and E, bacterial infections, and sexually transmitted infections continue to multiply, many of which have spread from coastal to inland provinces.

A recombinant rabies virus chimera expressing the DC-targeting molecular MAB2560 shows enhanced vaccine immunogenicity through activation of dendritic cells.

Gong Z, Huang P, Jin H, Bai Y, Li H, Qian M, Sun J, Jiao C, Zhang M, Li Y, Zhang H, Wang H.

24-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37093869/>

Background: Rabies, caused by the rabies virus (RABV), is an ancient and neglected zoonotic disease posing a large public health threat to humans and animals in developing countries. Immunization of animals with a rabies vaccine is the most effective way to control the epidemic and the occurrence of the disease in humans. Therefore, the development of cost-effective and efficient rabies vaccines is urgently needed. The activation of dendritic cells (DCs) is known to play an important role in improving the host immune response induced by rabies vaccines.

Methodology/principal findings: In this study, we constructed a recombinant virus, rCVS11-MAB2560, based on the reverse genetic system of the RABV CVS11 strain. The MAB2560 protein (a DC-targeting molecular) was chimeric expressed on the surface of the viral particles to help target and activate the DCs when this virus was used as inactivated vaccine. Our results demonstrated that inactivated rCVS11-MAB2560 was able to promote the recruitment and/or proliferation of DC cells, T cells and B cells in mice, and induce good immune memory after two immunizations. Moreover, the inactivated recombinant virus rCVS11-MAB2560 could produce higher levels of virus-neutralizing antibodies (VNAs) in both mice and dogs more quickly than rCVS11 post immunization.

Conclusions/significance: In summary, the recombinant virus rCVS11-MAB2560 chimeric-expressing the molecular adjuvant MAB2560 can stimulate high levels of humoral and cellular immune responses in vivo and can be used as an effective inactivated rabies vaccine candidate.

Rabies post-exposure prophylaxis of international travellers - Results from two major German travel clinics.

Saffar F, Heinemann M, Heitkamp C, Stelzl DR, Ramharter M, Schunk M, Rothe C, Bühler S.

20-04-2023

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37087082/>

Schistosomiasis

A Critical Review on Human Malaria and Schistosomiasis Vaccines: Current State, Recent Advancements, and Developments.

Siddiqui AJ, Bhardwaj J, Saxena J, Jahan S, Snoussi M, Bardakci F, Badraoui R, Adnan M.

04-04-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37112704/>

Malaria and schistosomiasis are two major parasitic diseases that remain leading causes of morbidity and mortality worldwide. Co-infections of these two parasites are common in the tropics, where both diseases are endemic. The clinical consequences of schistosomiasis and malaria are determined by a variety of host, parasitic, and environmental variables. Chronic schistosomiasis causes malnutrition and cognitive impairments in children, while malaria can cause fatal acute infections. There are effective drugs available to treat malaria and schistosomiasis. However, the occurrence of allelic polymorphisms and the rapid selection of parasites with genetic mutations can confer reduced susceptibility and lead to the emergence of drug resistance. Moreover, the successful elimination and complete management of these parasites are difficult due to the lack of effective vaccines against *Plasmodium* and *Schistosoma* infections. Therefore, it is important to highlight all current vaccine candidates undergoing clinical trials, such as pre-erythrocytic and erythrocytic stage malaria, as well as a next-generation RTS,S-like vaccine, the R21/Matrix-M vaccine, that conferred 77% protection against clinical malaria in a Phase 2b trial. Moreover, this review also discusses the progress and development of schistosomiasis vaccines. Furthermore, significant information is provided through this review on the effectiveness and progress of schistosomiasis vaccines currently under clinical trials, such as Sh28GST, Sm-14, and Sm-p80. Overall, this review provides insights into recent progress in malarial and schistosomiasis vaccines and their developmental approaches.

Molluscicidal and Larvicidal Potency of N-Heterocyclic Analogs against Biomphalaria alexandrina Snails and Schistosoma mansoni Larval Stages.

Sheir SK, Elmongy EI, Mohamad AH, Osman GY, Bendary SE, Ahmed AAS, Binsuwaidan R, El-Sayed IE.

10-04-2023

Pharmaceutics.

<https://pubmed.ncbi.nlm.nih.gov/37111685/>

This work describes the synthesis of quinoline-based N-heterocyclic arenes and their biological evaluation as molluscicides against adult *Biomphalaria alexandrina* snails as well as larvicides against *Schistosoma mansoni* larvae (miracidia and cercariae). Molecular docking studies

were demonstrated to investigate their affinity for cysteine protease protein as an interesting target for antiparasitics. Compound **AEAN** showed the best docking results followed by **APAN** in comparison to the co-crystallized ligand D1R reflected by their binding affinities and RMSD values. The egg production, hatchability of *B. alexandrina* snails and ultrastructural topography of *S. mansoni* cercariae using SEM were assessed. Biological evaluations (hatchability and egg-laying capacity) revealed that the quinoline hydrochloride salt **CAAQ** was the most effective compound against adult *B. alexandrina* snails, whereas the indolo-quinoline derivative **APAN** had the most efficiency against miracidia, and the acridinyl derivative **AEAA** was the most effective against cercariae and caused 100% mortality. **CAAQ** and **AEAA** were found to modulate the biological responses of *B. alexandrina* snails with/without *S. mansoni* infection and larval stages that will affect *S. mansoni* infection. **AEAA** caused deleterious morphological effects on cercariae. **CAAQ** caused inhibition in the number of eggs/snail/week and reduced reproductive rate to 43.8% in all the experimental groups. **CAAQ** and **AEAA** can be recommended as an effective molluscicide of plant origin for the control program of schistosomiasis.

Establishment of a Simple and Rapid Nucleic Acid Detection Method for Hookworm Identification.

Ding X, Yang Y, Zhang Y, Zhang Q, Mao F, Dai Y.

21-04-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111516/>

HGPRT and PNP: Recombinant Enzymes from *Schistosoma mansoni* and Their Role in Immunotherapy during Experimental Murine Schistosomiasis.

de Lima Fragelli BD, Fattori ACM, de Almeida Montija E, de Almeida Rodolpho JM, de Castro CA, de Godoy KF, Nogueira CT, Rodrigues V, Soares EG, Romanello L, Torini JR, Pereira HD, de Freitas Anibal F.

29-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111413/>

Schistosomiasis is a parasitic infection caused by trematode worms (also called blood flukes) of the genus *Schistosoma* sp., which affects over 230 million people worldwide, causing 200,000 deaths annually. There is no vaccine or new drugs available, which represents a worrying aspect, since there is loss of sensitivity of the parasite to the medication recommended by the World Health Organization, Praziquantel. The present study evaluated the effects of the recombinant enzymes of *S. mansoni* Hypoxanthine-Guanine Phosphoribosyltransferase (HGPRT), Purine Nucleoside Phosphorylase (PNP) and the MIX of both enzymes in the immunotherapy of schistosomiasis in murine model. These enzymes are part of the purine salvage pathway, the only metabolic pathway present in the parasite for this purpose, being essential for the synthesis of DNA and RNA. Female mice of Swiss and BALB/c strains were infected

with cercariae and treated, intraperitoneally, with three doses of 100 µg of enzymes. After the immunotherapy, the eggs and adult worms were counted in the feces; the number of eosinophils from the fluid in the peritoneal cavity and peripheral blood was observed; and the quantification of the cytokine IL-4 and the production of antibodies IgE was analyzed. The evaluation of the number of granulomas and collagen deposition via histological slides of the liver was performed. The results demonstrate that immunotherapy with the enzyme HGPRT seems to stimulate the production of IL-4 and promoted a significant reduction of granulomas in the liver in treated animals. The treatment with the enzyme PNP and the MIX was able to reduce the number of worms in the liver and in the mesenteric vessels of the intestine, to reduce the number of eggs in the feces and to negatively modulate the number of eosinophils. Therefore, immunotherapy with the recombinant enzymes of *S. mansoni* HGPRT and PNP might contribute to the control and reduction of the pathophysiological aspects of schistosomiasis, helping to decrease the morbidity associated with the infection in murine model.

Correlation of Cytokines with Parasitic Infections, Undernutrition and Micronutrient Deficiency among Schoolchildren in Rural Tanzania: A Cross-Sectional Study.

Mrimi EC, Palmeirim MS, Minja EG, Long KZ, Keiser J.

15-04-2023

Nutrients.

<https://pubmed.ncbi.nlm.nih.gov/37111135/>

Two Molecular Plasma-Based Diagnostic Methods to Evaluate Early Infection of *Schistosoma japonicum* and Schistosomiasis Japonica.

Hong Y, Guo Q, Zhou X, Tang L, Chen C, Shang Z, Zhou K, Zhang Z, Liu J, Lin J, Xu B, Chen JH, Fu Z, Hu W.

18-04-2022

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/37110482/>

The prevalence and infectious intensity of schistosomiasis japonica has decreased significantly in China in the past few decades. However, more accurate and sensitive diagnostic methods are urgently required for the further control, surveillance, and final elimination of the disease. In this study, we assessed the diagnostic efficacy of a real-time fluorescence quantitative PCR (qPCR) method and recombinase polymerase amplification (RPA) combined with a lateral-flow dipstick (LFD) assay for detecting early infections of *Schistosoma japonicum* and different infection intensities. The sensitivity of the qPCR at 40 days post-infection (dpi) was 100% (8/8) in mice infected with 40 cercariae, which was higher than in mice infected with 10 cercariae (90%, 9/10) or five cercariae (77.8%, 7/9). The results of the RPA-LFD assays were similar, with sensitivities of 55.6% (5/9), 80% (8/10), and 100% (8/8) in mice infected with 5, 10, and 40 cercariae, respectively. In goats, both the qPCR and RPA-LFD assays showed 100% (8/8) sensitivity at 56 dpi. In the early detection of *S.*

japonicum infection in mice and goats with qPCR, the first peak in positivity appeared at 3-4 dpi, when the positivity rate exceeded 40%, even in the low infection, intensity mice. In the RPA-LFD assays, positive results first peaked at 4-5 dpi in the mice, and the positivity rate was 37.5% in the goats at 1 dpi. In conclusion, neither of the molecular methods produced exceptional results for the early diagnosis of *S. japonicum* infection. However, they were useful methods for the regular diagnosis of schistosomiasis in mice and goats.

Programmatic Implications for Schistosomiasis Elimination Based on Community-Based Survey in the Blue Nile, North Kordofan, and Sennar States, Sudan.

Ismail HAHA, Cha S, Jin Y, Hong ST.

19-04-2023

Life (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37109578/>

Schistosomiasis prevalence has remained high in some areas due to reinfection despite repeated mass drug administration interventions. We aimed to explore its risk factors in order to help to design adequate interventions in such high-transmission areas. A total of 6225 individuals residing in 60 villages in 8 districts of North Kordofan, Blue Nile, or Sennar States, Sudan participated in the community-based survey in March 2018. First, we investigated *Schistosoma haematobium* and *Schistosoma mansoni* prevalences among school-aged children and adults. Second, the associations between risk factors and schistosomiasis were explored. Those without any type of latrine in their households had higher odds of being infected with schistosomiasis than those with a latrine (odds ratio (OR) = 1.53; 95% confidence interval (CI) 1.20-1.94; $p = 0.001$), and the odds of being positive for schistosomiasis among people living in a household without an improved latrine were higher than for their counterparts with an improved latrine (OR = 1.63; CI 1.05-2.55; $p = 0.03$). Furthermore, people with households or outside compounds found to contain human faeces had higher odds of being infected with schistosomiasis than their counterparts (OR = 1.36, 95% CI 1.01-1.83, $p = 0.04$). Installing an improved latrine and eliminating open defecation should be highlighted in schistosomiasis elimination projects in high-transmission areas.

Impact of the National Wetland Park in the Poyang Lake Area on *Oncomelania hupensis*, the Intermediate Host of *Schistosoma japonicum*.

Li Z, Wen Y, Lin D, Hu F, Wang Q, Li Y, Zhang J, Liu K, Li S.

27-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104320/>

Prevalence and risk distribution of schistosomiasis among adults in Madagascar: a cross-sectional study.

Gruninger SK, Rasamoelina T, Rakotoarivelo RA, Razafindrakoto AR, Rasolojaona ZT, Rakotozafy RM, Soloniaina PR, Rakotozandrindrainy N, Rausche P, Doumbia CO, Jaeger A, Zerbo A, von Thien H, Klein P, van Dam G, Tannich E, Schwarz NG, Lorenz E, May J, Rakotozandrindrainy R, Fusco D.

25-04-2023

Infect Dis Poverty.

<https://pubmed.ncbi.nlm.nih.gov/37098581/>

Spectrum of Helminth Infections in Migrants from Sub-Saharan Africa to Europe: A Literature Review.

Grzegorek K, Kroidl I, Prazeres da Costa C, Rothe C.

24-04-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37094791/>

Sub-Saharan Africa (SSA) is endemic to numerous neglected tropical diseases, including many helminth diseases. With the migration of people from this part of the world to Europe, as has been happening on a large scale since 2015, these diseases are becoming more relevant to European physicians. This work aims to summarize the recent literature on this topic and to raise awareness of helminth diseases afflicting SSA migrants. The databases PubMed, Embase, and MEDLINE were screened for literature published in English and German between January 1, 2015 and December 31, 2020. In total, 74 articles were included in this review. The spectrum of helminth infections in migrants from SSA found in the literature review is broad; current research, however, is particularly focused on infections with *Schistosoma* spp. and *Strongyloides stercoralis*. Both diseases are often characterized by a long course, with few or no symptoms, with the risk of long-term organ damage. Successful and reliable screening for schistosomiasis and strongyloidiasis is strongly recommended. However, the current diagnostic methods lack sensitivity and specificity, rendering the diagnosis challenging and reliable assessment of disease prevalence difficult. Novel diagnostic methods and a greater awareness of these diseases are urgently needed.

A Simple Purification Method for Heat-Stable Recombinant Low Molecular Weight Proteins and Peptides Via GST-Fusion Products.

Okoto PS, Sonniata S, Sakhel B, Muhoza D, Adams P, Kumar TKS.

2023

Methods Mol Biol.

<https://pubmed.ncbi.nlm.nih.gov/37093474/>

Characteristics of Th9 cells in *Schistosoma japonicum*-infected C57BL/6 mouse mesenteric lymph node.

Qiu H, Wang R, Xing J, Li L, Gao Z, Li J, Fang C, Shi F, Mo F, Liu L, Zhao Y, Xie H, Zhao S, Huang J.

20-04-2032

Mol Biochem Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37086898/>

Interleukin 9 (IL-9) is an effective cytokine secreted by newly defined Th9 cells, which is involved in allergic and infectious diseases. In this study, lymphocytes were isolated from mesenteric lymph node (MLN), spleen, liver, lung, and Peyer's patches (PP) of C57BL/6 mice 5-6 weeks after *S. japonicum* infection, intracellular cytokine staining was done to detect the percentage of IL-9-producing CD4⁺ T cells. The qPCR and ELISA were used to verify the content of IL-9 in MLN. The population of IL-9-producing lymphocyte subset was identified by FACS. In addition, the dynamic changes and cytokine profiles of Th9 cells in the MLN of infected mice were detected by FACS. ELISA was used to detect IL-9 induced by soluble egg antigen (SEA) from isolated lymphocytes in mouse MLN. The results showed that the percentage of IL-9-secreting Th9 cells in the MLN of the infected mouse was higher than that in the spleen, liver, lung, or PP. Though CD8⁺ Tc cells, NKT cells, and γ δT cells could secrete IL-9, CD4⁺ Th cells were the main source of IL-9 in *S. japonicum*-infected C57BL/6 mice ($P < 0.05$). The percentage of Th9 cells in MLN of infected mouse increased from week 3-4, and reached a peak at week 5-6, then began to decrease from week 7-8 ($P < 0.05$). Moreover, Th9 cells could also secrete a small amount of IL-4, IFN- γ , IL-5, and IL-10. Our results suggested a higher percentage of Th9 cells was induced in the MLN of *S. japonicum*-infected mice, which might play an important role in the early stage of *S. japonicum*-induced disease.

Perspective on Schistosomiasis Drug Discovery: Highlights from a Schistosomiasis Drug Discovery Workshop at Wellcome Collection, London, September 2022.

Caldwell N, Afshar R, Baragaña B, Bustinduy AL, Caffrey CR, Collins JJ, Fusco D, Garba A, Gardner M, Gomes M, Hoffmann KF, Hsieh M, Lo NC, McNamara CW, Nono JK, Padalino G, Read KD, Roestenberg M, Spangenberg T, Specht S, Gilbert IH.

21-04-2023

ACS Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37083395/>

Ultrasound aspects and risk factors associated with urogenital schistosomiasis among primary school children in Mali.

Agniwo P, Sidibé B, Diakité A, Niaré SD, Guindo H, Akplogan A, Ibikounlé M, Boissier J, Dabo A.

20-04-2023

Infect Dis Poverty.

<https://pubmed.ncbi.nlm.nih.gov/37081494/>

Background: Urogenital schistosomiasis is endemic in Mali and is a major cause of serious morbidity in large parts of the world. This disease is responsible for many socio-economic and public health issues. The aim of this study was to investigate the impact of the disease on morbidity and to describe demographic and socioeconomic factors in relation to the status of children with urogenital schistosomiasis in Mali. **Methods:** We conducted a cross-

sectional study in November 2021 of 971 children aged 6 to 14 years selected at random from six schools in three districts in the Kayes Region of Mali. Demographic and socioeconomic data were collected on survey forms. Clinical data were collected following a medical consultation. Hematuria was systematically searched for through the use of strips. The search for *Schistosoma haematobium* eggs in urine was done via the filtration method. The urinary tract was examined by ultrasound. Associations between each of these variables and disease infection were tested using multivariate logistic regression. **Results:** The overall prevalence of urinary schistosomiasis detected was 50.2%. The average intensity of infection was 36 eggs/10 ml of urine. The associated risk factors for urogenital schistosomiasis showed that children who bathed, used the river/pond as a domestic water source, and who habitually urinated in the river/pond were more affected ($P < 0.05$). Children with farming parents were most affected ($P = 0.032$). The collection of clinical signs revealed that boys had more pollakiuria (58.6%) and dysuria (46.4%) than girls. Ultrasound data showed that focal lesion rates were recorded in all villages with the lowest rate in Diakalel (56.1%). Ultrasound and parasitological findings showed that irregularity and thickening were strongly associated with urinary schistosomiasis ($P < 0.0001$). **Conclusions:** *Schistosoma haematobium* infection was still endemic in the study site despite more than a decade of mass treatment with praziquantel. However, the high percentage of symptoms associated with high intensity reinforces the idea that further studies in terms of schistosomiasis-related morbidity are still needed.

Repetitive schistosoma exposure causes perivascular lung fibrosis and persistent pulmonary hypertension.

Kumar R, Lee MH, Kassa B, Fonseca Balladares DC, Mickael C, Sanders L, Andruska A, Kumar M, Spiekerkoetter E, Bandeira A, Stenmark KR, Tuder RM, Graham BB.

26-04-2032

Clin Sci (Lond).

<https://pubmed.ncbi.nlm.nih.gov/37014925/>

Background: Pulmonary hypertension (PH) can occur as a complication of schistosomiasis. In humans, schistosomiasis-PH persists despite antihelminthic therapy and parasite eradication. We hypothesized that persistent disease arises as a consequence of exposure repetition. **Methods:** Following intraperitoneal sensitization, mice were experimentally exposed to *Schistosoma* eggs by intravenous injection, either once or three times repeatedly. The phenotype was characterized by right heart catheterization and tissue analysis. **Results:** Following intraperitoneal sensitization, a single intravenous *Schistosoma* egg exposure resulted in a PH phenotype that peaked at 7-14 days, followed by spontaneous resolution. Three sequential exposures resulted in a persistent PH phenotype. Inflammatory cytokines were not significantly different between mice exposed to one or three egg doses, but there was an increase in perivascular fibrosis in those who received three egg doses. Significant perivascular fibrosis was also

observed in autopsy specimens from patients who died of this condition. **Conclusions:** Repeatedly exposing mice to schistosomiasis causes a persistent PH phenotype, accompanied by perivascular fibrosis. Perivascular fibrosis may contribute to the persistent schistosomiasis-PH observed in humans with this disease.

CD193 (CCR3) expression by B cells correlates with reduced IgE production in paediatric schistosomiasis.

Onkanga IO, Sang H, Hamilton R, Ondigo BN, Jaoko W, Odiere MR, Ganley-Leal L.

Mai-2023

Parasite Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36971331/>

Trachome

Meandered and muddled: a systematic review on the impact of air pollution on ocular health.

Muruganandam N, Mahalingam S, Narayanan R, Rajadurai E.

25-04-2023

Environ Sci Pollut Res Int.

<https://pubmed.ncbi.nlm.nih.gov/37097565/>

From the years 1970-2023, a systematic overview of the diverse consequences of particulate matter on eye health and a disease classification according to acute, chronic, and genetic are presented using the PubMed, Research Gate, Google Scholar, and Science Direct databases. Various studies on medical aspects correlate with the eye and health. However, from an application perspective, there is limited research on the ocular surface and air pollution. The main objective of the study is to uncover the relationship between eye health and air pollution, particularly particulate matter, along with other external factors acting as aggravators. The secondary goal of the work is to examine the existing models for mimicking human eyes. The study is followed by a questionnaire survey in a workshop, in which the exposure-based investigation was tagged based on their activity. This paper establishes a relationship between particulate matter and its influence on human health, leading to numerous eye diseases like dry eyes, conjunctivitis, myopia, glaucoma, and trachoma. The results of the questionnaire survey indicate that about 68% of the people working in the workshop are symptomatic with tears, blurred vision, and mood swings, while 32% of the people were asymptomatic. Although there are approaches for conducting experiments, the evaluation is not well defined; empirical and numerical solutions for particle deposition on the eye are needed. There prevails a broad gap in the arena of ocular deposition modeling.

Trématodoses d'origine alimentaire (clonorchiose, opisthorchiose, fasciolose et paragonimose)

Establishment of a Simple and Rapid Nucleic Acid Detection Method for Hookworm Identification.

Ding X, Yang Y, Zhang Y, Zhang Q, Mao F, Dai Y.

21-04-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111516/>

Intra-Species Variations of Bioactive Compounds of Two Dictyota Species from the Adriatic Sea: Antioxidant, Antimicrobial, Dermatological, Dietary, and Neuroprotective Potential.

Martić A, Čižmek L, Ul'yanovskii NV, Paradžik T, Perković L, Matijević G, Vujović T, Baković M, Babić S, Kosyakov DS, Trebše P, Čož-Rakovac R.

01-04-2023

Antioxidants (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37107232/>

The marine environment has a significant impact on life on Earth. Organisms residing in it are vital for the ecosystem but also serve as an inexhaustible source of biologically active compounds. Herein, the biodiversity of two brown seaweeds, *Dictyota dichotoma* and *Dictyota fasciola* from the Adriatic Sea, was evaluated. The aim of the study was the determination of differences in compound composition while comparing their activities, including antioxidant, antimicrobial, and enzyme inhibition, in connection to human digestion, dermatology, and neurological disorders. Chemical analysis revealed several terpenoids and steroids as dominant molecules, while fucoxanthin was the main identified pigment in both algae. *D. dichotoma* had higher protein, carbohydrate, and pigment content. Omega-6 and omega-3 fatty acids were identified, with the highest amount of dihomo- γ -linolenic acid and α -linolenic acid in *D. dichotoma*. Antimicrobial testing revealed a dose-dependent inhibitory activity of methanolic fraction against *Escherichia coli* and *Staphylococcus aureus*. Moderate antioxidant activity was observed for both algae fractions, while the dietary potential was high, especially for the *D. fasciola* dichloromethane fraction, with inhibition percentages of around 92% for α -amylase and 57% for pancreatic lipase at 0.25 mg/mL. These results suggest that *Dictyota* species might be a potent source of naturally derived agents for obesity and diabetes.

Correction: Perakanya et al. Prevalence and Risk Factors of Opisthorchis viverrini Infection in Sakon Nakhon

Province, Thailand. Trop. Med. Infect. Dis. 2022, 7, 313.

Perakanya P, Ungcharoen R, Worabannakorn S, Ongari P, Artchayasawat A, Boonmars T, Boueroy P.

11-04-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104365/>

Prevalence of Human and Animal Fasciolosis in Butajira and Gilgel Gibe Health Demographic Surveillance System Sites in Ethiopia.

Abaya SW, Mereta ST, Tulu FD, Mekonnen Z, Ayana M, Girma M, Vineer HR, Mor SM, Caminade C, Graham-Brown J.

30-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104334/>

Characterization of Monoamine Oxidase-A in tropical liver fluke, *Fasciola gigantica*.

Beg MA, Rehman A, Rehman L, Ullah R, Farhat F, Wasim S, Abidi SMA.

27-03-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37104309/>

Fasciola gigantica, responsible for the zoonotic disease fasciolosis, pose a great threat to the livestock and human health worldwide. The triclabendazole (TCBZ) has been used for decades as a broad spectrum anthelmintic to control this perilous disease but the emergence of resistance in flukes against TCBZ has prompted researchers across the world to explore for new drugs and antigenic targets. World Health Organization has strongly recommended the utilization of neurobiologically significant biomolecules as new drug/antigenic targets because of their significant role in the physiology of parasites. Monoamine Oxidase (MAO) is an important neurobiological enzyme which catabolizes aminergic neurotransmitters thus preventing prolonged excitation of neurons and in non-neuronal cells it prevents cellular toxicity due to accumulation of toxic monoamines. Owing to the important role of MAO in the survival and perpetuation of parasites, multipronged approaches were undertaken for the characterization of MAO-A in *F. gigantica*. The activity of MAO was found to be 1.5 times higher in the mitochondrial samples than the whole homogenate samples. The adult worms of the *F. gigantica* appeared to possess both the isoforms of MAO i.e., MAO-A and MAO-B. The zymographic studies revealed strong enzyme activity in its native state as assessed through prominent dark bands at 250KDa in the zymogram. The enzyme was also found to be highly immunogenic as revealed by high antibody titer at 1:6400 dilution. The immunogenicity of MAO-A enzyme was further established in the Western Blots in which a strong band of 50KDa was distinctly evident. Despite ubiquitous presence of MAO in *F. gigantica* some regions like tegumental surface and intestinal caecae displayed strong immunofluorescence as compared to other regions. The

detection of MAO-A in the *F. gigantica* samples in Dot-Blot assay indicate a great potential of this molecule for the immunodiagnostics of fasciolosis, particularly in the field conditions. The enzyme activity was sensitive to the specific inhibitor clorgyline in a concentration dependant manner, particularly in the late incubation period. The zymographic results also exhibited similar trend. The strong intensity of spots in Dot-blot indicate high immunogenicity of the MAO protein. The intensity of bands/spots in the samples of worms treated with clorgyline also declined, clearly indicating that the tropical liver fluke possesses prominent MAO-A activity.

Mitogenomic and nuclear ribosomal transcription unit datasets support the synonymy of *Paragonimus iloktsuenensis* and *P. ohirai* (Paragonimidae: Platyhelminthes).

Le TH, Nguyen KT, Pham LTK, Doan HTT, Roan DT, Le XTK, Agatsuma T, Blair D.

27-04-2032

Parasitol Res.

<https://pubmed.ncbi.nlm.nih.gov/37101088/>

The complete mitogenome (mtDNA) of nominal *Paragonimus iloktsuenensis* (Paragonimidae: Trematoda) and the nuclear ribosomal transcription unit (rTU) coding region (rTU*: from 5'-terminus of 18S to 3'-terminus of 28S rRNA gene, excluding the external spacer region) of this species and of *P. ohirai* were obtained and used to further support the previously suggested synonymy of these taxa in the *P. ohirai* complex. The complete mitogenome of *P. iloktsuenensis* was 14,827 bp long (GenBank: ON961029) and nearly identical to that of *P. ohirai* (14,818 bp; KX765277), with a 99.12% nucleotide identity. The rTU* was 7543 bp and 6932 bp in these two taxa, respectively. All genes and spacers in the rTU were identical in length, with exception of the first internal transcribed spacer, which contained multiple tandem repeat units (6.7 for *P. iloktsuenensis* and 5.7 for *P. ohirai*). There was near 100% identity for the rTU genes. The phylogenetic topology inferred from the mtDNA and from individual gene regions (partial *cox1* of 387 bp and the ITS-2 of 282 bp - 285 bp) indicated a very close relationship consistent with synonymy of *P. iloktsuenensis* and *P. ohirai*. The datasets provided here will be useful for taxonomic reappraisal as well as studies of evolutionary and population genetics of the genus *Paragonimus* and family Paragonimidae.

***Clonorchis sinensis* granulin promotes malignant transformation of human intrahepatic biliary epithelial cells through interaction with M2 macrophages via regulation of STAT3 phosphorylation and the MEK/ERK pathway.**

He Q, Pan X, Yin Y, Xu A, Yi X, Wu Y, Li X.

24-04-2032

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37095578/>

Prevalence and hepatic histopathological findings of fascioliasis in sheep slaughtered in Jeddah, Saudi Arabia.

Ashoor SJ, Wakid MH.

24-04-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37095133/>

Hepatic fascioliasis is an important parasitic disease responsible for morbidity and mortality in many domestic ruminants, especially sheep, goats, and cattle, due to *Fasciola* (F.) *hepatica* and *F. gigantica*. This study aimed to determine the prevalence of fascioliasis in sheep slaughtered in Jeddah, Saudi Arabia, and to describe the morphological and histopathological changes in the liver. A total of 109,253 sheep slaughtered between July 2017 and July 2018 were screened to assess the prevalence of fascioliasis. The livers were grossly investigated for *Fasciola* infection and morphological changes. Tissue samples were collected for proper histopathological examinations. Livers of local and imported sheep represented infection rates of 0.67% and 2.12%, respectively, and the highest infection rate was in the spring season. Macroscopically, the affected liver showed hepatomegaly, thickened capsule and discoloration with necrosis, fibrosis, dilation of the bile duct, engorgement of the gallbladder and enlargement of the portal lymph nodes. Microscopic examination showed fibrotic thickening, calcification and hyperplasia of the bile ducts filled with debris, as well as massive hemorrhagic foci. Histopathological examinations of the infected liver showed a central vein region with disturbed parenchyma cells, focal lymphocytic infiltration, elongated endothelial cells, blood sinusoids that showed enlarged Kupffer cells, patches of lysed or necrotic hepatocytes, eosinophil infiltration, lymphocytes and proliferating fibroblast, thickening of hepatic artery and arteriolar walls. We concluded that fascioliasis among sheep slaughtered in Jeddah is not uncommon. The identified histopathological changes in the liver of infected sheep reflect tissue damage, which can lead to significant economic losses for the animals.

Fasciola hepatica juveniles interact with the host fibrinolytic system as a potential early-stage invasion mechanism.

Serrat J, Becerro-Recio D, Torres-Valle M, Simón F, Valero MA, Bargues MD, Mas-Coma S, Siles-Lucas M, González-Miguel J.

21-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37083884/>

Development and application of a new liver pathology recording system for use in cattle abattoirs.

Owen H, Jones E, Kowald C, Hand S, McGowan M, Cobbold R, Barnes TS, Gibson JS, Ranjbar S, Palmieri C, Allavena R.

Mai-2023

Res Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37023570/>

Trypanosomes (trypanosomiasis et maladie de Chagas)

Poly-ε-caprolactone Implants for Benznidazole Prolonged Release: An Alternative to Chagas Disease Oral Treatment.

Mazzeti AL, Gonçalves KR, Boasquívís PF, Barbosa J, Pereira BG, Soeiro MNC, Mosqueira VCF, Bahia MT.

02-04-2023

Pharmaceutics.

<https://pubmed.ncbi.nlm.nih.gov/37111612/>

Benznidazole (BZ) tablets are the currently prescribed treatment for Chagas disease. However, BZ presents limited efficacy and a prolonged treatment regimen with dose-dependent side effects. The design and development of new BZ subcutaneous (SC) implants based on the biodegradable poly-ε-caprolactone (PCL) is proposed in this study for a controlled release of BZ and to improve patient compliance. The BZ-PCL implants were characterized by X-ray diffraction, differential scanning calorimetry, and scanning electron microscopy, which indicated that BZ remains in its crystalline state dispersed in the polymer matrix with no polymorphic transitions. BZ-PCL implants, even at the highest doses, induce no alteration of the levels of hepatic enzymes in treated animals. BZ release from implants to blood was monitored in plasma during and after treatment in healthy and infected animals. Implants at equivalent oral doses increase the body's exposure to BZ in the first days compared with oral therapy, exhibiting a safe profile and allowing sustained BZ concentrations in plasma to induce a cure of all mice in the experimental model of acute infection by the Y strain of *T. cruzi*. BZ-PCL implants have the same efficacy as 40 daily oral doses of BZ. Biodegradable BZ implants are a promising option to reduce failures related to poor adherence to treatment, with more comfort for patients, and with sustained BZ plasma concentration in the blood. These results are relevant for optimizing human Chagas disease treatment regimens.

Evaluation of Molecular Methods to Identify Chagas Disease and Leishmaniasis in Blood Donation Candidates in Two Brazilian Centers.

Ferreira JGG, Costa SCB, Addas-Carvalho M, Pereira MB, França AO, de Lima RG, Andrade PD, Wanderley JDS, Martins LC, de Almeida EA, Marcon GEB.

24-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/37111394/>

Meroterpenoids from *Gongolaria abies-marina* against Kinetoplastids: In Vitro Activity and Programmed Cell Death Study.

Nicolás-Hernández DS, Rodríguez-Expósito RL, López-Arencibia A, Bethencourt-Estrella CJ, Sifaoui I, Salazar-Villatoro L, Omaña-Molina M, Fernández JJ, Díaz-Marrero AR, Piñero JE, Lorenzo-Morales J.
23-03-2023

Pharmaceuticals (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37111233/>

Leishmaniasis and Chagas disease affect millions of people worldwide. The available treatments against these parasitic diseases are limited and display multiple undesired effects. The brown alga belonging to the genus *Gongolaria* has been previously reported as a source of compounds with different biological activities. In a recent study from our group, *Gongolaria abies-marine* was proven to present antiamebic activity. Hence, this brown alga could be a promising source of interesting molecules for the development of new antiprotozoal drugs. In this study, four meroterpenoids were isolated and purified from a dichloromethane/ethyl acetate crude extract through a bioguided fractionation process targeting kinetoplastids. Moreover, the in vitro activity and toxicity were evaluated, and the induction of programmed cell death was checked in the most active and less toxic compounds, namely gongolarone B (2), 6Z-1'-methoxyamentadione (3) and 1'-methoxyamentadione (4). These meroterpenoids triggered mitochondrial malfunction, oxidative stress, chromatin condensation and alterations of the tubulin network. Furthermore, a transmission electron microscopy (TEM) image analysis showed that meroterpenoids (2-4) induced the formation of autophagy vacuoles and ER and Golgi complex disorganization. The obtained results demonstrated that the mechanisms of action at the cellular level of these compounds were able to induce autophagy as well as an apoptosis-like process in the treated parasites.

Comparative Assessment of Two Commercial Real-Time PCR Assays for the Diagnosis of *Trypanosoma cruzi* DNA in Serum.

Kann S, Concha G, Weinreich F, Hahn A, Rückert C, Kalinowski J, Landt O, Frickmann H.
30-03-2023

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/37110326/>

This study was performed to comparably assess two commercial real-time PCR assays for the identification of *Trypanosoma cruzi* DNA in serum. A total of 518 Colombian serum samples with high pre-test probability for infections with either *T. cruzi* or apathogenic *Trypanosoma rangeli* were assessed. The assessment comprised the NDO real-time PCR (TIB MOLBIOL, ref. no. 53-0755-96, referred to as the TibMolBiol assay in the following) with specificity for *T. cruzi* and the RealStar Chagas PCR Kit 1.0 (altona DIAGNOSTICS, order no. 611013, referred to as the RealStar assay in the following) targeting a kinetoplast sequence of both *T. cruzi* and *T. rangeli* without further discrimination. To discriminate between *T. cruzi*- and *T. rangeli*-specific real-time PCR amplicons, Sanger sequencing results were available for a minority of cases with discordant real-time PCR results, while the amplicons of the remaining discordant samples

were subjected to nanopore sequencing. The study assessment indicated a proportion of 18.1% (n = 94) *T. cruzi*-positive samples next to 24 samples (4.6%) containing DNA of the phylogenetically related but apathogenic parasite *T. rangeli*. The observed diagnostic accuracy as expressed by sensitivity and specificity was 97.9% (92/94) and 99.3% (421/424) with the TibMolBiol assay and 96.8% (91/94) and 95.0% (403/424) with the RealStar assay, respectively. Reduced specificity resulted from cross-reaction with *T. rangeli* in all instances (3 cross-reactions with the TibMolBiol assay and 21 cross-reactions with the RealStar assay). DNA from the six discrete typing units (DTUs) of *T. cruzi* was successfully amplified by both real-time PCR assays. In summary, both assays showed a comparable diagnostic accuracy for the diagnosis of *T. cruzi* from human serum, with a slightly higher specificity seen for the TibMolBiol assay. The pronounced co-amplification of DNA from apathogenic *T. rangeli* according to the RealStar assay may be a disadvantage in areas of co-circulation with *T. cruzi*, while the test performance of the two compared assays will be quite similar in geographic settings where *T. rangeli* infections are unlikely.

Detection of Pathogens and Ticks on Sedentary and Migratory Birds in Two Corsican Wetlands (France, Mediterranean Area).

Defaye B, Moutailler S, Vollot B, Galon C, Gonzalez G, Moraes RA, Leoncini AS, Rataud A, Le Guillou G, Pasqualini V, Quilichini Y.

28-03-2023

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/37110292/>

Increased *Trypanosoma cruzi* Growth during Infection of Macrophages Cultured on Collagen I Matrix.

Logullo J, Diniz-Lima I, Rocha JDB, Cortê-Real S, Silva-Júnior EBD, Guimarães-de-Oliveira JC, Morrot A, Fonseca LMD, Freire-de-Lima L, Decote-Ricardo D, Freire-de-Lima CG.

21-04-2023

Life (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37109592/>

The interactions between cell and cellular matrix confers plasticity to each body tissue, influencing the cellular migratory capacity. Macrophages rely on motility to promote their physiological function. These phagocytes are determinant for the control of invasive infections, and their immunological role largely depends on their ability to migrate and adhere to tissue. Therefore, they interact with the components of the extracellular matrix through their adhesion receptors, conferring morphological modifications that change their shape during migration. Nevertheless, the need to use in vitro cell growth models with the conditioning of three-dimensional synthetic matrices to mimic the dynamics of cell-matrix interaction has been increasingly studied. This becomes more important to effectively understand the changes occurring in phagocyte morphology in the context of infection

progression, such as in Chagas disease. This disease is caused by the intracellular pathogen *Trypanosoma cruzi*, capable of infecting macrophages, determinant cells in the anti-trypanosomatid immunity. In the present study, we sought to understand how an in vitro extracellular matrix model interferes with *T. cruzi* infection in macrophages. Using different time intervals and parasite ratios, we evaluated the cell morphology and parasite replication rate in the presence of 3D collagen I matrix. Nevertheless, microscopy techniques such as scanning electron microscopy were crucial to trace macrophage-matrix interactions. In the present work, we demonstrated for the first time that the macrophage-matrix interaction favors *T. cruzi* in vitro replication and the release of anti-inflammatory cytokines during macrophage infection, in addition to drastically altering the morphology of the macrophages and promoting the formation of migratory macrophages.

Genetic Ablation and Pharmacological Blockade of Bradykinin B1 Receptor Unveiled a Detrimental Role for the Kinin System in Chagas Disease Cardiomyopathy.

Oliveira AC, Vicentino ARR, Andrade D, Pereira IR, Saboia-Vahia L, Moreira ODC, Carvalho-Pinto CE, Mota JBD, Maciel L, Vilar-Pereira G, Pesquero JB, Lannes-Vieira J, Sirois P, Campos de Carvalho AC, Scharfstein J.

15-04-2023

J Clin Med.

<https://pubmed.ncbi.nlm.nih.gov/37109224/>

Phytochemical Screening, GC-MS Analysis, and Evaluating In Vivo Antitrypanosomal Effects of a Methanolic Extract of Garcinia kola Nuts on Rats.

Rufa'i FA, Baecker D, Mukhtar MD.

06-04-2023

Antibiotics (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37107074/>

Cardiac Magnetic Resonance Imaging Detects Myocardial Abnormalities in Naturally Infected Dogs with Chronic Asymptomatic Chagas Disease.

Matthews DJ, Fries RC, Jeffery ND, Hamer SA, Saunders AB.

18-04-2023

Animals (Basel).

<https://pubmed.ncbi.nlm.nih.gov/37106957/>

Trypanosoma cruzi infection causes inflammation and fibrosis, resulting in cardiac damage in dogs. The objectives of this study were to describe cardiac magnetic resonance imaging (CMR) in naturally infected dogs with chronic Chagas disease and the frequency of abnormalities for CMR and cardiac diagnostic tests. Ten asymptomatic, client-owned dogs seropositive for *T. cruzi* were prospectively enrolled in an observational study evaluating echocardiography, ECG (standard and

ambulatory), cardiac troponin I (cTnI), and CMR. Standard ECG measurements (3/10) and cTnI concentration (1/10) outside the reference range were uncommon. Ambulatory ECG abnormalities were documented more frequently (6/10 dogs) than with standard ECG and included ventricular arrhythmias (4), supraventricular premature beats (3), second-degree atrioventricular block (2), and sinus arrest (1). Echocardiographic abnormalities were documented in 6/10 dogs including mildly increased left ventricular internal dimension in diastole (1) and decreased right ventricular (RV) systolic function based on reductions in tricuspid annular plane systolic excursion (3) and RV S' (4). Abnormalities were detected with CMR in 7/10 dogs including delayed myocardial enhancement in 5 of which 2 also had increased extracellular volume, abnormal wall motion in 5, and loss of apical compact myocardium in 1. In conclusion, CMR abnormalities were common, and the results of this study suggest CMR can provide useful information in dogs with *T. cruzi* infection and may support naturally infected dogs for future clinical investigation as an animal model for Chagas disease.

Cryo-EM structures of Trypanosoma brucei gambiense ISG65 with human complement C3 and C3b and their roles in alternative pathway restriction.

Sülzen H, Began J, Dhillon A, Kereiche S, Pompach P, Votrubova J, Zahedifard F, Šubrtova A, Šafner M, Hubalek M, Thompson M, Zoltner M, Zoll S.

27-04-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37105991/>

Cultivation of Protozoa Parasites In Vitro: Growth Potential in Conventional Culture Media versus RPMI-PY Medium.

Castelli G, Oliveri E, Valenza V, Giardina S, Facciponte F, La Russa F, Vitale F, Bruno F.

27-03-2023

Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37104407/>

Chagas Disease Maternal Seroprevalence and Maternal-Fetal Health Outcomes in a Parturition Cohort in Western El Salvador.

Lynn MK, Rodriguez Aquino MS, Cornejo Rivas PM, Kanyangarara M, Self SCW, Campbell BA, Nolan MS.

20-04-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37104358/>

Congenital Chagas disease is a growing concern, prioritized by the World Health Organization for public health action. El Salvador is home to some of the highest Chagas disease (*Trypanosoma cruzi* infection) burdens in the Americas, yet pregnancy screening remains neglected. This pilot investigation performed a maternal *T. cruzi* surveillance study in Western El Salvador among women presenting for labor and delivery. From 198 consented and enrolled pregnant women, 6% were *T. cruzi* positive by serology or molecular diagnosis. Half of the infants born to

T. cruzi-positive women were admitted to the NICU for neonatal complications. Geospatial statistical clustering of cases was noted in the municipality of Jujutla. Older women and those knowing an infected relative or close friend were significantly more likely to test positive for *T. cruzi* infection at the time of parturition. In closing, maternal *T. cruzi* infections were significantly higher than national HIV or syphilis maternal rates, creating an urgent need to add *T. cruzi* to mandatory pregnancy screening programs.

Evaluating the Effect of Irradiation on the Densities of Two RNA Viruses in *Glossina morsitans morsitans*.

Mirieri CK, Abd-Alla AMM, Ros VID, van Oers MM.

20-04-2023

Insects.

Tsetse flies are cyclic vectors of *Trypanosoma* parasites, which cause debilitating diseases in humans and animals. To decrease the disease burden, the number of flies is reduced using the sterile insect technique (SIT), where male flies are sterilized through irradiation and released into the field. This procedure requires the mass rearing of high-quality male flies able to compete with wild male flies for mating with wild females. Recently, two RNA viruses, an iflavirus and a negevirus, were discovered in mass-reared *Glossina morsitans morsitans* and named GmmIV and GmmNegeV, respectively. The aim of this study was to evaluate whether the densities of these viruses in tsetse flies are affected by the irradiation treatment. Therefore, we exposed tsetse pupae to various doses (0-150 Gy) of ionizing radiation, either in air (normoxia) or without air (hypoxia), for which oxygen was displaced by nitrogen. Pupae and/or emerging flies were collected immediately afterwards, and at three days post irradiation, virus densities were quantified through RT-qPCR. Generally, the results show that irradiation exposure had no significant impact on the densities of GmmIV and GmmNegeV, suggesting that the viruses are relatively radiation-resistant, even at higher doses. However, sampling over a longer period after irradiation would be needed to verify that densities of these insect viruses are not changed by the sterilisation treatment.

<https://pubmed.ncbi.nlm.nih.gov/37103212/>

Evaluation of the susceptibility of *Tritrichomonas foetus* to extracts of *Lantana camara* (Verbenaceae) by flow cytometry.

López LA, Luque ME, Rivero MB, Abdala ME, Carranza PG, Luna BE, Di Lullo D, Volta BJ, Rodríguez SA, Rivero FD.

27-04-2023

Vet Res Commun.

<https://pubmed.ncbi.nlm.nih.gov/37100969/>

A description of the epidemiological dynamics of Chagas disease via mathematical modeling.

Lozada-Yavina R, Marchant C, Cancino-Faure B, Hernández-Rodríguez EW, Córdova-Lepe F.

23-04-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37098356/>

Chemical Inhibition of Bromodomain Proteins in Insect-Stage African Trypanosomes Perturbs Silencing of the Variant Surface Glycoprotein Repertoire and Results in Widespread Changes in the Transcriptome.

Ashby EC, Havens JL, Rollosso LM, Hardin J, Schulz D.

25-04-2023

Microbiol Spectr.

<https://pubmed.ncbi.nlm.nih.gov/37097159/>

The eukaryotic protozoan parasite *Trypanosoma brucei* is transmitted by the tsetse fly to both humans and animals, where it causes a fatal disease called African trypanosomiasis. While the parasite lacks canonical DNA sequence-specific transcription factors, it does possess histones, histone modifications, and proteins that write, erase, and read histone marks. Chemical inhibition of chromatin-interacting bromodomain proteins has previously been shown to perturb bloodstream specific trypanosome processes, including silencing of the variant surface glycoprotein (VSG) genes and immune evasion. Transcriptomic changes that occur in bromodomain-inhibited bloodstream parasites mirror many of the changes that occur as parasites developmentally progress from the bloodstream to the insect stage. We performed transcriptome sequencing (RNA-seq) time courses to determine the effects of chemical bromodomain inhibition in insect-stage parasites using the compound I-BET151. We found that treatment with I-BET151 causes large changes in the transcriptome of insect-stage parasites and also perturbs silencing of VSG genes. The transcriptomes of bromodomain-inhibited parasites share some features with early metacyclic-stage parasites in the fly salivary gland, implicating bromodomain proteins as important for regulating transcript levels for developmentally relevant genes. However, the downregulation of surface procyclin protein that typically accompanies developmental progression is absent in bromodomain-inhibited insect-stage parasites. We conclude that chemical modulation of bromodomain proteins causes widespread transcriptomic changes in multiple trypanosome life cycle stages. Understanding the gene-regulatory processes that facilitate transcriptome remodeling in this highly diverged eukaryote may shed light on how these mechanisms evolved. **IMPORTANCE** The disease African trypanosomiasis imposes a severe human and economic burden for communities in sub-Saharan Africa. The parasite that causes the disease is transmitted to the bloodstream of a human or ungulate via the tsetse fly. Because the environments of the fly and the bloodstream differ, the parasite modulates the expression of its genes to accommodate two different lifestyles in these disparate niches. Perturbation of bromodomain proteins that interact with histone proteins around which DNA is wrapped (chromatin) causes profound changes in gene expression in bloodstream-stage parasites. This paper

reports that gene expression is also affected by chemical bromodomain inhibition in insect-stage parasites but that the genes affected differ depending on life cycle stage. Because trypanosomes diverged early from model eukaryotes, an understanding of how trypanosomes regulate gene expression may lend insight into how gene-regulatory mechanisms evolved. This could also be leveraged to generate new therapeutic strategies.

Prevalence of *Trypanosoma cruzi* infection in a cohort of people living with HIV-AIDS from an urban area.

Kesper N, Ignácio Junior JC, Rocci RA, Cunha MA, Lauletta Lindoso JA.

25-04-2023

Epidemiol Infect.

<https://pubmed.ncbi.nlm.nih.gov/37096666/>

The Pampa del Indio project: District-wide quasi-elimination of *Triatoma infestans* after a 9-year intervention program in the Argentine Chaco.

Gürtler RE, Gaspe MS, Macchiaverna NP, Enriquez GF, Rodríguez-Planes LI, Fernández MDP, Provecho YM, Cardinal MV.

24-04-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37093886/>

Transcriptomic analysis of the adaptation to prolonged starvation of the insect-dwelling *Trypanosoma cruzi* epimastigotes.

Smircich P, Pérez-Díaz L, Hernández F, Duhagon MA, Garat B.

06-04-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37091675/>

Omics data integration facilitates target selection for new antiparasitic drugs against *TriTryp* infections.

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06-04-2023

Front Pharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37089958/>

Introduction: *Trypanosoma cruzi*, *Trypanosoma brucei*, and *Leishmania spp.*, commonly referred to as *TriTryps*, are a group of protozoan parasites that cause important human diseases affecting millions of people belonging to the most vulnerable populations worldwide. Current treatments have limited efficiencies and can cause serious side effects, so there is an urgent need to develop new control strategies. Presently, the identification and prioritization of appropriate targets can be aided by integrative genomic and computational approaches.

Methods: In this work, we conducted a genome-wide multidimensional data integration strategy to prioritize

drug targets. We included genomic, transcriptomic, metabolic, and protein structural data sources, to delineate candidate proteins with relevant features for target selection in drug development. **Results and Discussion:** Our final ranked list includes proteins shared by *TriTryps* and covers a range of biological functions including essential proteins for parasite survival or growth, oxidative stress-related enzymes, virulence factors, and proteins that are exclusive to these parasites. Our strategy found previously described candidates, which validates our approach as well as new proteins that can be attractive targets to consider during the initial steps of drug discovery.

Blocking activation of CD4-CD8- T cells modulates their cytotoxic potential and decreases the expression of inflammatory and chemotactic receptors.

Neves EGA, Koh CC, Lucinda PPD, Souza-Silva TG, Medeiros NI, Pantaleão A, Mutarelli A, de Assis Silva Gomes J, de Araújo Silva S, Gollob KJ, do Carmo Pereira Nunes M, Dutra WO.

21-04-2023

Clin Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37088297/>

Targeted Protein Degradation Might Present a Novel Therapeutic Approach in the Fight Against African Trypanosomiasis.

Danazumi AU, Ishmam IT, Idris S, Izert MA, Balogun EO, Góna MW.

21-04-2023

Eur J Pharm Sci.

<https://pubmed.ncbi.nlm.nih.gov/37088149/>

In vitro and in vivo evaluation of efficacy of berberine chloride: Phyto-alternative approach against *Trypanosoma evansi* infection.

Gupta S, Vohra S, Sethi K, Rani R, Gupta S, Kumar S, Kumar R.

20-04-2023

Mol Biochem Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37084956/>

Current chemotherapy against the Surra organism, *Trypanosoma evansi* has several limitations in terms of efficacy, toxicity, availability and emerging resistance. These reasons make the search of new chemo-preventive and chemo-therapeutic agent with high potency and low toxicity. Alkaloid phyto-molecules, berberine has shown promising anti-kinetoplastid activity against *T. cruzi*, *T. congolense*, *T. brucei*, *Leishmania donovani* and *L. tropica*. However, till date, there is no investigation of therapeutic efficacy of berberine chloride (BC) against *T. evansi*. The IC₅₀ value of BC for growth inhibition of *T. evansi* at 24 h of culture was calculated as 12.15 µM. The specific selectivity index (SSI) of BC was calculated as 19.01 and 10.43 against Vero cell line and Equine PBMC's, respectively. Thirteen drug target genes affecting various metabolic pathways

were studied to investigate the mode of trypanocidal action of BC. In transcript analysis, the mRNA expression of arginine kinase 1 remained refractory to exposure with BC, which provides metabolic plasticity in adverse environmental conditions. In contrary, rest all the drug target gene were down-regulated, which indicates that drug severely affect DNA replication, cell proliferation, energy homeostasis, redox homeostasis and calcium homeostasis of *T. evansi*, leading to the death of parasite in low concentrations. It is the first attempt to investigate in vitro anti-trypanosomal activity of BC against *T. evansi*. These data imply that phytochemicals as alternative strategies can be explored in the future as an alternative treatment for Surra in animal.

Systematic study of 1,2,3-triazolyl sterols for the development of new drugs against parasitic Neglected Tropical Diseases.

Porta EOJ, Ballari MS, Carlucci R, Wilkinson S, Ma G, Tekwani BL, Labadie GR.

13-04-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37084599/>

A series of thirty 1,2,3-triazolylsterols, inspired by azasterols with proven antiparasitic activity, were prepared by a stereocontrolled synthesis. Ten of these compounds constitute chimeras/hybrids of 22,26-azasterol (AZA) and 1,2,3-triazolyl azasterols. The entire library was assayed against the kinetoplastid parasites *Leishmania donovani*, *Trypanosoma cruzi*, and *Trypanosoma brucei*, the causatives agents for visceral leishmaniasis, Chagas disease, and sleeping sickness, respectively. Most of the compounds were active at submicromolar/nanomolar concentrations with high selectivity index, when compared to their cytotoxicity against mammalian cells. Analysis of in silico physicochemical properties were conducted to rationalize the activities against the neglected tropical disease pathogens. The analogs with selective activity against *L. donovani* (E4, IC₅₀ 0.78 µM), *T. brucei* (E1, IC₅₀ 0.12 µM) and *T. cruzi* (B1- IC₅₀ 0.33 µM), and the analogs with broad-spectrum antiparasitic activities against the three kinetoplastid parasites (B1 and B3), may be promising leads for further development as selective or broad-spectrum antiparasitic drugs.

Genome-Wide Libraries for Protozoan Pathogen Drug Target Screening Using Yeast Surface Display.

Heslop R, Gao M, Brito Lira A, Sternlieb T, Loock M, Sanghi SR, Cestari I.

21-04-2023

ACS Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37083339/>

Ulcère de Buruli

Mycobacterium ulcerans culture results according to duration of prior antibiotic treatment: A cohort study.

Tweeddale B, Collier F, Waidyatillake NT, Athan E, O'Brien DP.

24-04-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37093836/>

Mycobacterium ulcerans disease is a necrotising disease of the skin and subcutaneous tissue and is effectively treated with eight-weeks antibiotic therapy. Significant toxicities, however, are experienced under this prolonged regimen. Here, we investigated the length of antibiotic duration required to achieve negative cultures of *M. ulcerans* disease lesions and evaluated the influence of patient characteristics on this outcome. *M. ulcerans* cases from an observational cohort that underwent antibiotic treatment prior to surgery and had post-excision culture assessment at Barwon Health, Victoria, from May 25 1998 to June 30 2019, were included. Antibiotic duration before surgery was grouped as <2 weeks, ≥2-<4 weeks, ≥4-<6 weeks, ≥6-<8 weeks, ≥8-<10 weeks and ≥10-20 weeks. Cox regression analyses were performed to assess the association between variables and culture positive results. Ninety-two patients fitted the inclusion criteria. The median age was 60 years (IQR 28-74.5) and 51 (55.4%) were male. Rifampicin-based regimens were predominantly used in combination with clarithromycin (47.8%) and ciprofloxacin (46.7%), and the median duration of antibiotic treatment before surgery was 23 days (IQR, 8.0-45.5). There were no culture positive results after 19 days of antibiotic treatment and there was a significant association between antibiotic duration before surgery and a culture positive outcome ($p<0.001$). The World Health Organisation category of the lesion and the antibiotic regimen used had no association with the culture outcome. Antibiotics appear to be effective at achieving negative cultures of *M. ulcerans* disease lesions in less than the currently recommended eight-week duration.