Réseau MTN Francophone

Veille scientifique
Maladies tropicales négligées

Semaine 29
17 au 23 juillet 2023

Cysticercose

Emerging Infectious Diseases of the Skin: A Review of Clinical and Histologic Findings.

McMahon DE, Schuetz AN, Kovarik CL.
14-07-2023
Hum Pathol.
https://pubmed.ncbi.nlm.nih.gov/37454994/

Emerging infectious diseases are of great importance to public health and clinical practice. This review aims to characterize the clinical and histopathologic features of emerging infectious diseases with cutaneous manifestations in order to increase awareness of these entities among dermatologists, pathologists, and dermatopathologists.

Albendazole - Ivermectin combination decreases inflammation in experimental neurocysticercosis.

da Silva Santana RC, Prudente TP, de Sousa Guerra CH, de Lima NF, de Souza Lino Junior R, Vinaud MC.
Août-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37327965/

Intraventricular neurocysticercosis: A correlative radiopathological image.

Mansour MA, Tahir M.
Août-2023
Neurol Sci.
https://pubmed.ncbi.nlm.nih.gov/37178212

Efficacy and safety of antiparasitic therapy for neurocysticercosis in rural Tanzania: a prospective cohort study.

Stelzle D, Makasi C, Schmidt V, Trevisan C, Van Damme I, Ruether C, Dorny P, Magnussen P, Zulu G, Mwape KE, Bottieau E, Prazeres da Costa C, Prodjinotho UF, Carabin H, Jackson E, Fleury A, Gabriël S, Ngowi BJ, Winkler AS.
Août-2023
Infection.
https://pubmed.ncbi.nlm.nih.gov/36961623/

Purpose: Neurocysticercosis is common in regions endemic for Taenia solium. Active-stage neurocysticercosis can be treated with antiparasitic medication, but so far no study on efficacy and safety has been conducted in Africa. Methods: We conducted a prospective cohort study on treatment of neurocysticercosis in Tanzania between August 2018 and January 2022. Patients were initially treated with albendazole (15 mg/kg/d) for 10 days and followed up for 6 months. Additionally in July 2021, all participants who then still had cysts were offered a combination therapy consisting of albendazole (15 mg/kg/d) and praziquantel (50 mg/kg/d). Antiparasitic treatment was accompanied by corticosteroid medication and anti-seizure medication if the patient had experienced epileptic seizures before treatment. Results: Sixty-three patients were recruited for this study, of whom 17 had a complete follow-up after albendazole monotherapy. These patients had a total of 138 cysts at baseline, of which 58 (42%) had disappeared or calcified by the end of follow-up. The median cyst reduction was 40% (interquartile range 11-63%). Frequency of epileptic seizures reduced considerably ($p < 0.001$). Three patients had all active cysts resolved or calcified and of the remaining 14, eight received the combination therapy which resolved 63 of 66 cysts (95%). Adverse events were infrequent and mild to moderate during both treatment cycles. Conclusion: Cyst resolution was unsatisfactory with albendazole monotherapy but was very high when it was followed by a combination of albendazole and praziquantel.

Disseminated cysticercosis with multi-system involvement in a child.

Kaur L, Bansal A, Dayal S, Karwal A, Singh S.
Juil-Août 2023
Pediatr Dermatol.
https://pubmed.ncbi.nlm.nih.gov/36724898/

Dengue, chikungunya et maladie à virus Zika

Differences in proteome perturbations caused by the Wolbachia strain wAu suggest multiple mechanisms of Wolbachia-mediated antiviral activity.

Rainey SM, Geoghegan V, Lefteri DA, Ant TH, Martinez J, McNamara CJ, Kamel W, de Laurent ZR, Castello A, Sinkins SP.
20-07-2023
Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/37474590/

Insights into the structure, functional perspective, and pathogenesis of ZIKV: an updated review.

Bhat EA, Ali T, Sajjad N, Kumar R, Bron P.
18-07-2023
Biomed Pharmacother.
https://pubmed.ncbi.nlm.nih.gov/37473686/

Zika virus (ZIKV) poses a serious threat to the entire world. The rapid spread of ZIKV and recent outbreaks since 2007 have caused worldwide concern about the virus. Diagnosis is complicated because of the cross-reactivity of the virus with other viral antibodies. Currently, the virus is diagnosed by molecular techniques such as RT-PCR and IgM-linked enzyme immunoassays (MAC-ELISA). Recently, outbreaks and epidemics have been caused by ZIKV, and severe clinical symptoms and congenital malformations have also been associated with the virus. Although most ZIKV infections present with a subclinical or moderate flu-like course of illness, severe symptoms such as Guillain-Barre syndrome in adults and microcephaly in children of infected mothers have also been reported. Because there is no reliable cure for ZIKV and no vaccine is available, the public health response has focused primarily on

preventing infection, particularly in pregnant women. A comprehensive approach is urgently needed to combat this infection and stop its spread and imminent threat. In view of this, this review aims to present the current structural and functional viewpoints, structure, etiology, clinical prognosis, and measures to prevent this transmission based on the literature and current knowledge. Moreover, we provide thorough description of the current understanding about ZIKV interaction with receptors, and a comparative examination of its similarities and differences with other viruses.

The reemergence of dengue virus in Sudan.

Mustafa MI, Makhawi AM.
07-07-2023
J Infect Public Health.
https://pubmed.ncbi.nlm.nih.gov/37473544/

Dengue fever (DF) is a mosquito-transmitted arboviral disease caused by 1 of 4 closely related but antigenically distinct serotypes of dengue virus (DENV), DENV-1-4. The primary vector of DENV is Aedes aegypti and Aedes albopictus mosquitoes. Humans are the main carrier of the virus and the amplifying host with non-human primates plays a considerable role in sylvatic cycle. On November 8, 2022, an outbreak of dengue fever has killed at least five people in North Kordofan State. On 23 Nov 2022, the Sudanese Ministry of Health reported 3326 cases of dengue fever across 8 Sudanese States; while 23 patients died from the fever. Sudan is witnessing its worst outbreak of dengue fever in over a decade, especially in North and South Kordofan and Red Sea State are hit hard. In this review, we will focus on the recent outbreak of dengue fever in many Sudanese states.

Investigating the aggregation perspective of Dengue virus proteome.

Kapuganti SK, Saumya KU, Verma D, Giri R.
13-07-2023
Virology.
https://pubmed.ncbi.nlm.nih.gov/37473502/

Notes from the Field: Autism Spectrum Disorder Among Children with Laboratory Evidence of Prenatal Zika Virus Exposure - Puerto Rico, 2023.

Roth NM, Delgado-López C, Wiggins LD, Muñoz NN, Mulkey SB, Nieves-Ferrer L, Woodworth KR, Rosario GM, Huertas MM, Moore CA, Tong VT, Gilboa SM, Valencia-Prado M.
21-07-2023
MMWR Morb Mortal Wkly Rep.
https://pubmed.ncbi.nlm.nih.gov/37471268/

Mayaro virus detection by integrating sample preparation with isothermal amplification in portable devices.

Alipanah M, Manzanas C, Hai X, Lednicky JA, Paniz-Mondolfi A, Morris JG, Fan ZH.
20-07-2023
Anal Bioanal Chem.
https://pubmed.ncbi.nlm.nih.gov/37470813/

Etiological Profile and Clinico Epidemiological Patterns of Acute Encephalitis Syndrome in Tamil Nadu, India.

Kumar VS, Sivasubramanian S, Padmanabhan P, Anupama CP, Ramesh K, Gunasekaran P, Krishnasamy K, Kitambi SS.
02-05-2023
J Glob Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37469472/

Introduction: Establishing the etiological cause of acute encephalitis syndrome (AES) is challenging due to the distinct distribution of various etiological agents. This study aims to determine the etiological profiles of both viruses and bacteria and their associated clinico-epidemiological features among the AES suspected cases in Tamil Nadu, India. Methods: Samples of 5136 suspected AES cases from January 2016 to December 2020 (5 years) were subjected to the detection of etiological agents for AES through serological and molecular diagnosis methods. Further, the clinical profile, age- and gender-wise susceptibility of cases, co-infection with other AES etiological agents, and seasonality pattern with respect to various etiological agents were examined. Results: AES positivity was established in 1480 cases (28.82%) among the 5136 suspected cases and the positivity for male and female groups were 57.77% and 42.23%, respectively. The pediatric group was found to be more susceptible than others. Among the etiological agents tested, the Japanese encephalitis virus (JEV) was the predominant followed by *Cytomegalovirus*, Herpes Simplex virus, Epstein-Barr virus, Varicella Zoster virus, and others. Co-infection with other AES etiological agents was observed in 3.5% of AES-positive cases. Seasonality was observed only for vector-borne diseases such as JEV, dengue virus, and West Nile virus infections in this study. Conclusion: AES was found to be a significant burden for Tamil Nadu with a diverse etiological spectrum including both sporadic and outbreak forms. Overlapping clinical manifestations of AES agents necessitate the development of region-specific diagnostic algorithm with distinct etiological profiles for early detection and effective case management.

Consideration of serum IL-36α and β levels trends in two patients with chikungunya fever.

Kondo M, Matsushima Y, Nakanishi T, Iida S, Habe K, Yamanaka K.
17-07-2023
Clin Case Rep.
https://pubmed.ncbi.nlm.nih.gov/37469370/

Key clinical message: IL-36 might play a role as an initial immune mechanism against chikungunya fever, and regulating IL-36 production could be a potential treatment approach for this condition. Abstract: Two Japanese siblings visited Cook Islands in 2015 and developed Chikungunya fever upon their return. The sister experienced high fever, joint pain, and leg swelling, while

the brother had joint pain and a rash. Both siblings had a confirmed CHIKV infection and continued to experience prolonged joint pain, with the sister enduring chronic pain for about a year. In this study, the levels of IL-36 in the serum of two siblings who were infected with chikungunya fever during the acute and recovery phases were compared using ELISA. IL-36 is a cytokine that induces inflammation and is produced by cells in tissues such as the skin and mucosa. It was hypothesized that IL-36 may be involved in persistent joint pain after chikungunya fever infection. Both siblings experienced long-lasting joint pain after chikungunya fever infection. The levels of IL-36α and IL-36β decreased by 56 days after infection. In the results, IL-36 plays an important role in host immunity and may act as part of the immune response during chikungunya virus infection. Inhibiting the release of IL-36 could be a promising approach for developing new treatment methods for chikungunya fever.

Importation of a novel Indian Ocean lineage carrying E1-K211E and E2-V264A of Chikungunya Virus in Zhejiang Province, China, in 2019.

Su L, Lou X, Yan H, Yang Z, Mao H, Yao W, Sun Y, Pan J, Zhang Y.
19-07-2023
Virus Genes.
https://pubmed.ncbi.nlm.nih.gov/37468826/

CRISPR-Cas Systems: Programmable Nuclease Revolutionizing the Molecular Diagnosis.

Pandya K, Jagani D, Singh N.
19-07-2023
Mol Biotechnol.
https://pubmed.ncbi.nlm.nih.gov/37466850/

Neurodevelopmental outcomes in congenital and perinatal infections.

Fortin O, Mulkey SB.
20-07-2023
Curr Opin Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37466092/

Purpose of review: Congenital infections are a major cause of childhood multidomain neurodevelopmental disabilities. They contribute to a range of structural brain abnormalities that can cause severe neurodevelopmental impairment, cerebral palsy, epilepsy, and neurosensory impairments. New congenital infections and global viral pandemics have emerged, with some affecting the developing brain and causing neurodevelopmental concerns. This review aims to provide current understanding of fetal infections and their impact on neurodevelopment. Recent findings: There are a growing list of congenital infections causing neurodevelopmental issues, including cytomegalovirus, Zika virus, syphilis, rubella, lymphocytic choriomeningitis virus, and toxoplasmosis. Fetal exposure to maternal SARS-CoV-2 may also pose risk to the developing brain and impact neurodevelopmental outcomes, although studies have conflicting results. As Zika virus was a recently identified congenital infection, there are several new reports on child neurodevelopment in the Caribbean and Central and South America. For many congenital infections, children with in-utero exposure, even if asymptomatic at birth, may have neurodevelopmental concerns manifest over time. Summary: Congenital infections should be considered in the differential diagnosis of a child with neurodevelopmental impairments. Detailed pregnancy history, exposure risk, and testing should guide diagnosis and multidisciplinary evaluation. Children with congenital infections should have long-term follow-up to assess for neurodevelopmental delays and other neurosensory impairments. Children with confirmed delays or high-risk should be referred for rehabilitation therapies.

Euphopias G - J, macrocyclic diterpenes with anti-zika virus activity from Euphorbia helioscopia L.

Qiu X, Jiang YJ, Huang YX, Pang WH, Wu ZK, Zhou YL, Li R, Bi DW, Cheng B, Xiao WL, Zheng CB, Li XL.
16-07-2023
Fitoterapia.
https://pubmed.ncbi.nlm.nih.gov/37463646/

Global prevalence of Asymptomatic Dengue infections - A systematic review and meta-analysis.

Asish PR, Dasgupta S, Rachel G, Bagepally BS, Kumar CPG.
16-07-2023
Int J Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37463631/

Unique Immune Blood Markers Between Severe Dengue and Sepsis in Children.

Salgado DM, Rivera GM, Pinto WA, Rodríguez J, Acosta G, Castañeda DM, Vega R, Perdomo-Celis F, Bosch I, Narváez CF.
18-07-2023
Pediatr Infect Dis J.
https://pubmed.ncbi.nlm.nih.gov/37463399/

Background: Pediatric dengue and sepsis share clinical and pathophysiologic aspects. Multiple inflammatory and regulatory cytokines, decoy receptors and vascular permeability factors have been implicated in the pathogenesis of both diseases. The differential pattern and dynamic of these soluble factors, and the relationship with clinical severity between pediatric dengue and sepsis could offer new diagnosis and therapeutic strategies. Methods: We evaluated the concentration levels of 11 soluble factors with proinflammatory, regulatory and vascular permeability involvement, in plasma from children with dengue or sepsis, both clinically ranging from mild to severe, in the early, late and convalescence phases of the disease. Results: During early acute infection, children with sepsis exhibited specific higher concentration levels of IL-6, vascular endothelial growth factor (VEGF), and its soluble decoy receptor II (sVEGFR2) and lower concentration levels of IL-10 and the soluble tumor necrosis factor receptor 2 (sTNFR2), in comparison with children with severe dengue. In addition, the

circulating amounts of soluble ST2, and VEGF/sVEGFR2 were widely associated with clinical and laboratory indicators of dengue severity, whereas secondary dengue virus infections were characterized by an enhanced cytokine response, relative to primary infections. In severe forms of dengue, or sepsis, the kinetics and the cytokines response during the late and convalescence phases of the disease also differentiate. **Conclusions:** Dengue virus infection and septic processes in children are characterized by cytokine responses of a specific magnitude, pattern and kinetics, which are implicated in the pathophysiology and clinical outcome of these diseases.

Alphavirus-induced transcriptional and translational shutoffs play major roles in blocking the formation of stress granules.

Palchevska O, Dominguez F, Frolova EI, Frolov I.
05-07-2023
bioRxiv.
https://pubmed.ncbi.nlm.nih.gov/37461699/

Alphavirus infections cause multiple alterations in the intracellular environment that can have both positive and negative effects on viral replication. The Old World alphaviruses, such as Sindbis (SINV), chikungunya (CHIKV), and Semliki Forest viruses, hinder the ability of vertebrate cells to form stress granules (SGs). Previously, this inhibitory function was attributed to the hypervariable domain (HVD) of nsP3, which sequesters the key components of SGs, G3BP1 and G3BP2, and to the nsP3 macro domain. The macro domain possesses ADP-ribosylhydrolase activity, which can diminish the ADP-ribosylation of G3BP1 during viral replication. However, our recent findings do not support the prevailing notions. We demonstrate that the interactions between SINV- or CHIKV-specific nsP3s and G3BPs, and the ADP-ribosylhydrolase activity are not major contributors to the inhibitory process, at least when nsP3 is expressed at biologically relevant levels. Instead, the primary factors responsible for suppressing SG formation are virus-induced transcriptional and translational shutoffs that rapidly develop within the first few hours post infection. Poorly replicating SINV variants carrying mutated nsP3 HVD still inhibit SG development even in the presence of NaAs. Conversely, SINV mutants lacking transcription and/or translation inhibitory functions lose their ability to inhibit SGs, despite expressing high levels of wt nsP3. Moreover, we found that stable cell lines expressing GFP-nsP3 fusions retain the capacity to form SGs when exposed to sodium arsenite. However, our results do not rule out a possibility that additional virus-induced changes in cell biology may contribute to the suppression of SG formation. **Importance:** Our study highlights the mechanisms behind the cell's resistance to SG formation after infection with Old World alphaviruses. Shortly after infection, the replication of these viruses hinders the cell's ability to form SGs, even when exposed to chemical inducers such as sodium arsenite. This resistance is primarily attributed to virus-induced transcriptional and translational shutoffs, rather than interactions between the viral nsP3 and the key components of SGs, G3BP1/2, or the ADP-ribosylhydrolase activity of nsP3 macro domain. While interactions between G3BP and nsP3 are essential for the formation of viral replication complexes, their role in regulating SG development appears to be minimal, if any. Cells harboring replicating virus-specific RNA with modified abilities to inhibit transcription and/or translation, but encoding wt nsP3, retain the capacity for SG development. Understanding these mechanisms of regulation of SG development contributes to our knowledge of viral replication and the intricate relationships between alphaviruses and host cells.

Myeloid cell activation during Zika virus encephalitis predicts recovery of functional cortical connectivity.

Agner SC, Brier LM, Hill J, Liu E, Bice A, Rahn RM, Culver JP, Klein RS.
06-07-2023
bioRxiv.
https://pubmed.ncbi.nlm.nih.gov/37461558/

Unforeseen complications: a case of dengue shock syndrome presenting with multi-organ dysfunction in a subtropical region.

Owais SM, Ansar F, Saqib M, Wahid K, Rashid K, Mumtaz H.
17-07-2023
Trop Med Health.
https://pubmed.ncbi.nlm.nih.gov/37461097/

An ecological assessment of the potential pandemic threat of Dengue Virus in Zhejiang province of China.

Zhang Y, Wang L, Wang G, Xu J, Zhang T.
17-07-2023
BMC Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37461015/

Background and aim: Dengue fever, transmitted by Aedes mosquitoes, is a significant public health concern in tropical and subtropical regions. With the end of the COVID-19 pandemic and the reopening of the borders, dengue fever remains a threat to mainland China, Zhejiang province of China is facing a huge risk of importing the dengue virus. This study aims to analyze and predict the current and future potential risk regions for Aedes vectors distribution and dengue prevalence in Zhejiang province of China. **Method:** We collected occurrence records of DENV and DENV vectors globally from 2010 to 2022, along with historical and future climate data and human population density data. In order to predict the probability of DENV distribution in Zhejiang province of China under future conditions, the ecological niche of Ae. aegypti and Ae. albopictus was first performed with historical climate data based on MaxEnt. Then, predicted results along with a set of bioclimatic variables, elevation and human population density were included in MaxEnt model to analyze the risk region of DENV in Zhejiang province. Finally, the established model was utilized to predict the spatial pattern of DENV risk in the current and future scenarios in Zhejiang province of China.

Results: Our findings indicated that approximately 89.2% (90,805.6 KM^2) of Zhejiang province of China is under risk, within about 8.0% (8,144 KM^2) classified as high risk area for DENV prevalence. Ae. albopictus were identified as the primary factor influencing the distribution of DENV. Future predictions suggest that sustainable and "green" development pathways may increase the risk of DENV prevalence in Zhejiang province of China. Conversely, Fossil-fueled development pathways may reduce the risk due to the unsuitable environment for vectors. **Conclusions:** The implications of this research highlight the need for effective vector control measures, community engagement, health education, and environmental initiatives to mitigate the potential spread of dengue fever in high-risk regions of Zhejiang province of China.

Correction: Clinical Characteristics and Outcomes Among Travelers With Severe Dengue.

[No authors listed]
18-07-2023
Ann Intern Med.
https://pubmed.ncbi.nlm.nih.gov/37459620/

African ZIKV lineage fails to sustain infectivity in an in vitro mimetic urban cycle.

Molina BF, Marques NN, Bittar C, Batista MN, Rahal P.
17-07-2023
Braz J Microbiol.
https://pubmed.ncbi.nlm.nih.gov/37458982/

Zika virus infection histories in brain development.

Marcelino BLM, Dos Santos BL, Doerl JG, Cavalcante SF, Maia SN, Arrais NMR, Zin A, Jeronimo SMB, Queiroz C, Hedin-Pereira C, Sequerra EB.
01-07-2023
Dis Model Mech.
https://pubmed.ncbi.nlm.nih.gov/37458166/

An outbreak of births of microcephalic patients in Brazil motivated multiple studies on this incident. The data left no doubt that infection by Zika virus (ZIKV) was the cause, and that this virus promotes reduction in neuron numbers and neuronal death. Analysis of patients' characteristics revealed additional aspects of the pathology alongside the decrease in neuronal number. Here, we review the data from human, molecular, cell and animal model studies attempting to build the natural history of ZIKV in the embryonic central nervous system (CNS). We discuss how identifying the timing of infection and the pathways through which ZIKV may infect and spread through the CNS can help explain the diversity of phenotypes found in congenital ZIKV syndrome (CZVS). We suggest that intraneuronal viral transport is the primary mechanism of ZIKV spread in the embryonic brain and is responsible for most cases of CZVS. According to this hypothesis, the viral transport through the blood-brain barrier and cerebrospinal fluid is responsible for more severe pathologies in which ZIKV-induced malformations occur along the entire anteroposterior CNS axis.

Liver immunopathogenesis in fatal cases of dengue in children: detection of viral antigen, cytokine profile and inflammatory mediators.

Moragas LJ, Alves FAV, Oliveira LLS, Salomão NG, Azevedo CG, da Silva JFR, Basílio-de-Oliveira CA, Basílio-de-Oliveira R, Mohana-Borges R, de Carvalho JJ, Rosman FC, Paes MV, Rabelo K.
30-06-2023
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/37457689/

Introduction: Dengue virus (DENV), the etiologic agent of dengue fever illness, represents a global public health concern, mainly in tropical and subtropical areas across the globe. It is well known that this acute viral disease can progress to severe hemorrhagic stages in some individuals, however, the immunopathogenic basis of the development of more severe forms by these patients is yet to be fully understood. **Objective:** In this context, we investigated and characterized the histopathological features as well as the cytokine profile and cell subpopulations present in liver tissues from three fatal cases of DENV in children. **Methods:** Hematoxylin and Eosin, Periodic Acid Schiff and Picro Sirius Red staining were utilized for the histopathological analysis. Immunohistochemistry assay was performed to characterize the inflammatory response and cell expression patterns. **Results:** Vascular dysfunctions such as hemorrhage, vascular congestion and edema associated with a mononuclear infiltrate were observedin all three cases. Liver tissues exhibited increased presence of CD68+ and TCD8+ cells as well as high expression of MMP-9, TNF-a, RANTES, VEGFR-2 mediators. Viral replication was confirmed by the detection of NS3 protein. **Conclusion:** Taken together, these results evidenced key factors that may be involved in the development of severe alterations in liver tissues of children in response to DENV infection.

Characterizing antibody responses to mosquito salivary antigens of the Southeast Asian vectors of malaria and dengue with a human challenge model of controlled exposure: a protocol.

Sawasdichai S, Chaumeau V, Kearney E, Wasisakun P, Simpson JA, Price DJ, Chotirat S, Rénia L, Bergmann-Leitner E, Fowkes F, Nosten F.
11-07-2023
Wellcome Open Res.
https://pubmed.ncbi.nlm.nih.gov/37456919/

Next-generation diagnostic test for dengue virus detection using an ultrafast plasmonic colorimetric RT-PCR strategy.

Jiang K, Lee JH, Fung TS, Wu J, Liu C, Mi H, Rajapakse RPVJ, Balasuriya UBR, Peng YK, Go YY.
15-09-2023
Anal Chim Acta.
https://pubmed.ncbi.nlm.nih.gov/37455070/

Emerging Infectious Diseases of the Skin: A Review of Clinical and Histologic Findings.

McMahon DE, Schuetz AN, Kovarik CL.
14-07-2023
Hum Pathol.
https://pubmed.ncbi.nlm.nih.gov/37454994/

Emerging infectious diseases are of great importance to public health and clinical practice. This review aims to characterize the clinical and histopathologic features of emerging infectious diseases with cutaneous manifestations in order to increase awareness of these entities among dermatologists, pathologists, and dermatopathologists.

Analysis of dengue fever disease in West Africa.

Gyasi P, Bright Yakass M, Quaye O.
15-07-2023
Exp Biol Med (Maywood).
https://pubmed.ncbi.nlm.nih.gov/37452719/

Dengue fever disease (DFD) which is caused by four antigenically distinct dengue viruses (DENV) presents a global health threat, with tropical and subtropical regions at a greater risk. The paucity of epidemiological data on dengue in West African subregion endangers efforts geared toward disease control and prevention. A systematic search of DFD prevalence, incidence, and DENV-infected *Aedes* in West Africa was conducted in PubMed, Scopus, African Index Medicus, and Google Scholar in line with the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines. A total of 58 human prevalence studies involving 35,748 people from 8 countries were identified. Two incidence and six DENV-infected studies were also reviewed. Nigeria and Burkina Faso contributed the majority of the prevalence studies which spanned between 1968 and 2018, with a considerable variation in coverage among the countries reviewed in this study. An average prevalence of 20.97% was observed across both general prevalence and acute DENV infection study categories, ranging between 0.02% and 93%. The majority of these studies were conducted in acute febrile patients with a prevalence range of 0.02-93% while 19% (n = 11) of all studies were general population-based studies and reported a prevalence range of 17.2-75.8%. DENV-infected *Aedes aegypti* were reported in four out of the five countries with published reports; with DENV-2 found circulating in Cape Verde, Senegal, and Burkina Faso while DENV-3 and DENV-4 were also reported in Senegal and Cape Verde, respectively. High prevalence of DFD in human populations and the occurrence of DENV-infected *A. aegypti* have been reported in West Africa, even though weaknesses in study design were identified. Epidemiological data from most countries and population in the subregion were scarce or non-existent. This study highlights the epidemic risk of DFD in West Africa, and the need for research and surveillance to be prioritized to fill the data gap required to enact effective control measures.

Miconia albicans (Melastomataceae) to treat Chikungunya viral infection: An effectual symptom-driven ethnomedicinal repurposing of an anti-inflammatory species?

do Nascimento SN, Mazzei JL, Tostes JBF, Nakamura MJ, Valente LMM, de Lima RC, Nunes PCG, de Azeredo EL, Berrueta LA, Gallo B, Siani AC.
12-07-2023
J Ethnopharmacol.
https://pubmed.ncbi.nlm.nih.gov/37451491/

Ethnopharmacological relevance: Miconia albicans (MA) is consumed all over the Brazilian territory as a remedy to treat rheumatoid arthritis and has been increasingly used to alleviate the deleterious symptoms caused by Chikungunya virus (CHIKV). Aim of the study: To investigate the effect of MA leaf and stem hydroethanolic extracts (LE and SE, respectively), their fractions enriched in triterpene acids or polyphenols as well isolated constituents, on CHIKV hosted in Vero cells. Materials and methods: Polyphenol profiles of LE and SE were dereplicated by HPLC-DAD-ESI-MS/MS, aided by standards. Polyphenol-rich (LEx and SEx) and triterpenic acid-rich (LOH and SOH) fractions were obtained in Amberlite XAD-4 and alkalinized 95% ethanol (EtOH) extraction, respectively. TPC and TFC were assessed by colorimetric methods. Three representative flavonoids and two triterpenic acids were quantified by HPLC. CHIKV load suppression was evaluated in Vero cells by real-time qRT–PCR at noncytotoxic concentrations. Results: Fifteen flavonoids were characterized in LE and SE. LEx presented isoquercitrin, quercitrin, rutin (0.49-1.51%) and quercetin. The TPC was 48 and 62 mg QE/g extract, and the TFC was 11.93 and 0.76 mg QE/g extract for LEx and SEx, respectively. LOH presented ursolic (15.3%) and oleanolic (8.0%) acids. A reduction (91-97%) in the CHIKV load was produced by the triterpene fraction, quercitrin and quercetin; the latter maintained the activity down to one twentieth of the tolerated concentration. Conclusion: M. albicans contains flavonoids and triterpenic acids that are effective against CHIKV, which might justify its use to alleviate sequelae of CHIKV infection. However, further investigations on the species and its active constituents are needed.

Treatment with sofosbuvir attenuates the adverse neurodevelopmental consequences of Zika virus infection in infant rhesus macaques.

Medina A, Rusnak R, Richardson R, Zimmerman MG, Suthar M, Schoof N, Kovacs-Balint Z, Mavigner M, Sanchez M, Chahroudi A, Raper J.
07-07-2023
J Neuroimmunol.
https://pubmed.ncbi.nlm.nih.gov/37451078/

Differing taxonomic responses of mosquito vectors to anthropogenic land-use change in Latin America and the Caribbean.

Fletcher IK, Gibb R, Lowe R, Jones KE.
14-07-2023

PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37450491/

Anthropogenic land-use change, such as deforestation and urban development, can affect the emergence and re-emergence of mosquito-borne diseases, e.g., dengue and malaria, by creating more favourable vector habitats. There has been a limited assessment of how mosquito vectors respond to land-use changes, including differential species responses, and the dynamic nature of these responses. Improved understanding could help design effective disease control strategies. We compiled an extensive dataset of 10,244 Aedes and Anopheles mosquito abundance records across multiple land-use types at 632 sites in Latin America and the Caribbean. Using a Bayesian mixed effects modelling framework to account for between-study differences, we compared spatial differences in the abundance and species richness of mosquitoes across multiple land-use types, including agricultural and urban areas. Overall, we found that mosquito responses to anthropogenic land-use change were highly inconsistent, with pronounced responses observed at the genus- and species levels. There were strong declines in Aedes (-26%) and Anopheles (-35%) species richness in urban areas, however certain species such as Aedes aegypti, thrived in response to anthropogenic disturbance. When abundance records were coupled with remotely sensed forest loss data, we detected a strong positive response of dominant and secondary malaria vectors to recent deforestation. This highlights the importance of the temporal dynamics of land-use change in driving disease risk and the value of large synthetic datasets for understanding changing disease risk with environmental change.

Seroprevalence of Dengue, Chikungunya, and Zika viruses antibodies in a cohort of asymptomatic pregnant women in a low-income region of Minas Gerais, Brazil, 2018-2019.

Santos JD, Garcia BCC, Rocha KLS, Silva TJ, da Silva Lage SL, de Souza Macedo M, Teixeira RA, Rocha-Vieira E, de Oliveira DB.
15-07-2023
Braz J Microbiol.
https://pubmed.ncbi.nlm.nih.gov/37454038/

Dengue seroprevalence study in Bali.

Masyeni S, Fatawy RM, Paramasatiari AAAL, Maheraditya A, Dewi RK, Winianti NW, Santosa A, Setiabudy M, Sumadewi NT, Herawati S.
14-07-2023
PLoS One.
https://pubmed.ncbi.nlm.nih.gov/37450543/

Introduction: Dengue infection poses significant public health problems in tropical and subtropical regions worldwide. The clinical manifestations of dengue vary from asymptomatic to severe dengue manifestations. This serological survey highlighted the high incidence of asymptomatic cases. This study aimed to determine the prevalence of dengue in healthy and ill adults in Bali. Methods: Cross-sectional seroprevalence surveys were performed between July 2020 and June 2021 among healthy and ill adults in Denpasar Bali. Blood samples were collected from 539 randomly selected urban sites in Denpasar. Immunoglobulin G antibodies against the dengue virus were detected in serum using a commercial enzyme-linked immunosorbent assay kit. Results: Overall, the dengue seroprevalence rate among the 539 clinically healthy and ill adults was high (85.5%). The median age was 34.1 (18-86.1). Most of the participants in the study were younger than 40 years (61.2%). Men were the dominant sex (54.5%). The study found a significant association between dengue seropositivity among people aged > 40 years and healthy status ($p = 0.005$; odds ratio [OR] = 0.459 and $p < 0.001$; OR = 0.336, respectively). The study reported that as many as 60% of the subjects had a history of previously suspected dengue infection. This study reflected the proportion of asymptomatic dengue patients requiring better assessment with a serological test. Conclusion: The current study highlighted that real cases of dengue infection may be higher than reported, with a high prevalence of dengue seropositivity and a relatively dominant proportion of asymptomatic cases. The study guides physicians to be aware of every dengue infection in tropical countries and prevent the spread of the disease.

Mathematical modeling of Dengue virus serotypes propagation in Mexico.

Sánchez-González G, Condé R.
14-06-2023
PLoS One.
https://pubmed.ncbi.nlm.nih.gov/37450471/

The Dengue virus (DENV) constitutes a major vector borne virus disease worldwide. Prediction of the DENV spread dynamics, prevalence and infection rates are crucial elements to guide the public health services effort towards meaningful actions. The existence of four DENV serotypes further complicates the virus proliferation forecast. The different serotypes have varying clinical impacts, and the symptomatology of the infection is dependent on the infection history of the patient. Therefore, changes in the prevalent DENV serotype found in one location have a profound impact on the regional public health. The prediction of the spread and intensity of infection of the individual DENV serotypes in specific locations would allow the authorities to plan local pesticide spray to control the vector as well as the purchase of specific antibody therapy. Here we used a mathematical model to predict serotype-specific DENV prevalence and overall case burden in Mexico.

Retrospective Analysis of Spectrum of Infections and Antibiotic Resistance Pattern in Chronic Kidney Disease Patients on Maintenance Hemodialysis in a Tertiary Care Centre in North India.

Chhakchhuak M, Chaturvedy M, Agarwal J, Tak V, Bajpai NK.
Mai-Juin 2023
Indian J Nephrol.
https://pubmed.ncbi.nlm.nih.gov/37448889/

Antiviral Evaluation of New Synthetic Bioconjugates Based on GA-Hecate: A New Class of Antivirals Targeting Different Steps of Zika Virus Replication.

da Silva Sanches PR, Velazquez RS, Batista MN, Carneiro BM, Bittar C, De Lorenzo G, Rahal P, Patel AH, Cilli EM.
21-07-2023
Molecules.
https://pubmed.ncbi.nlm.nih.gov/37446546/

Re-emerging arboviruses represent a serious health problem due to their rapid vector-mediated spread, mainly in urban tropical areas. The 2013-2015 Zika virus (ZIKV) outbreak in South and Central America has been associated with cases of microcephaly in newborns and Guillain-Barret syndrome. We previously showed that the conjugate gallic acid-Hecate (GA-FALALKALKKALKKLKKALKKAL-$CONH_2$)-is an efficient inhibitor of the hepatitis C virus. Here, we show that the Hecate peptide is degraded in human blood serum into three major metabolites. These metabolites conjugated with gallic acid were synthesized and their effect on ZIKV replication in cultured cells was evaluated. The GA-metabolite 5 (GA-FALALKALKKALKKL-COOH) was the most efficient in inhibiting two ZIKV strains of African and Asian lineage at the stage of both virus entry (virucidal and protective) and replication (post-entry). We also demonstrate that GA-metabolite 5 does not affect cell growth after 7 days of continuous treatment. Thus, this study identifies a new synthetic antiviral compound targeting different steps of ZIKV replication in vitro and with the potential for broad reactivity against other flaviviruses. Our work highlights a promising strategy for the development of new antivirals based on peptide metabolism and bioconjugation.

Antiviral and Immunomodulatory Activities of Clinacanthus nutans (Burm. f.) Lindau.

Lin CM, Chen HH, Lung CW, Chen HJ.
28-06-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37445964/

Re-emerging arboviruses represent a serious health problem due to their rapid vector-mediated spread, mainly in urban tropical areas. The 2013-2015 Zika virus (ZIKV) outbreak in South and Central America has been associated with cases of microcephaly in newborns and Guillain-Barret syndrome. We previously showed that the conjugate gallic acid-Hecate (GA-FALALKALKKALKKLKKALKKAL-$CONH_2$)-is an efficient inhibitor of the hepatitis C virus. Here, we show that the Hecate peptide is degraded in human blood serum into three major metabolites. These metabolites conjugated with gallic acid were synthesized and their effect on ZIKV replication in cultured cells was evaluated. The GA-metabolite 5 (GA-FALALKALKKALKKL-COOH) was the most efficient in inhibiting two ZIKV strains of African and Asian lineage at the stage of both virus entry (virucidal and protective) and replication (post-entry). We also demonstrate that GA-metabolite 5 does not affect cell growth after 7 days of continuous treatment. Thus, this study identifies a new synthetic antiviral compound targeting different steps of ZIKV replication in vitro and with the potential for broad reactivity against other flaviviruses. Our work highlights a promising strategy for the development of new antivirals based on peptide metabolism and bioconjugation.

Heterologous DNA Prime- Subunit Protein Boost with Chikungunya Virus E2 Induces Neutralizing Antibodies and Cellular-Mediated Immunity.

Coirada FC, Fernandes ER, Mello LR, Schuch V, Soares Campos G, Braconi CT, Boscardin SB, Santoro Rosa D.
23-06-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37445695/

Chikungunya virus (CHIKV) has become a significant public health concern due to the increasing number of outbreaks worldwide and the associated comorbidities. Despite substantial efforts, there is no specific treatment or licensed vaccine against CHIKV to date. The E2 glycoprotein of CHIKV is a promising vaccine candidate as it is a major target of neutralizing antibodies during infection. In this study, we evaluated the immunogenicity of two DNA vaccines (a non-targeted and a dendritic cell-targeted vaccine) encoding a consensus sequence of $E2_{CHIKV}$ and a recombinant protein ($E2^*_{CHIKV}$). Mice were immunized with different homologous and heterologous DNAprime-E2* protein boost strategies, and the specific humoral and cellular immune responses were accessed. We found that mice immunized with heterologous non-targeted DNA prime- $E2^*_{CHIKV}$ protein boost developed high levels of neutralizing antibodies, as well as specific IFN-γ producing cells and polyfunctional $CD4^+$ and $CD8^+$ T cells. We also identified 14 potential epitopes along the $E2_{CHIKV}$ protein. Furthermore, immunization with recombinant $E2^*_{CHIKV}$ combined with the adjuvant AS03 presented the highest humoral response with neutralizing capacity. Finally, we show that the heterologous prime-boost strategy with the non-targeted pVAX-E2 DNA vaccine as the prime followed by E2* protein + AS03 boost is a promising combination to elicit a broad humoral and cellular immune response. Together, our data highlights the importance of $E2_{CHIKV}$ for the development of a CHIKV vaccine.

Exploring New Mechanism of Depression from the Effects of Virus on Nerve Cells.

Yu X, Wang S, Wu W, Chang H, Shan P, Yang L, Zhang W, Wang X.
03-07-2023
Cells.
https://pubmed.ncbi.nlm.nih.gov/37443801/

Depression is a common neuropsychiatric disorder with long-term recurrent depressed mood, pain and despair, pessimism and anxiety, and even suicidal tendencies as the main symptoms. Depression usually induces or aggravates the development of other related diseases, such as sleep disorders and endocrine disorders. In today's society, the incidence of depression is increasing

worldwide, and its pathogenesis is complex and generally believed to be related to genetic, psychological, environmental, and biological factors. Current studies have shown the key role of glial cells in the development of depression, and it is noteworthy that some recent evidence suggests that the development of depression may be closely related to viral infections, such as SARS-CoV-2, BoDV-1, ZIKV, HIV, and HHV6, which infect the organism and cause some degree of glial cells, such as astrocytes, oligodendrocytes, and microglia. This can affect the transmission of related proteins, neurotransmitters, and cytokines, which in turn leads to neuroinflammation and depression. Based on the close relationship between viruses and depression, this paper provides an in-depth analysis of the new mechanism of virus-induced depression, which is expected to provide a new perspective on the mechanism of depression and a new idea for the diagnosis of depression in the future.

Performance Evaluation of VIDAS® Diagnostic Assays Detecting Anti-Chikungunya Virus IgM and IgG Antibodies: An International Study.

Pereira GM, Manuli ER, Coulon L, Côrtes MF, Ramundo MS, Dromenq L, Larue-Triolet A, Raymond F, Tourneur C, Lázari CDS, Brasil P, Filippis AMB, Paranhos-Baccalà G, Banz A, Sabino EC.
07-07-2023
Diagnostics (Basel).
https://pubmed.ncbi.nlm.nih.gov/37443699/

Chikungunya (CHIK) is a debilitating mosquito-borne disease with an epidemiology and early clinical symptoms similar to those of other arboviruses-triggered diseases such as dengue or Zika. Accurate and rapid diagnosis of CHIK virus (CHIKV) infection is therefore challenging. This international study evaluated the performance of the automated VIDAS® anti-CHIKV IgM and IgG assays compared to that of manual competitor IgM and IgG ELISA for the detection of anti-CHIKV IgM and IgG antibodies in 660 patients with suspected CHIKV infection. Positive and negative agreements of the VIDAS® CHIKV assays with ELISA ranged from 97.5% to 100.0%. The sensitivity of the VIDAS® CHIKV assays evaluated in patients with a proven CHIKV infection confirmed reported kinetics of anti-CHIKV IgM and IgG response, with a positive detection of 88.2-100.0% for IgM ≥ 5 days post symptom onset and of 100.0% for IgG ≥ 11 days post symptom onset. Our study also demonstrated the superiority of ELISA and VIDAS® assays over rapid diagnostic IgM/IgG tests. The analytical performance of VIDAS® anti-CHIKV IgM and IgG assays was excellent, with a high precision (coefficients of variation ≤ 7.4%) and high specificity (cross-reactivity rate ≤ 2.9%). This study demonstrates the suitability of the automated VIDAS® anti-CHIKV IgM and IgG assays to diagnose CHIKV infections and supports its applicability for epidemiological surveillance and differential diagnosis in regions endemic for CHIKV.

Exclusion of pregnant people from emergency vaccine clinical trials: A systematic review of clinical trial protocols and reporting from 2009 to 2019.

Minchin J, Harris GH, Baumann S, Smith ER.
11-07-2023
Vaccine.
https://pubmed.ncbi.nlm.nih.gov/37442686/

Detection of dengue virus serotype 1 from gadfly in China.

Qi NS, Zhang X, Liao SQ, Li J, Liu JM, Shao JW, Sun MF.
11-07-2023
J Infect.
https://pubmed.ncbi.nlm.nih.gov/37442374/

Latin America in the clutches of an old foe: Dengue.

Alied M, Endo PT, Aquino VH, Vadduri VV, Huy NT.
10-07-2023
Braz J Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37442196/

Attitude towards dengue control efforts with the potential of digital technology during COVID-19: partial least squares-structural equation modeling.

Purnama SG, Susanna D, Achmadi UF, Eryando T.
27-06-2023
F1000Res.
https://pubmed.ncbi.nlm.nih.gov/37441548/

Background: Dengue fever is still a public health issue in Indonesia, and during the coronavirus disease 2019 (COVID-19) pandemic, integrated digital technology will be required for its control. This study aims to identify critical indicators influencing attitudes towards dengue control related to the potential for implementing digital technology. Methods: This was a cross-sectional survey, with 515 people willing to fill out an online questionnaire. The analysis was conducted using Partial Least Square-Structural Equation Modelling (PLS-SEM). There were 46 indicators used to assess attitudes toward dengue control, which were organized into six variables: the need for digital information systems, perceptions of being threatened with dengue, the benefits of dengue control programs, program constraints, environmental factors and attitudes in dengue control. Results: The source of information needed for dengue control was mainly through social media. There was a positive relationship between perception of environmental factors to perception of dengue threat, perception of program constraints, perception of program benefits, and perception of digital technology needs. Perception of program benefits and threatened perception of dengue have a positive relationship with perception of digital technology needs. Conclusions: This model showed the variables perception of digital technology and perception of benefits had a positive association with attitude towards dengue control.

The Aedes aegypti RNA interference response against Zika virus in the

context of co-infection with dengue and chikungunya viruses.

Leggewie M, Scherer C, Altinli M, Gestuveo RJ, Sreenu VB, Fuss J, Vazeille M, Mousson L, Badusche M, Kohl A, Failloux AB, Schnettler E.
13-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37440582/

Since its detection in 2015 in Brazil, Zika virus (ZIKV) has remained in the spotlight of international public health and research as an emerging arboviral pathogen. In addition to single infection, ZIKV may occur in co-infection with dengue (DENV) and chikungunya (CHIKV) viruses, with whom ZIKV shares geographic distribution and the mosquito Aedes aegypti as a vector. The main mosquito immune response against arboviruses is RNA interference (RNAi). It is unknown whether or not the dynamics of the RNAi response differ between single arboviral infections and co-infections. In this study, we investigated the interaction of ZIKV and DENV, as well as ZIKV and CHIKV co-infections with the RNAi response in Ae. aegypti. Using small RNA sequencing, we found that the efficiency of small RNA production against ZIKV -a hallmark of antiviral RNAi-was mostly similar when comparing single and co-infections with either DENV or CHIKV. Silencing of key antiviral RNAi proteins, showed no change in effect on ZIKV replication when the cell is co-infected with ZIKV and DENV or CHIKV. Interestingly, we observed a negative effect on ZIKV replication during CHIKV co-infection in the context of Ago2-knockout cells, though his effect was absent during DENV co-infection. Overall, this study provides evidence that ZIKV single or co-infections with CHIKV or DENV are equally controlled by RNAi responses. Thus, Ae. aegypti mosquitoes and derived cells support co-infections of ZIKV with either CHIKV or DENV to a similar level than single infections, as long as the RNAi response is functional.

Carbonic anhydrase inhibitory activity of phthalimide-capped benzene sulphonamide derivatives.

Shilkar D, Mohd Siddique MU, Bua S, Yasmin S, Patil M, Timiri AK, Supuran CT, Jayaprakash V.
Dec-2023
J Enzyme Inhib Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37439360/

Midgut transcriptomic responses to dengue and chikungunya viruses in the vectors Aedes albopictus and Aedes malayensis.

Modahl CM, Chowdhury A, Low DHW, Manuel MC, Missé D, Kini RM, Mendenhall IH, Pompon J.
12-07-2023
Sci Transl Med.
https://pubmed.ncbi.nlm.nih.gov/37438463/

Insights into dengue immunity from vaccine trials.

Ooi EE, Kalimuddin S.
12-07-2023
Sci Transl Med.
https://pubmed.ncbi.nlm.nih.gov/37437017/

The quest for an effective dengue vaccine has culminated in two approved vaccines and another that has completed phase 3 clinical trials. However, shortcomings exist in each, suggesting that the knowledge on dengue immunity used to develop these vaccines was incomplete. Vaccine trial findings could refine our understanding of dengue immunity, because these are experimentally derived, placebo-controlled data. Results from these trials suggest that neutralizing antibody titers alone are insufficient to inform protection against symptomatic infection, implicating a role for cellular immunity in protection. These findings have relevance for both future dengue vaccine development and application of current vaccines for maximal public health benefit.

Dengue virus M and E proteins belonging to genotype II (Cosmopolitan) of serotype 2 are influenced by the nature of M residue 36.

Decotter J, Desprès P, Gadea G.
Juil-2023
J Gen Virol.
https://pubmed.ncbi.nlm.nih.gov/37436433/

Mosquito-borne dengue disease is caused by the dengue virus serotype-1 to serotype-4. The contemporary dengue outbreaks in the southwestern Indian ocean coincided with the widespread of dengue virus serotype 2 genotype II (Cosmopolitan), including epidemic viral strains DES-14 and RUN-18 isolated in Dar es Salaam (Tanzania) in 2014 and La Reunion Island (France) in 2018, respectively. Heterodimeric interaction between prM (intracellular precursor of surface structural M protein) and envelope E proteins is required during the initial stage of dengue virus assembly. Amino acid 127 of DES-14 prM protein (equivalent to M36) has been identified as an infrequent valine whereas RUN-18 has a common isoleucine. In the present study, we examined the effect of M-I36V mutation on the expression of a recombinant RUN-18 E protein co-expressed with prM in human epithelial A549 cells. The M ectodomain of dengue virus serotype 2 embeds a pro-apoptotic peptide referred as D_2AMP. The impact of M-I36V mutation on the death-promoting capability of D_2AMP was assessed in A549 cells. We showed that valine at position M36 affects expression of recombinant RUN-18 E protein and potentiates apoptosis-inducing activity of D_2AMP. We propose that the nature of M residue 36 influences the virological characteristics of dengue 2 M and E proteins belonging to genotype II that contributes to global dengue burden.

Design, synthesis, and biological evaluation of a series of new anthraquinone derivatives as anti-ZIKV agents.

Zhu Y, Yu J, Chen T, Liu W, Huang Y, Li J, Zhang B, Zhu G, He Z, Long Y, Yuan J.
05-10-2023
Eur J Med Chem.

https://pubmed.ncbi.nlm.nih.gov/37421888/

The organization of double-stranded RNA in the chikungunya virus replication organelle.

Laurent T, Carlson LA.
05-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37406010/

Alphaviruses are mosquito-borne, positive-sense single-stranded RNA viruses. Amongst the alphaviruses, chikungunya virus is notable as a large source of human illness, especially in tropical and subtropical regions. When they invade a cell, alphaviruses generate dedicated organelles for viral genome replication, so-called spherules. Spherules form as outward-facing buds at the plasma membrane, and it has recently been shown that the thin membrane neck that connects this membrane bud with the cytoplasm is guarded by a two-megadalton protein complex that contains all the enzymatic functions necessary for RNA replication. The lumen of the spherules contains a single copy of the negative-strand template RNA, present in a duplex with newly synthesized positive-sense RNA. Less is known about the organization of this double-stranded RNA as compared to the protein components of the spherule. Here, we analyzed cryo-electron tomograms of chikungunya virus spherules in terms of the organization of the double-stranded RNA replication intermediate. We find that the double-stranded RNA has a shortened apparent persistence length as compared to unconstrained double-stranded RNA. Around half of the genome is present in either of five conformations identified by subtomogram classification, each representing a relatively straight segment of ~25-32 nm. Finally, the RNA occupies the spherule lumen at a homogeneous density, but has a preferred orientation to be perpendicular to a vector pointing from the membrane neck towards the spherule center. Taken together, this analysis lays another piece of the puzzle of the highly coordinated alphavirus genome replication.

Seroprevalence of Dengue, Chikungunya and Zika at the epicenter of the congenital microcephaly epidemic in Northeast Brazil: A population-based survey.

Braga C, Martelli CMT, Souza WV, Luna CF, Albuquerque MFPM, Mariz CA, Morais CNL, Brito CAA, Melo CFCA, Lins RD, Drexler JF, Jaenisch T, Marques ETA, Viana IFT.
03-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37399197/

Discovery of Acyl-Indole Derivatives as Pan-Serotype Dengue Virus NS4B Inhibitors.

Kesteleyn B, Bardiot D, Bonfanti JF, De Boeck B, Goethals O, Kaptein SJF, Stoops B, Coesemans E, Fortin J, Muller P, Doublet F, Carlens G, Koukni M, Smets W, Raboisson P, Chaltin P, Simmen K, Van Loock M, Neyts J, Marchand A, Jonckers THM.
13-07-2023
J Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37389813/

In the absence of any approved dengue-specific treatment, the discovery and development of a novel small-molecule antiviral for the prevention or treatment of dengue are critical. We previously reported the identification of a novel series of 3-acyl-indole derivatives as potent and pan-serotype dengue virus inhibitors. We herein describe our optimization efforts toward preclinical candidates **24a** and **28a** with improved pan-serotype coverage (EC_{50}'s against the four DENV serotypes ranging from 0.0011 to 0.24 μM for **24a** and from 0.00060 to 0.084 μM for **28a**), chiral stability, and oral bioavailability in preclinical species, as well as showing a dose-proportional increase in efficacy against DENV-2 infection in vivo in mice.

The effects of allosteric and competitive inhibitors on ZIKV protease conformational dynamics explored through smFRET, nanoDSF, DSF, and ^{19}F NMR.

Maus H, Hammerschmidt SJ, Hinze G, Barthels F, Pérez Carrillo VH, Hellmich UA, Basché T, Schirmeister T.
05-10-2023
Eur J Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37379675/

Zika and dengue viruses cause mosquito-borne diseases of high epidemic relevance. The viral NS2B-NS3 proteases play crucial roles in the pathogen replication cycle and are validated drug targets. They can adopt at least two conformations depending on the position of the NS2B cofactor. Recently, we reported ligand-induced conformational changes of dengue virus NS2B-NS3 protease by single-molecule Förster resonance energy transfer (smFRET). Here, we investigated the conformational dynamics of the homologous Zika virus protease through an integrated methodological approach combining smFRET, thermal shift assays (DSF and nanoDSF) and ^{19}F NMR spectroscopy. Our results show that allosteric inhibitors favor the open conformation and competitive inhibitors stabilize the closed conformation of the Zika virus protease.

Design, synthesis, antiviral evaluation, and In silico studies of acrylamides targeting nsP2 from Chikungunya virus.

Souza BG, Choudhary S, Vilela GG, Passos GFS, Costa CACB, Freitas JD, Coelho GL, Brandão JA, Anderson L, Bassi ÊJ, Araújo-Júnior JX, Tomar S, Silva-Júnior EFD.
05-10-2023
Eur J Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37364511/

The Togaviridae family comprises several New- and Old-World Alphaviruses that have been responsible for thousands of human illnesses, including the RNA arbovirus Chikungunya virus (CHIKV). Firstly, it was reported in Tanzania in 1952 but rapidly it spread to several countries from Europe, Asia, and the Americas. Since then, CHIKV has been circulating in diverse countries around the world,

leading to increased morbidity rates. Currently, there are no FDA-approved drugs or licensed vaccines to specifically treat CHIKV infections. Thus, there is a lack of alternatives to fight against this viral disease, making it an unmet need. Structurally, CHIKV is composed of five structural proteins (E3, E2, E1, C, and 6k) and four non-structural proteins (nsP1-4), in which nsP2 represents an attractive antiviral target for designing novel inhibitors since it has an essential role in the virus replication and transcription. Herein, we used a rational drug design strategy to select some acrylamide derivatives to be synthesized and evaluated against CHIKV nsP2 and also screened on CHIKV-infected cells. Thus, two regions of modifications were considered for these types of inhibitors, based on a previous study of our group, generating 1560 possible inhibitors. Then, the 24 most promising ones were synthesized and screened by using a FRET-based enzymatic assay protocol targeting CHIKV nsP2, identifying LQM330, 333, 336, and 338 as the most potent inhibitors, with K_i values of 48.6 ± 2.8, 92.3 ± 1.4, 2.3 ± 1.5, and 181.8 ± 2.5 μM, respectively. Still, their K_m and V_{max} kinetic parameters were also determined, along with their competitive binding modes of CHIKV nsP2 inhibition. Then, ITC analyses revealed K_D values of 127, 159, 198, and 218 μM for LQM330, 333, 336, and 338, respectively. Also, their ΔH, ΔS, and ΔG physicochemical parameters were determined. MD simulations demonstrated that these inhibitors present a stable binding mode with nsP2, interacting with important residues of this protease, according to docking analyzes. Moreover, MM/PBSA calculations displayed that van der Waals interactions are mainly responsible for stabilizing the inhibitor-nsP2 complex, and their binding energies corroborated with their K_i values, having -198.7 ± 15.68, -124.8 ± 17.27, -247.4 ± 23.78, and -100.6 ± 19.21 kcal/mol for LQM330, 333, 336, and 338, respectively. Since Sindbis (SINV) nsP2 is similar to CHIKV nsP2, these best inhibitors were screened against SINV-infected cells, and it was verified that LQM330 presented the best result, with an EC_{50} value of 0.95 ± 0.09 μM. Even at 50 μM concentration, LQM338 was found to be cytotoxic on Vero cells after 48 h. Then, LQM330, 333, and 336 were evaluated against CHIKV-infected cells in antiviral assays, in which LQM330 was found to be the most promising antiviral candidate in this study, exhibiting an EC_{50} value of 5.2 ± 0.52 μM and SI of 31.78. The intracellular flow cytometry demonstrated that LQM330 is able to reduce the CHIKV cytopathogenic effect on cells, and also reduce the percentage of CHIKV-positive cells from 66.1% ± 7.05 to 35.8% ± 5.78 at 50 μM concentration. Finally, qPCR studies demonstrated that LQM330 was capable of reducing the number of viral RNA copies/μL, suggesting that CHIKV nsP2 is targeted by this inhibitor as its mechanism of action.

Interventions against Aedes/dengue at the household level: a systematic review and meta-analysis.

Montenegro-Quiñonez CA, Louis VR, Horstick O, Velayudhan R, Dambach P, Runge-Ranzinger S.
Juil-2023
EBioMedicine.
https://pubmed.ncbi.nlm.nih.gov/37352828/

DENV and ZIKV cross paths.

Du Toit A.
12-07-2023
Nat Rev Microbiol.
https://pubmed.ncbi.nlm.nih.gov/37340087/

Clinical Characteristics and Outcomes Among Travelers With Severe Dengue : A GeoSentinel Analysis.

Huits R, Angelo KM, Amatya B, Barkati S, Barnett ED, Bottieau E, Emetulu H, Epelboin L, Eperon G, Medebb L, Gobbi F, Grobusch MP, Itani O, Jordan S, Kelly P, Leder K, Díaz-Menéndez M, Okumura N, Rizwan A, Rothe C, Saio M, Waggoner J, Yoshimura Y, Libman M, Hamer DH, Schwartz E.
Juil-2023
Ann Intern Med.
https://pubmed.ncbi.nlm.nih.gov/37335991/

Dengue hepatitis: Incidence, spectrum and outcome.

Prajapati R, Mehta R, Kabrawala M, Nandwani S, Patel N, Sethia M, Magnani K, Tandel R, Kumar A.
Juin-2023
Indian J Gastroenterol.
https://pubmed.ncbi.nlm.nih.gov/37335522/

Background and aims: While dengue infection is common in India, there is scarce information on dengue hepatitis. The aim of this study was to analyze the incidence, spectrum and outcome of dengue hepatitis. Methods: We retrospectively analyzed consecutive patients, who had hepatitis among those with dengue infection admitted to two tertiary care hospitals in western India from January 2016 to March 2021. Diagnosis of dengue infection was made by serology. Dengue hepatitis was diagnosed and the severity of dengue was categorized by standard criteria. Results: Of 1664 patients admitted with dengue fever during the study period, 199 patients had hepatitis (i.e. incidence of dengue hepatitis was 11.9%). Of the 199 dengue hepatitis patients (age: 29 [13 - 80] years, median [range], 67% males), 100 patients (50%) had severe dengue, 73 (36%) had severe dengue hepatitis, 32 (16%) had dengue shock syndrome and eight (4%) had acute liver failure. Forty-five patients (23%) had acute lung injury and 32 (16%) had acute kidney injury. The dengue hepatitis patients were treated with standard medical care, including vital organ support, as needed-166 (83%) patients survived, while 33 patients (17%) died (cause of death: multi-organ failure: 24 patients, septic shock: nine patients). The presence of shock independently predicted mortality (odds ratio 6.4, 95% confidence interval: 1.2 - 34). Among patients with dengue hepatitis, mortality rate was higher in those with severe dengue (23%), dengue shock syndrome (47%), severe dengue hepatitis (24%) and acute liver failure (38%). Conclusion: In this large series of hospitalized patients with dengue infection, the incidence of dengue hepatitis was 11.9%. Among 199 dengue hepatitis, 17% died; multi-organ failure was the commonest cause for death and death rate was higher in patients with more severe disease. The presence of shock at presentation independently predicted mortality.

Crude saliva of Amblyomma cajennense sensu stricto (Acari: Ixodidae) reduces locomotor activity and increases the hemocyte number in the females of Aedes aegypti (Diptera: Culicidae).

Cerri F, Araujo MDS, Aguirre AAR, Evaristo GPC, Evaristo JAM, Nogueira FCS, de Medeiros JF, Dias QM.
12-07-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37330106/

Insecticidal and Repellent Properties of Rapid-Acting Fluorine-Containing Compounds against Aedes aegypti Mosquitoes.

Zhu X, Valbon W, Qiu M, Hu CT, Yang J, Erriah B, Jankowska M, Dong K, Ward MD, Kahr B.
14-07-2023
ACS Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37311068/

The development of safe and potent insecticides remains an integral part of a multifaceted strategy to effectively control human-disease-transmitting insect vectors. Incorporating fluorine can dramatically alter the physiochemical properties and bioavailability of insecticides. For example, 1,1,1-trichloro-2,2-bis(4-fluorophenyl)ethane (DFDT)–a difluoro congener of trichloro-2,2-bis(4-chlorophenyl)ethane (DDT)–was demonstrated previously to be 10-fold less toxic to mosquitoes than DDT in terms of LD_{50} values, but it exhibited a 4-fold faster knockdown. Described herein is the discovery of fluorine-containing 1-aryl-2,2,2-trichloro-ethan-1-ols (FTEs, for fluorophenyl-trichloromethyl-ethanols). FTEs, particularly per-fluorophenyl-trichloromethyl-ethanol (PFTE), exhibited rapid knockdown not only against *Drosophila melanogaster* but also against susceptible and resistant *Aedes aegypti* mosquitoes, major vectors of Dengue, Zika, yellow fever, and Chikungunya viruses. The *R* enantiomer of any chiral FTE, synthesized enantioselectively, exhibited faster knockdown than its corresponding *S* enantiomer. PFTE does not prolong the opening of mosquito sodium channels that are characteristic of the action of DDT and pyrethroid insecticides. In addition, pyrethroid/DDT-resistant *Ae. aegypti* strains having enhanced P450-mediated detoxification and/or carrying sodium channel mutations that confer knockdown resistance were not cross-resistant to PFTE. These results indicate a mechanism of PFTE insecticidal action distinct from that of pyrethroids or DDT. Furthermore, PFTE elicited spatial repellency at concentrations as low as 10 ppm in a hand-in-cage assay. PFTE and MFTE were found to possess low mammalian toxicity. These results suggest the substantial potential of FTEs as a new class of compounds for controlling insect vectors, including pyrethroid/DDT-resistant mosquitoes. Further investigations of FTE insecticidal and repellency mechanisms could provide important insights into how incorporation of fluorine influences the rapid lethality and mosquito sensing.

Mitophagy Activation Targeting PINK1 Is an Effective Treatment to Inhibit Zika Virus Replication.

Huang Y, Li Q, Kang L, Li B, Ye H, Duan X, Xie H, Jiang M, Li S, Zhu Y, Tan Q, Chen L.
14-07-2023
ACS Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37300493/

Flavivirus Antibodies Reactive to Zika Virus Detected in Multiple Species of Nonhuman Primates in Kenya, 2008-2017.

Makio A, Widdowson MA, Ambala P, Ozwara H, Munyua P, Hunsperger E.
Juil-2023
Vector Borne Zoonotic Dis.
https://pubmed.ncbi.nlm.nih.gov/37205849/

The 2022 dengue outbreak in Bangladesh: hypotheses for the late resurgence of cases and fatalities.

Haider N, Hasan MN, Khalil I, Tonge D, Hegde S, Chowdhury MAB, Rahman M, Khan MH, Ansumana R, Zumla A, Uddin MJ.
12-07-2023
J Med Entomol.
https://pubmed.ncbi.nlm.nih.gov/37202843/

Bangladesh reported the highest number of annual deaths (n = 281) related to dengue virus infection in 2022 since the virus reappeared in the country in 2000. Earlier studies showed that >92% of the annual cases occurred between the months of August and September. The 2022 outbreak is characterized by late onset of dengue cases with unusually higher deaths in colder months, that is, October-December. Here we present possible hypotheses and explanations for this late resurgence of dengue cases. First, in 2022, the rainfall started late in the season. Compared to the monthly average rainfall for September and October between 2003 and 2021, there was 137 mm of additional monthly rainfall recorded in September and October 2022. Furthermore, the year 2022 was relatively warmer with a 0.71°C increased temperature than the mean annual temperature of the past 20 yr. Second, a new dengue virus serotype, DENV-4, had recently reintroduced/reappeared in 2022 and become the dominant serotype in the country for a large naïve population. Third, the post-pandemic return of normalcy after 2 yr of nonpharmaceutical social measures facilitates extra mosquito breeding habitats, especially in construction sites. Community engagement and regular monitoring and destruction of Aedes mosquitoes' habitats should be prioritized to control dengue virus outbreaks in Bangladesh.

Broad-Spectrum Small-Molecule Inhibitors Targeting the SAM-Binding Site of Flavivirus NS5 Methyltransferase.

Samrat SK, Bashir Q, Huang Y, Trieshmann CW, Tharappel AM, Zhang R, Chen K, Zheng YG, Li Z, Li H.

14-07-2023
ACS Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37348028/

Flavivirus infections, such as those caused by dengue virus (DENV), West Nile virus (WNV), yellow fever virus (YFV), and Zika virus (ZIKV), pose a rising threat to global health. There are no FDA-approved drugs for flaviviruses, although a small number of flaviviruses have vaccines. For flaviviruses or unknown viruses that may appear in the future, it is particularly desirable to identify broad-spectrum inhibitors. The NS5 protein is regarded as one of the most promising flavivirus drug targets because it is conserved across flaviviruses. In this study, we used FL-NAH, a fluorescent analog of the methyl donor *S*-adenosyl methionine (SAM), to develop a fluorescence polarization (FP)-based high throughput screening (HTS) assay to specifically target methyltransferase (MTase), a vital enzyme for flaviviruses that methylates the N7 and 2'-O positions of the viral 5'-RNA cap. Pilot screening identified two candidate MTase inhibitors, NSC 111552 and 288387. The two compounds inhibited the FL-NAH binding to the DENV3 MTase with low micromolar IC_{50}. Functional assays verified the inhibitory potency of these molecules for the flavivirus MTase activity. Binding studies indicated that these molecules are bound directly to the DENV3 MTase with similar low micromolar affinity. Furthermore, we showed that these compounds greatly reduced ZIKV replication in cell-based experiments at dosages that did not cause cytotoxicity. Finally, docking studies revealed that these molecules bind to the SAM-binding region on the DENV3 MTase, and further mutagenesis studies verified residues important for the binding of these compounds. Overall, these compounds are innovative and attractive candidates for the development of broad-spectrum inhibitors for the treatment of flavivirus infections.

Spatial repellency and attractancy responses of some chemical lures against Aedes albopictus (Diptera: Culicidae) and Anopheles minimus (Diptera: Culicidae) using the high-throughput screening system.

Boonyuan W, Tisgratog R, Ahebwa A, Leepasert T, Thanispong K, Chareonviriyaphap T.
12-07-2023
J Med Entomol.
https://pubmed.ncbi.nlm.nih.gov/37167551/

El Niño Southern Oscillation (ENSO) effects on local weather, arboviral diseases, and dynamics of managed and unmanaged populations of Aedes aegypti (Diptera: Culicidae) in Puerto Rico.

Barrera R, Acevedo V, Amador M, Marzan M, Adams LE, Paz-Bailey G.
12-07-2023
J Med Entomol.
https://pubmed.ncbi.nlm.nih.gov/37156093/

We investigated the effects of interannual El Niño Southern Oscillation (ENSO) events on local weather, Aedes aegypti populations, and combined cases of dengue (DENV), chikungunya (CHIKV), and Zika (ZIKV) viruses in 2 communities with mass mosquito trapping and 2 communities without mosquito control in southern Puerto Rico (2013-2019). Gravid adult Ae. aegypti populations were monitored weekly using Autocidal Gravid Ovitraps (AGO traps). Managing Ae. aegypti populations was done using 3 AGO traps per home in most homes. There were drought conditions in 2014-2015 concurrent with the emergence of a strong El Niño (2014-2016), wetter conditions during La Niña (2016-2018), a major hurricane (2017), and a weaker El Niño (2018-2019). The main factor explaining differences in Ae. aegypti abundance across sites was mass trapping. Populations of Ae. aegypti reached maximum seasonal values during the wetter and warmer months of the year when arbovirus epidemics occurred. El Niño was significantly associated with severe droughts that did not impact the populations of Ae. aegypti. Arbovirus cases at the municipality level were positively correlated with lagged values (5-12 mo.) of the Oceanic El Niño Index (ONI), droughts, and abundance of Ae. aegypti. The onset of strong El Niño conditions in Puerto Rico may be useful as an early warning signal for arboviral epidemics in areas where the abundance of Ae. aegypti exceeds the mosquito density threshold value.

Nasopharyngeal swabs as alternative specimens for the diagnosis of dengue virus infection.

Maia AC, Quintão TSC, de Oliveira PM, Cassemiro ÉM, Cilião-Alves DC, Alves PPM, Martins FDAP, Araújo ELL, Gurgel HDC, Noronha EF, Ramalho WM, Pereira AL, Slavov SN, de Araújo WN, Haddad R.
Août-2023
J Infect.
https://pubmed.ncbi.nlm.nih.gov/37003524/

Regulation of ribonucleoprotein condensates by RNase L during viral infection.

Burke JM.
Juil-Août 2023
Wiley Interdiscip Rev RNA.
https://pubmed.ncbi.nlm.nih.gov/36479619/

In response to viral infection, mammalian cells activate several innate immune pathways to antagonize viral gene expression. Upon recognition of viral double-stranded RNA, protein kinase R (PKR) phosphorylates the alpha subunit of eukaryotic initiation factor 2 (eIF2α) on serine 51. This inhibits canonical translation initiation, which broadly antagonizes viral protein synthesis. It also promotes the assembly of cytoplasmic ribonucleoprotein complexes termed stress granules (SGs). SGs are widely thought to promote cell survival and antiviral signaling. However, co-activation of the OAS/RNase L antiviral pathway inhibits the assembly of SGs and promotes the assembly of an alternative ribonucleoprotein complex termed an RNase L-dependent body (RLB). The formation of RLBs has been observed in response to double-stranded RNA, dengue virus infection, or SARS-CoV-2 infection. Herein, we review the distinct biogenesis pathways and

properties of SGs and RLBs, and we provide perspective on their potential functions during the antiviral response. This article is categorized under: RNA Interactions with Proteins and Other Molecules > RNA-Protein Complexes RNA Turnover and Surveillance > Regulation of RNA Stability RNA Export and Localization > RNA Localization.

Lassa Virus Countermeasures.

Melnik LI.
2023
Curr Top Microbiol Immunol.
https://pubmed.ncbi.nlm.nih.gov/36253593/

Dracunculose

Comparative Study of Chromium Phytoremediation by Two Aquatic Macrophytes.

Sharma K, Saxena P, Kumari A.
17-07-2023
Bull Environ Contam Toxicol.
https://pubmed.ncbi.nlm.nih.gov/37460624/

Chromium (Cr) occurs in several oxidation states from trivalent to hexavalent. However, hexavalent forms are more toxic and mainly produced by anthropogenic activities. A hydroponic experiment was conducted to analyse the comparative remediation of Cr by Marsilea minuta and Pistia stratiotes. Plants were exposed to four concentrations of Cr (0.5, 1.0, 1.5, and 2.0 mM) for 3 days. The highest accumulation of Cr was seen at the 1.5 mM concentration after 3 days in Marsilea (11.96 mg/g) and Pistia (18.78 mg/g). Dry weights decreased and malondialdehyde (MDA) levels increased in response to increasing Cr concentrations. Results indicate that both macrophytes are suitable candidates for Cr phytoremediation. Antioxidant-enzyme activity as a function of metal tolerance is imperative for a coherent understanding of plant physiology under metal stress.

Potential contribution of floral thermogenesis to cold adaptation, distribution pattern, and population structure of thermogenic and non/slightly thermogenic Symplocarpus species.

Sato MP, Matsuo A, Otsuka K, Takano KT, Maki M, Okano K, Suyama Y, Ito-Inaba Y.
15-07-2023
Ecol Evol.
https://pubmed.ncbi.nlm.nih.gov/37456070/

The genus *Symplocarpus* in basal Araceae includes both thermogenic and non/slightly thermogenic species that prefer cold environments. If floral thermogenesis of *Symplocarpus* contributes to cold adaptation, it would be expected that thermogenic species have a larger habitat than non/slightly thermogenic species during an ice age, leading to increased genetic diversity in the current population. To address this question, potential distribution in past environment predicted by ecological niche modeling (ENM), genetic diversity, and population structure of chloroplast and genome-wide single nucleotide polymorphisms were compared between thermogenic *Symplocarpus renifolius* and non/slightly thermogenic *Symplocarpus nipponicus*. ENM revealed that the distribution of *S. nipponicus* decreased, whereas that of *S. renifolius* expanded in the Last Glacial Maximum. Phylogeographic analyses have shown that the population structures of the two species were genetically segmented and that the genetic diversity of *S. renifolius* was higher than that of *S. nipponicus*. The phylogenetic relationship between chloroplast and nuclear DNA is topologically different in the two species, which may be due to the asymmetric gene flow ubiquitously observed in plants. The results of this study imply that floral thermogenesis of *Symplocarpus* contributes to expanding the distribution during an ice age, resulting in increased genetic diversity due to cold adaptation.

Evaluation of konjac noodle as a microsurgery training model: learning curve analysis.

Avelar TM, Lovato RM, Barbosa TG, Xander PAW, Rodrigues LHDS, Campos AJB, Riechelmann RS, Flores JAC, Aguiar GB, Oliveira JG, Veiga JCE.
10-07-2023
Rev Col Bras Cir.
https://pubmed.ncbi.nlm.nih.gov/37436283/

Background: classical models of microsurgical anastomosis training are expensive and have ethical implications. Some alternatives join low cost and easiness to store. However, the translation of knowledge acquired by training in these methods into the traditional ones is not clear. This project aims to assess the feasibility of konjac noodles as a reliable microsurgery-training model. Methods: 10 neurosurgery residents performed an end-to-end anastomosis in a 2-3mm placenta artery. The anastomoses were evaluated quantitatively, recording time; and qualitatively, applying a validated score (Anastomosis Lapse Index - ALI) by three experienced neurosurgeons and verifying the presence of gross leakage through the infusion of fluorescein. Subsequently, they performed 10 non-consecutive sessions of anastomosis training in the konjac noodle. Eventually, a final anastomosis in the placenta model was performed and the same parameters were scored. Results: we observed a 17min reduction in the mean time to perform the anastomosis in the placenta model after the training in the konjac ($p<0.05$). There was a non-significant 20% reduction in gross leakage, but the training sessions were not able to consistently improve the ALI score. Conclusions: we demonstrate a reduction in anastomosis performing time in placental arteries after training sessions in the konjac noodle model, which can be regarded as a feasible low-cost method, particularly useful in centers with surgical microscopes only in the operation room.

Efficacy and safety of Banxia-Houpo-Tang (Banha-Hubak-Tang) for depression: A systematic review and meta-analysis.

Kim DW, Kwon HW, Kim SH.
Août-2023
Complement Ther Clin Pract.
https://pubmed.ncbi.nlm.nih.gov/37224584/

Echinococcose

Impact of Echinococcus granulosus Antigens on Monocyte Development and Dendritic Cell Differentiation.

Wang M, Qiao F, Li Z, Wang Q, Shang Z, Hei J, Ma X, Wang Y.
17-07-2023
Iran J Immunol.
https://pubmed.ncbi.nlm.nih.gov/37458144/

Background: Different subtypes of dendritic cells (DCs) can induce different types of immune responses. Our previous study found that Echinococcus granulosus (E. granulosus) antigens (Eg.ferritin, Eg.mMDH and Eg.10) stimulated DC differentiation to different subtypes and produced different immune responses. Objective: To further understand whether Eg.ferritin, Eg.mMDH and Eg.10 affect the DC-mediated immune response by promoting the differentiation of monocytes to DCs. Methods: Bone marrow-derived monocytes were exposed to three antigens of E. granulosus on days 0, 3, 5, and 7. The percentage of monocyte-derived DCs (moDCs), DCs subsets, and the expression of surface molecules of DCs at different time points in different groups were assessed by flow cytometry. The levels of cytokines of IL-1β, IL-4, IL-6, IL-10, IL-13, IFN-γ, TNF-α, IL-12p70, IL-18, IL-23, and IL-27 in the cell culture supernatant were detected by multi-factorial detection technology. Results: The percentage of moDCs revealed that none of the three antigens blocked monocyte differentiation to DCs. The monocytes of 7-day-old cultures showed increased sensitivity to these antigens. The Eg.ferritin induced more mature DCs, which expressed high levels of MHC II and costimulatory molecules, and secreted Th1 cytokines. Eg10 and Eg.mMDH induced lower degrees of DC maturation, however differentiated DCs were in a semi-mature state due to low expression of MHC II and costimulatory molecules and secretion of higher Th2 and lower Th1 cytokines.

Status of human cystic echinococcosis based on hospital records in Mazandaran Province: A first registry-based evidence.

Tabaripour R, Sharifpour A, Fakhar M, Asadi S, Esmaeili Reykandeh S, Montazeri M, Keighobadi M.
04-07-2023
Parasite Epidemiol Control.
https://pubmed.ncbi.nlm.nih.gov/37457119/

Isolated renal hydatid cyst in a ten-year-old female child: A rare case report.

Hailu SS, Gebremariam M, Nigussie T, Girma K, Misgea A, Arega G.
30-06-2023
Urol Case Rep.
https://pubmed.ncbi.nlm.nih.gov/37455774/

[Single-cell RNA sequencing deciphers transcriptional profiles of hepatocytes in mouse with hepatic alveolar echinococcosis].

Yang Q, Jia W, Wang X, Cai Q, Ge X, Wang W, Han X.
29-06-2023
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
https://pubmed.ncbi.nlm.nih.gov/37455093/

Objective: To investigate the cell composition and the transcriptional characteristics in microenvironments of hepatic tissues in mice at late stage of *Echinococcus multilocularis* infection at a single-cell level. Methods: Peri-lesion and paired distal hepatic specimens were collected from two BALB/c mice (6 to 8 weeks old) infected with *E. multilocularis* for single-cell RNA sequencing. The Seurat package in the R software was employed for quality control of data, multi-sample integration and correction of batch effects, and uniform manifold approximation and projection (UMAP) algorithm was used for cell clustering. Cell types were annotated using classical marker genes. Differentially expressed genes were screened in each cell type through differential gene expression analysis, and the biological roles of cells were predicted using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses. Results: A total of 43 710 cells from peri-lesion and distal hepatic tissues of *E. multilocularis*-infected mice were analyzed, and were classified into 11 cell types, including neutrophils, T cells, macrophages, granulocyte-monocyte progenitor cells, B cells, plasma cells, basophils, hepatic stellate cells, endothelial cells, hepatocytes, and platelets. T cells were the largest population of immune cells in the microenvironment of hepatic tissues, including five $CD4^+$ T cell subsets, two $CD8^+$ T cell subsets and phosphoantigen-reactive γδT cells. The proportions of $CD4^+$ helper T cells and cytotoxic $CD4^+$ T cells decreased and the proportion of T helper 2 (Th2) cells increased in peri-lesion tissues relative to distal hepatic tissues. In addition, the differentially expressed genes in Th2 cells were associated with negative regulation of the immune system, and the highly expressed genes in cytotoxic $CD4^+$ T cells correlated with activation of the immune system. Conclusions: Single-cell RNA sequencing deciphers the cell composition and distribution in microenvironments of hepatic tissues from mice infected with *E. multilocularis*, and the increased proportion of Th2 cells in peri-lesion hepatic tissues may be associated with formation of immunosuppressive microenvironments.

Design of ion channel blocking, toxin-like Kunitz inhibitor peptides from the tapeworm, Echinococcus granulosus, with potential anti-cancer activity.

Rashno Z, Rismani E, Ghasemi JB, Mansouri M, Shabani M, Afgar A, Dabiri S, Rezaei Makhouri F, Hatami A, Harandi MF.
15-07-2023
Sci Rep.

https://pubmed.ncbi.nlm.nih.gov/37454225/

Over-expression of K+ channels has been reported in human cancers and is associated with the poor prognosis of several malignancies. EAG1, a particular potassium ion channel, is widely expressed in the brain but poorly expressed in other normal tissues. Kunitz proteins are dominant in metazoan including the dog tapeworm, Echinococcus granulosus. Using computational analyses on one A-type potassium channel, EAG1, and in vitro cellular methods, including major cancer cell biomarkers expression, immunocytochemistry and whole-cell patch clamp, we demonstrated the anti-tumor activity of three synthetic small peptides derived from E. granulosus Kunitz4 protease inhibitors. Experiments showed induced significant apoptosis and inhibition of proliferation in both cancer cell lines via disruption in cell-cycle transition from the G0/G1 to S phase. Western blotting showed that the levels of cell cycle-related proteins including P27 and P53 were altered upon kunitz4-a and kunitz4-c treatment. Patch clamp analysis demonstrated a significant increase in spontaneous firing frequency in Purkinje neurons, and exposure to kunitz4-c was associated with an increase in the number of rebound action potentials after hyperpolarized current. This noteworthy component in nature could act as an ion channel blocker and is a potential candidate for cancer chemotherapy based on potassium channel blockage.

Pulmonary cystic echinococcosis acquired during a short-term tourist travel.

Svensgaard SNH, Jokelainen P, Stensvold CR, Lausch KR, Højsgaard A, Keller JL, Nielsen HV, Larsen CS.
28-06-2023
IDCases.
https://pubmed.ncbi.nlm.nih.gov/37448378/

What do we know about the epidemiology and the management of human echinococcosis in Albania?

Luga P, Gjata A, Akshija I, Mino L, Gjoni V, Pilaca A, Zobi M, Martinez GE, Richter J.
Août-2023
Parasitol Res.
https://pubmed.ncbi.nlm.nih.gov/37272973/

Echinococcosis is a life-threatening neglected zoonotic disease. Cystic echinococcosis (CE) due to Echinococcus (E.) granulosus usually involves livestock and dogs; alveolar echinococcosis (AE) due to E. multilocularis involves rodents and canines such as foxes and dogs. Human hosts are infected accidentally via hand to mouth and/or foodborne/waterborne pathways. Albania is deemed to be endemic for cystic echinococcosis (CE), but there is a scarcity of data to confirm this. A systematic literature search was performed in PubMed, Google Scholar, and in other medical sources. Because of the scarcity of existing information, data confirming CE cases were reviewed from the medical hospital records of Albania's largest Hospital, the Mother Teresa University Hospital (UHCMT) Tirana, and from a large private laboratory in Tirana (Pegasus laboratory). A total of eight eligible publications on 540 CE patients were found. Three hundred forty seven additional cases hospitalized in UHCMT from 2011 to 2020 were confirmed, as well as 36 laboratory cases and 10 Albanian cases notified in Germany. Taking all cases into account and considering 162 overlapping cases, 771 cases were documented from 2011 to 2020. The only case reported as AE was most likely a multi-organic CE. Surgery was the most frequent therapy approach used (84.7%). Autochthonous human CE seems to be widespread, and transmission is ongoing in Albania. CE patients in Albania undergo surgery more frequently compared with CE cases in other European countries. In order to establish a realistic estimate of prevalence and incidence of CE in Albania, mandatory notification should be reinforced. Stage-specific therapy can be used in CE to reduce therapy cost and diminish mortality by avoiding surgical overtreatment.

Molecular characterization of cattle and sheep isolates of Echinococcus granulosus from Elazig province in Turkey and expression analysis of the non-coding RNAs, egr-miR-7, egr-miR-71 and egr-miR-96.

Irehan B, Celik F, Koroglu E, Tektemur A, Simsek S.
Août-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37257717/

In vitro and ex vivo protoscolicidal effects of hydroalcoholic extracts of Eucalyptus microtheca on protoscoleces of Echinococcus granulosus sensu stricto: A light and scanning electron microscopy (SEM) study.

Mahmoodpour H, Spotin A, Hatam GR, Pourmahdi Ghaemmaghami A, Sadjjadi SM.
Août-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37230322

Filariose lymphatique

Applying community health systems lenses to identify determinants of access to surgery among mobile & migrant populations with hydrocele in Zambia: A mixed methods assessment.

Maritim P, Chewe M, Munakaampe MN, Silumbwe A, Sichone G, Zulu JM.
18-07-2023
PLOS Glob Public Health.
https://pubmed.ncbi.nlm.nih.gov/37463160/

Hydrocele which is caused by long term lymphatic filariasis infection can be treated through the provision of surgery. Access to surgeries remains low particularly for hard to reach populations. This study applied community health system lenses to identify determinants to the adoption, implementation and integration of hydrocele surgeries

among migrants &mobile populations in Luangwa District, Zambia. A concurrent mixed methods design consisting of cross-sectional survey with hydrocele patients (n = 438) and in-depth interviews with different community actors (n = 38) was conducted in October 2021. Data analysis was based on the relational and programmatic lenses of Community Health Systems. Under the Programmatic lens, insufficient resources resulted in most health facilities being incapable of providing the minimum package of care for lymphatic filariasis. The absence of cross border collaborative structures limits the continuity of care for patients moving across the three countries. Other programmatic barriers include language barriers, inappropriate appointment systems, direct and indirect costs. In the relational lens, despite the key role that community leaders play their engagement in service delivery was low. Community actors including patients were rarely included in planning, implementation or evaluation of hydrocele services. Some patients utilized their power within to act as champions for the surgery but local groups such as fishing associations remained underutilized. Community health systems provide a potential avenue through which access amongst mobile and migrant populations can be enhanced through strategies such engagement of patient groups, knowledge sharing across borders and use of community monitoring initiatives.

Individual longitudinal compliance to neglected tropical disease mass drug administration programmes, a systematic review.

Maddren R, Phillips A, Rayment Gomez S, Forbes K, Collyer BS, Kura K, Anderson R.
17-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37459369/

Repeated distribution of preventative chemotherapy (PC) by mass drug administration forms the mainstay of transmission control for five of the 20 recognised neglected tropical diseases (NTDs); soil-transmitted helminths, schistosomiasis, lymphatic filariasis, onchocerciasis and trachoma. The efficiency of such programmes is reliant upon participants swallowing the offered treatment consistently at each round. This is measured by compliance, defined as the proportion of eligible participants swallowing treatment. Individually linked longitudinal compliance data is important for assessing the potential impact of MDA-based control programmes, yet this accurate monitoring is rarely implemented in those for NTDs. Longitudinal compliance data reported by control programmes globally for the five (PC)-NTDs since 2016 is examined, focusing on key associations of compliance with age and gender. PubMed and Web of Science was searched in January 2022 for articles written in English and Spanish, and the subsequent extraction adhered to PRISMA guidelines. Study title screening was aided by Rayyan, a machine learning software package. Studies were considered for inclusion if primary compliance data was recorded for more than one time point, in a population larger than 100 participants. All data analysis was conducted in R. A total of 89 studies were identified containing compliance data, 57 were longitudinal studies, of which 25 reported individually linked data reported by varying methods. The association of increasing age with the degree of systematic treatment was commonly reported. The review is limited by the paucity of data published on this topic. The varying and overlapping terminologies used to describe coverage (receiving treatment) and compliance (swallowing treatment) is reviewed. Consequently, it is recommended that WHO considers clearly defining the terms for coverage, compliance, and longitudinal compliance which are currently contradictory across their NTD treatment guidelines. This review is registered with PROSPERO (number: CRD42022301991).

Gale

A study of pattern and assessment of life quality index in patients of nonvenereal dermatoses of external genitalia at a tertiary care center.

Vellaisamy SG, Muthukumarasamy V, Gopalan K.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457522/

Clinico-epidemiological profile of genital dermatoses in people living with HIV: A shifting paradigm from venereal to nonvenereal dermatoses.

Dhillon SK, Kura MM.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457512/

Context: The protean mucocutaneous manifestations of HIV and the resultant opportunistic infections are well documented. Genital dermatoses can be either venereal or nonvenereal in origin. As the presence of HIV infection greatly increases the chances of acquiring another sexually transmitted pathogen, these are often presumed to be venereal in origin. **Aims:** The aims of the study were to record the different morphologies of genital skin lesions in seropositive patients and to classify them as venereal or nonvenereal in origin. **Settings and design:** This was an observational study undertaken in seropositive patients with genital skin lesions attending the outpatient department of dermatology at a tertiary health-care center. **Subjects and methods:** One hundred and seventy-seven seropositive patients with genital lesions were enrolled. A detailed history was taken; the genital and dermatological examination was performed. **Statistical analysis used:** None. **Results:** Males predominated the study population with the majority (79.1%) falling into the reproductive age group of 15-49 years. Nonvenereal genital dermatoses (59%) outnumbered sexually transmitted infections (STIs) (41%) out of which the most frequently encountered were dermatophytosis, scabies, and intertrigo. Other entities recorded were inflammatory dermatoses, cutaneous adverse drug reactions, and tumors. The most common STIs were herpes genitalis (55.4%) and anogenital warts (32.5%). **Conclusion:** This

study showed that nonvenereal genital dermatoses are more common than STIs in people living with HIV. Our findings reiterate the fact that genital lesions should be approached with caution as a presumptive and hasty diagnosis of STI adds greatly to the morbidity of the patient in terms of guilt and shame, and adversely affects the quality of life. **Keywords:** Genital dermatoses; HIV; nonvenereal genital dermatoses.

Using ultraviolet light in diagnosing scabies: Scabies' Sign via Wood's Lamp.

Yürekli A, Can İ, Oğuz M.
12-07-2023
J Am Acad Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37451622/

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

Anthelmintic Activities of Extract and Ellagitannins from Phyllanthus urinaria against Caenorhabditis elegans and Zoonotic or Animal Parasitic Nematodes.

Jato J, Waindok P, Ngnodandi FNBF, Orman E, Agyare C, Bekoe EO, Strube C, Hensel A, Liebau E, Spiegler V.
17-07-2023
Planta Med.
https://pubmed.ncbi.nlm.nih.gov/37459860

The aerial parts of *Phyllanthus urinaria* are used in traditional medicine in West Africa against helminthiasis, but their anthelmintic potential has not been evaluated until now. Within the current study, a hydroacetonic extract (AWE) and fractions and isolated ellagitannins from *P. urinaria* were, therefore, tested *in vitro* against *Caenorhabditis elegans* and the larvae of the animal parasites *Toxocara canis, Ascaris suum, Ancylostoma caninum,* and *Trichuris suis*. Compounds 1: - 13: , mainly representing ellagitannins, were isolated using different chromatographic methods, and their structures were elucidated by HR-MS and $^{1}H/^{13}C$-NMR. AWE exerted concentration-dependent lethal effects (LC_{50} of 2.6 mg/mL) against *C. elegans* and inhibited larval migration of all animal parasites tested (*T. suis* L1 IC_{50} 24.3 µg/mL, *A. suum* L3 IC_{50} 35.7 µg/mL, *A. caninum* L3 IC_{50} 112.8 µg/mL, *T. canis* L3 IC_{50} 1513.2 µg/mL). The anthelmintic activity of AWE was mainly related to the polar, tannin-containing fractions. Geraniin 1: , the major ellagitannin in the extract, showed the strongest anthelmintic activity in general (IC_{50} between 0.6 and 804 µM, depending on parasite species) and was the only compound active against *A. caninum* (IC_{50} of 35.0 µM). Furosin 9: was least active despite structural similarities to 1: . Among the parasites tested, *Trichuris suis* L1 larvae turned out to be most sensitive with IC_{50} of 0.6, 6.4, 4.0, 4.8, and 2.6 µM for geraniin 1: , repandusinic acid A 3: , punicafolin 8: , furosin 9: , and phyllanthusiin A 10: , respectively.

Emergence of canine hookworm treatment resistance: Novel detection of Ancylostoma caninum anthelmintic resistance markers by fecal PCR in 11 dogs from Canada.

Evason MD, Weese JS, Polansky B, Leutenegger CM.
18-07-2023
Am J Vet Res.
https://pubmed.ncbi.nlm.nih.gov/37442544/

Objective: To describe dogs with detected Ancylostoma caninum anthelmintic treatment resistance markers in Canada. **Animals:** 11 client-owned dogs with fecal quantitative PCR (qPCR) assay detected A caninum with benzimidazole (BZ) resistance genotypic markers. **Methods:** Signalment, presenting concern, duration of clinical signs, fecal testing, treatment, and outcomes were obtained. Where available, follow-up data were collected via telephone or email with the primary veterinarian. **Results:** Ancylostoma spp was detected from 184/32,205 dog fecal samples by reference laboratory qPCR surveillance, between May 15, 2022, and April 26, 2023. 11 of these 184 samples had A caninum with genetic BZ F167Y resistance marker detection. 4 dogs had not traveled outside Canada, 6 had been imported from the US, and the travel history was unclear in 1 dog. 7 of the dogs had gastro-intestinal signs (diarrhea or soft stool) on initial presentation. Clinical improvement was reported in 6 of these dogs (resolution of diarrhea and soft stool), with 1 dog lost to follow-up. All 11 dogs received anthelmintic treatment (varied drugs and duration). **Clinical relevance:** Identification of genetic markers of BZ resistance raises concerns about the potential animal and human impacts of resistant hookworms. 4 dogs lacked an origin from or travel history to the US, indicating true emergence and/or novel spread within Canada, not just importation from an area where resistance has been reported. Fecal surveillance was performed with a qPCR test incorporating treatment (BZ) resistance markers. There is a need to raise clinician awareness around treatment-resistant hookworm in dogs and the capability of fecal surveillance for genotypic and phenotypic resistance.

Prevalence and associated risk factors of intestinal parasitic infections among children in pastoralist and agro-pastoralist communities in the Adadle woreda of the Somali Regional State of Ethiopia.

Lanker KC, Muhummed AM, Cissé G, Zinsstag J, Hattendorf J, Yusuf RB, Hassen SB, Tschopp R, Vonaesch P.
03-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37399193/

Leishmaniose

Identification of a small-molecule inhibitor that selectively blocks DNA-binding by Trypanosoma brucei replication protein A1.

Mukherjee A, Hossain Z, Erben E, Ma S, Choi JY, Kim HS.
20-07-2023
Nat Commun.
https://pubmed.ncbi.nlm.nih.gov/37474515/

Balancing the functions of DNA extracellular traps in intracellular parasite infections: implications for host defense, disease pathology and therapy.

Koh CC, Gollob KJ, Dutra WO.
20-07-2023
Cell Death Dis.
https://pubmed.ncbi.nlm.nih.gov/37474501/

The release of DNA to the extracellular milieu is a biological process referred to as etosis, which is involved in both physiological and pathological functions. Although the release of DNA extracellular traps (ETs) was initially attributed to innate immune cells such as neutrophils, eosinophils, and macrophages, recent studies have shown that T cells, as well as non-immune cells, are capable of releasing ETs. These structures were described primarily for their potential to trap and kill pathogens, presenting an important strategy of host defense. Intriguingly, these functions have been associated with intracellular pathogens such as the parasites Leishmania sp. and Trypanosoma cruzi, causative agents of leishmaniasis and Chagas disease, respectively. These are two devastating tropical diseases that lead to thousands of deaths every year. In an apparent contradiction, ETs can also induce and amplify inflammation, which may lead to worsening disease pathology. This has prompted the concept of targeting ETs' release as a means of controlling tissue destruction to treat human diseases. What is the best approach to prevent disease severity: inducing ETs to kill pathogens or preventing their release? In this Perspective article, we will discuss the importance of understanding ETs released by different cell types and the need to balance their potentially complementary functions. In addition, we will explore other functions of ETs and their translational applications to benefit individuals infected with intracellular parasites and other pathogens. Ultimately, a better understanding of the role of ETs in disease pathogenesis will provide valuable insights into developing novel therapies for human diseases.

The adaptive roles of aneuploidy and polyclonality in Leishmania in response to environmental stress.

Negreira GH, de Groote R, Van Giel D, Monsieurs P, Maes I, de Muylder G, Van den Broeck F, Dujardin JC, Domagalska MA.
20-07-2023
EMBO Rep.
https://pubmed.ncbi.nlm.nih.gov/37470283/

Aneuploidy is generally considered harmful, but in some microorganisms, it can act as an adaptive mechanism against environmental stress. Here, we use Leishmania-a protozoan parasite with remarkable genome plasticity-to study the early steps of aneuploidy evolution under high drug pressure (using antimony or miltefosine as stressors). By combining single-cell genomics, lineage tracing with cellular barcodes, and longitudinal genome characterization, we reveal that aneuploidy changes under antimony pressure result from polyclonal selection of pre-existing karyotypes, complemented by further and rapid de novo alterations in chromosome copy number along evolution. In the case of miltefosine, early parasite adaptation is associated with independent point mutations in a miltefosine transporter gene, while aneuploidy changes only emerge later, upon exposure to increased drug levels. Therefore, polyclonality and genome plasticity are hallmarks of parasite adaptation, but the scenario of aneuploidy dynamics depends on the nature and strength of the environmental stress as well as on the existence of other pre-adaptive mechanisms.

Localized Leishmania major infection disrupts systemic iron homeostasis that can be controlled by oral iron supplementation.

Banerjee S, Datta R.
17-07-2023
J Biol Chem.
https://pubmed.ncbi.nlm.nih.gov/37468101/

The estimated distribution of autochthonous leishmaniasis by Leishmania infantum in Europe in 2005-2020.

Maia C, Conceição C, Pereira A, Rocha R, Ortuño M, Muñoz C, Jumakanova Z, Pérez-Cutillas P, Özbel Y, Töz S, Baneth G, Monge-Maillo B, Gasimov E, Van der Stede Y, Torres G, Gossner CM, Berriatua E.
19-07-20233
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37467280/

Background: This study describes the spatial and temporal distribution between 2005 and 2020 of human and animal leishmaniasis by Leishmania infantum in European countries reporting autochthonous cases, and highlights potential activities to improve disease control. Methodology/principal findings: It was based on a review of the scientific literature and data reported by the World Health Organization (WHO), the World Organization for Animal Health (WOAH) and the Ministries of Health, including hospital discharges in some countries. Autochthonous infections were reported in the scientific literature from 22 countries, including 13 and 21 countries reporting human and animal infections, respectively. In contrast, only 17 countries reported autochthonous human leishmaniasis cases to the WHO and 8 countries animal infections to the WOAH. The number of WOAH reported cases were 4,203, comprising 4,183 canine cases and 20 cases in wildlife. Of 8,367 WHO reported human cases, 69% were visceral leishmaniasis cases-of which 94% were autochthonous-and 31% cutaneous leishmaniasis cases-of which 53% were imported and mostly in France. The resulting cumulative incidence per 100,000 population of visceral leishmaniasis between 2005-2020, was highest in Albania (2.15 cases), followed by Montenegro, Malta, Greece, Spain and North Macedonia (0.53-0.42), Italy (0.16), Portugal (0.09) and lower in other

endemic countries (0.07-0.002). However, according to hospital discharges, the estimated human leishmaniasis incidence was 0.70 in Italy and visceral leishmaniasis incidences were 0.67 in Spain and 0.41 in Portugal. Conclusions/significance: Overall, there was no evidence of widespread increased incidence of autochthonous human leishmaniasis by L. infantum in European countries. Visceral leishmaniasis incidence followed a decreasing trend in Albania, Italy and Portugal, and peaked in Greece in 2013, 2014 and 2017, and in Spain in 2006-2007 and 2011-2013. Animal and human cutaneous leishmaniasis remain highly underreported. In humans, hospital discharge databases provide the most accurate information on visceral leishmaniasis and may be a valuable indirect source of information to identify hotspots of animal leishmaniasis. Integrated leishmaniasis surveillance and reporting following the One Health approach, needs to be enhanced in order to improve disease control.

4',7-dihydroxyflavone conjugated carbon nanotube formulation demonstrates improved efficacy against Leishmania parasite.

Sasidharan S, Saudagar P.
16-06-2023
Biochim Biophys Acta Gen Subj.
https://pubmed.ncbi.nlm.nih.gov/37463617/

[Investigation of Leishmania RNA Virus 2 in Leishmania major and Leishmania tropica Strains Isolated from Cutaneous Leishmaniasis Patients in Türkiye].

Karabulut C, Aksoy T, Yıldırım A, Balcıoğlu IC.
Juil-2023
Mikrobiyol Bul.
https://pubmed.ncbi.nlm.nih.gov/37462309/

Leishmania RNA virus (LRV) is a double-stranded RNA (dsRNA) virus that is thought to contribute to the severe inflammatory response of the causative Leishmania parasite in the mammalian host by being present in many isolates of Leishmania spp. In our study, it was aimed to obtain data on the presence of Leishmania RNA Virus 2 (LRV2), which is thought to cause a change in the clinical course of leishmaniasis, in Leishmania major and Leishmania tropica isolates isolated from cutaneous leishmaniasis (CL) patients in Türkiye. Leishmania strains stored in liquid nitrogen tank by cryopreservation in Manisa Celal Bayar University Faculty of Medicine Parasite Bank were resuscitated under suitable conditions and cultivated in NNN and RPMI-1640 media. Then, the isolates were allowed to enter the logarithmic phase in a 26ºC incubator and DNA isolations were made using the "High Pure PCR Template Preparation Kit". Real-time polymerase chain reaction (Rt-PCR) melting analyzes were applied to the DNAs obtained by using primers and probes specific to the internal transcribed spacer-1 (ITS-1) gene region of Leishmania. After RNA isolation from promastigote suspension, cDNA synthesis was performed by reverse transcription. After gel electrophoresis with PCR amplification products, dsRNA band formation was evaluated in terms of LRV2 positivity under ultraviolet light. Among the 20 examined Leishmania spp. isolates (10 L.tropica and 10 L.major), four (three L.tropica, one L.major) were found to be positive for the presence of LRV2. Although the mechanism of LRV in recent studies has not been fully understood, it is known that it exacerbates the clinic of the disease and even has an effect on the formation of drug resistance by the parasite. It is important to obtain data on the presence of LRV in our country and to contribute to various clinical, drug development, prevalence studies, diagnosis and treatment of the disease in the future.

Emerging Infectious Diseases of the Skin: A Review of Clinical and Histologic Findings.

McMahon DE, Schuetz AN, Kovarik CL.
14-07-2023
Hum Pathol.
https://pubmed.ncbi.nlm.nih.gov/37454994/

Emerging infectious diseases are of great importance to public health and clinical practice. This review aims to characterize the clinical and histopathologic features of emerging infectious diseases with cutaneous manifestations in order to increase awareness of these entities among dermatologists, pathologists, and dermatopathologists.

The association between rLiHyp1 protein plus adjuvant and amphotericin B is an effective immunotherapy against visceral leishmaniasis in mice.

Lage DP, Martins VT, Vale DL, Freitas CS, Pimenta BL, Moreira GJL, Ramos FF, Pereira IAG, Bandeira RS, de Jesus MM, Ludolf F, Tavares GSV, Chávez-Fumagalli MA, Roatt BM, Christodoulides M, Coelho EAF.
13-07-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/37453579/

Treatment of visceral leishmaniasis (VL) is compromised by drug toxicity, high cost and/or the emergence of resistant strains. Though canine vaccines are available, there are no licensed prophylactic human vaccines. One strategy to improve clinical outcome for infected patients is immunotherapy, which associates a chemotherapy that acts directly to reduce parasitism and the administration of an immunogen-adjuvant that activates the host protective Th1-type immune response. In this study, we evaluated an immunotherapy protocol in a murine model by combining recombinant (r)LiHyp1 (a hypothetical amastigote-specific Leishmania protein protective against Leishmania infantum infection), with monophosphoryl-lipid A (MPLA) as adjuvant and amphotericin B (AmpB) as reference antileishmanial drug. We used this protocol to treat L. infantum infected-BALB/c mice, and parasitological, immunological and toxicological evaluations were performed at 1 and 30 days after treatment. Results showed that mice treated with rLiHyp1/MPLA/AmpB presented the lowest parasite burden in all organs evaluated, when both a limiting dilution technique and qPCR were used. In addition, these

animals produced higher levels of IFN-γ and IL-12 cytokines and IgG2a isotype antibody, which were associated with lower production of IL-4 and IL-10 and IgG1 isotype. Furthermore, low levels of renal and hepatic damage markers were found in animals treated with rLiHyp1/MPLA/AmpB possibly reflecting the lower parasite load, as compared to the other groups. We conclude that the rLiHyp1/MPLA/AmpB combination could be considered in future studies as an immunotherapy protocol to treat against VL.

Blood meal analysis and molecular detection of mammalian Leishmania DNA in wild-caught Sergentomyia spp. from Tunisia and Saudi Arabia.

Remadi L, Farjallah D, Chargui N, Belgacem S, Baba H, Zrieq R, Alzain MA, Babba H, Haouas N.
14-07-2023
Parasitol Res.
https://pubmed.ncbi.nlm.nih.gov/37449994/

Temporal Evaluation of the Surface Area of Treated Skin Ulcers Caused by Cutaneous Leishmaniasis and Relation with Optical Parameters in an Animal Model: A Proof of Concept.

Londoño S, Viloria C, Pérez-Buitrago S, Murillo J, Botina D, Zarzycki A, Garzón J, Torres-Madronero MC, Robledo SM, Marzani F, Treuillet S, Castaneda B, Galeano J.
24-06-2023
Sensors (Basel).
https://pubmed.ncbi.nlm.nih.gov/37447709/

Cutaneous leishmaniasis (CL) is a neglected disease caused by an intracellular parasite of the *Leishmania* genus. CL lacks tools that allow its understanding and treatment follow-up. This article presents the use of metrical and optical tools for the analysis of the temporal evolution of treated skin ulcers caused by CL in an animal model. *Leishmania braziliensis* and *L. panamensis* were experimentally inoculated in golden hamsters, which were treated with experimental and commercial drugs. The temporal evolution was monitored by means of ulcers' surface areas, as well as absorption and scattering optical parameters. Ulcers' surface areas were obtained via photogrammetry, which is a procedure that allowed for 3D modeling of the ulcer using specialized software. Optical parameters were obtained from a spectroscopy study, representing the cutaneous tissue's biological components. A one-way ANOVA analysis was conducted to identify relationships between both the ulcers' areas and optical parameters. As a result, ulcers' surface areas were found to be related to the following optical parameters: epidermis thickness, collagen, keratinocytes, volume-fraction of blood, and oxygen saturation. This study is a proof of concept that shows that optical parameters could be associated with metrical ones, giving a more reliable concept during the assessment of a skin ulcer's healing.

Mechanochemical Studies on Coupling of Hydrazines and Hydrazine Amides with Phenolic and Furanyl Aldehydes-Hydrazones with Antileishmanial and Antibacterial Activities.

Kapusterynska A, Bijani C, Paliwoda D, Vendier L, Bourdon V, Imbert N, Cojean S, Loiseau PM, Recchia D, Scoffone VC, Degiacomi G, Akhir A, Saxena D, Chopra S, Lubenets V, Baltas M.
07-07-2023
Molecules.
https://pubmed.ncbi.nlm.nih.gov/37446945/

Non-Vesicular Lipid Transport Machinery in Leishmania donovani: Functional Implications in Host-Parasite Interaction.

Das K, Nozaki T.
26-06-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37445815/

Characterization of Leishmania Parasites Isolated from Naturally Infected Mammals.

Burguete-Mikeo A, Fernández-Rubio C, Peña-Guerrero J, El-Dirany R, Gainza L, Carasa Buj B, Nguewa PA.
29-06-2023
Animals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37443951/

Leishmaniasis is spreading in Europe, especially in endemic countries such as Italy and Spain, in part due to ongoing climate change and the increase in travel and migration. Although *Leishmania infantum* is the main agent responsible for this disease in humans and animals, other species and hybrids have been detected. This highlights the need to continue isolating and characterizing *Leishmania* strains from biological samples of infected hosts. In this study, we characterized the recently isolated parasites *L. infantum* NAV and *L. infantum* TDL, obtained from naturally infected mammals (dogs), and we compared them with the widely distributed and studied strain *L. infantum* BCN 150. Both NAV and TDL promastigotes showed a slower growth rate than BCN 150 and were significantly more sensitive to amphotericin B and miltefosine. Furthermore, the expression of the *CYCA* gene (involved in cell cycle and proliferation) was significantly downregulated in NAV and TDL isolates. On the other hand, *CYC6* (implicated in treatment resistance) and *APG9* (related to the recycling of protein under stress conditions and/or while undergoing a differentiation process and treatment resistance) levels were upregulated, compared to those measured in BCN 150. Both isolates displayed a higher infection capacity (>3 amastigotes per macrophage and >70% of infected macrophages) compared to controls (<2 amastigotes/cells and <50% of infected macrophages). Finally, a higher susceptibility to miltefosine treatment was observed in intracellular NAV and TDL amastigotes. In conclusion, TDL and NAV are novel *Leishmania* isolates that might be useful for in vitro and in vivo assays that will allow a better understanding of the parasite biology in Mediterranean areas.

Increased CCL-5 (RANTES) Gene Expression in the Choroid Plexus of Dogs with Canine Leishmaniosis.

Silva JEDS, Jussiani GG, Grano FG, Pelissari MCC, de Melo GD, Negrão Watanabe TT, de Lima VF, Machado GF.
22-06-2023
Animals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37443858/

Visceral canine leishmaniasis (CanL) can cause several clinical manifestations, including neurological lesions. Few reports have characterized the lesions observed in the central nervous system (CNS) during CanL; however, its pathogenesis remains unclear. The choroid plexus (CP) is a specialized structure responsible for the production and secretion of cerebrospinal fluid (CSF) and considered an interface between the peripheral immune system and CNS. It can allow the passage of inflammatory cells or pathogens and has the potential to act as a source of inflammatory mediators in several diseases. Thus, this study aimed to evaluate the role of CP as a possible route of inflammatory cells in the development of brain lesions in dogs with CanL, as well as its association with blood-CSF barrier (BCSFB) dysfunction. Samples were collected from 19 dogs that were naturally infected with CanL. We evaluated the histopathological lesions in the brain and investigated the gene expression of the cytokines. Capture enzyme-linked immunosorbent assay (ELISA) was used to evaluate the presence of the same cytokines in the CSF. Biochemical analysis was performed to compare the presence of albumin in the serum and CSF. Indirect ELISA was performed to measure the presence of anti-Leishmania antibodies in the CSF, which would suggest the disruption of the BCSFB. Histopathological evaluation of the dogs' brains revealed mild-to-severe inflammatory infiltrates, mainly in the CP and meninges. We also detected the presence of anti-Leishmania antibodies and albumin in the CSF, as well as Leishmania DNA in the CP. The gene expression of CCL-5 was increased in the CP of infected dogs compared with that of controls, and there was a tendency for the increase in the gene expression of CXCL-10. Thus, our findings confirm the disfunction of the BCSFB during CanL and suggest that the chemokines CCL-5 and CXCL-10 can be responsible for the recruitment of inflammatory cells found in CP.

Same parasite, different outcomes: unraveling the epidemiology of Leishmania infantum infection in Brazil and Spain.

de Freitas Milagres T, López-de-Felipe M, da Silva WJ, Martín-Martín I, Gálvez R, da Silva OS.
11-07-2023
Trends Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37442747/

Clinical, hematological, biochemical, and histopathological evaluations in domestic cats (Felis catus) infected by Leishmania infantum.

Batista JF, Magalhães Neto FDCR, Lopes KSPDP, Sousa CMG, Alcântara DS, Baêta SAF, Alves MMM, Mendonça IL.
07-07-2023
Rev Bras Parasitol Vet.
https://pubmed.ncbi.nlm.nih.gov/37436206/

A high frequency of feline leishmaniasis has been reported in several countries. However, much information about disease progression in cats still needs to be clarified. This study aimed to verify the occurrence of clinicopathological changes in cats infected with Leishmania infantum. A total of 60 cats were divided into three groups of 20 animals each: control, suspects, and infected. All 60 cats underwent blood count and biochemical analyses. Serum samples from 20 animals with leishmaniasis were also used to diagnose feline immunodeficiency virus and feline leukemia virus. A total of five of the infected animals underwent necropsy for a histopathological study. The main clinical findings in cats with leishmaniasis were lymphadenomegaly (65%), alopecia (55%), ulcerative skin lesions and weight loss (40%), skin nodules (25%), a significant reduction in red blood cells (p=0.0005) and hematocrit (p=0.0007), hyperplasia in spleen 4/5(80%), presence of Leishmania in the spleen 2/5(40%), hepatitis 3/5(60%), liver degeneration 4/5(80%) and inflammatory nephropathy 3/5(60%). It was concluded that cats with leishmaniasis presented significant clinical, hematological, and histopathological alterations compatible with L. infantum infection. The observation of lymphadenomegaly, weight loss, skin lesions and low concentration of red blood cells, contributes significantly to the diagnosis and analysis of progression of feline leishmaniasis.

The role of natural anti-parasitic guided development of synthetic drugs for leishmaniasis.

Pal R, Teli G, Akhtar MJ, Matada GSP.
05-10-2023
Eur J Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37421889/

Delving in folate metabolism in the parasite Leishmania major through a chemogenomic screen and methotrexate selection.

Bigot S, Leprohon P, Ouellette M.
29-06-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37384801/

Canine Parvovirus 2 in Free-Living Wild Mammals from Southern Brazil.

Bertolazzi S, Paz FR, da Silveira VP, Prusch F, Agnes I, Santana WO, Ikuta N, Streck AF, Lunge VR.
01-07-2023
J Wildl Dis.
https://pubmed.ncbi.nlm.nih.gov/37270203/

Pathogens from domestic canines represent a significant and constant threat to wildlife. This study looked for four

common canine pathogens, Babesia vogeli, Ehrlichia canis, Leishmania infantum, and canine parvovirus 2 (CPV-2) in mammals from the Pampa Biome, southern Brazil. Animals killed by vehicular trauma on a road traversing this biome were evaluated over a 1-yr period. Tissues collected from 31 wild mammals and six dogs were further analyzed by specific real-time PCR assays for each pathogen. Babesia vogeli and L. infantum were not detected in any investigated animal. Ehrlichia canis was detected in one dog and CPV-2 in nine animals: four dogs, three white-eared opossums (Didelphis albiventris), one pampas fox (Lycalopex gymnocercus), and one brown rat (Rattus norvegicus). These results demonstrate the occurrence of important carnivore pathogens (E. canis and CPV-2) in domestic dogs and wild mammals from the Pampa Biome in southern Brazil.

Promising natural products for the treatment of cutaneous leishmaniasis: A review of in vitro and in vivo studies.

Afonso RC, Yien RMK, de Siqueira LBO, Simas NK, Dos Santos Matos AP, Ricci-Júnior E.
Août-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37268108/

Although there are available treatments for cutaneous leishmaniasis (CL), the drugs used are far from ideal, toxic, and costly, in addition to the challenge faced by the development of resistance. Plants have been used as a source of natural compounds with antileishmanial action. However, few have reached the market and become phytomedicines with registration in regulatory agencies. Difficulties related to the extraction, purification, chemical identification, efficacy, safety, and production in sufficient quantity for clinical studies, hinder the emergence of new effective phytomedicines against leishmaniasis. Despite the difficulties reported, the major research centers in the world see that natural products are a trend concerning the treatment of leishmaniasis. The present work consists of a literature review of articles with in vivo studies, covering the period from January 2011 to December 2022, providing an overview of promising natural products for CL treatment. The papers show encouraging antileishmanial action of natural compounds with reduced parasite load and lesion size in animal models, suggesting new strategies for the treatment of the disease. The results reported in this review show advances in using natural products as safe and effective formulations, which can stimulate clinical studies to establish clinical therapy. In conclusion, the information in this review article serves as a preliminary basis for establishing a therapeutic protocol for future clinical trials that can validate the safety and efficacy of natural compounds, providing the development of affordable and safe phytomedicines for the treatment of CL.

In vitro evaluation of antileishmanial activity, mode of action and cellular response induced by vanillin synthetic derivatives against Leishmania species able to cause cutaneous and visceral leishmaniasis.

Freitas CS, Santiago SS, Lage DP, Antinarelli LMR, Oliveira FM, Vale DL, Martins VT, Magalhaes LND, Bandeira RS, Ramos FF, Pereira IAG, de Jesus MM, Ludolf F, Tavares GSV, Costa AV, Ferreira RS, Coimbra ES, Teixeira RR, Coelho EAF.
Août-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37247802/

The treatment against leishmaniasis presents problems, mainly due to their toxicity of the drugs, high cost and/or by the emergence of parasite resistant strains. In this context, new therapeutics should be searched. In this study, two novel synthetic derivatives from vanillin: [4-(2-hydroxy-3-(4-octyl-1H-1,2,3-triazol-1-yl)propoxy)-3-methoxybenzaldehyde] or 3s and [4-(3-(4-decyl-1H-1,2,3-triazol-1-yl)-2-hydroxypropoxy)-3-methoxybenzaldehyde] or 3t, were evaluated regarding their antileishmanial activity against distinct parasite species able to cause cutaneous and visceral leishmaniasis. Results showed that compounds 3s and 3t were effective against Leishmania infantum, L. amazonensis and L. braziliensis promastigote and amastigote-like forms, showing selectivity index (SI) of 25.1, 18.2 and 22.9, respectively, when 3s was used against promastigotes, and of 45.2, 7.5 and 15.0, respectively, against amastigote-like stage. Using the compound 3t, SI values were 45.2, 53.0 and 80.0, respectively, against promastigotes, and of 35.9, 46.0 and 58.4, respectively, against amastigote-like forms. Amphotericin B (AmpB) showed SI values of 5.0, 7.5 and 15.0, respectively, against promastigotes, and of 3.8, 5.0 and 7.5, respectively, against amastigote-like stage. The treatment of infected macrophages and inhibition of the infection upon pre-incubation with the molecules showed that they were effective in reducing the infection degree and inhibiting the infection in pre-incubated parasites, respectively, as compared to data obtained using AmpB. The mechanism of action of 3s and 3t was evaluated in L. infantum, revealing that both 3s and 3t altered the parasite mitochondrial membrane potential leading to reactive oxygen species production, increase in lipid corps and changes in the cell cycle, causing the parasite' death. A preliminary assay using the cell culture supernatant from treated and infected macrophages showed that 3s and 3t induced higher IL-12 and lower IL-10 values; suggesting the development of an in vitro Th1-type response in the treated cells. In this context, data indicated that 3s and 3t could be considered therapeutic agents to be tested in future studies against leishmaniasis.

Leishmania species: A narrative review on surface proteins with structural aspects involved in host-pathogen interaction.

Kaushal RS, Naik N, Prajapati M, Rane S, Raulji H, Afu NF, Upadhyay TK, Saeed M.
Août-2023
Chem Biol Drug Des.
https://pubmed.ncbi.nlm.nih.gov/36872849/

The new way to identify Leishmania amastigotes in peripheral blood smear

using digital cell morphology instrument.

Zhang W, Lei N, Xu Y, Wang Y, Chen S, Wang T, Zhang L.
Août-2023
Int J Lab Hematol.
https://pubmed.ncbi.nlm.nih.gov/36808880/

Synthesis of aminochalcones and in silico evaluation of their antiparasitic potential against Leishmania.

Bezerra LL, Almeida-Neto FWQ, Marinho MM, Santos Oliveira L, Teixeira AMR, Bandeira PN, Dos Santos HS, Lima-Neto P, Marinho ES.
Août-Sept 2023
J Biomol Struct Dyn.

Leishmaniasis disease is a serious public health problem. This disease reaches about 10 to 12 million people, and 20-30 thousand people die yearly. The disease treatment is realized through pentavalent antimonial and glucantime. However, some studies indicated that these drugs presented high toxicity and cost. Therefore, it is urgent the search for new drugs that may combat this disease and are less toxic. This work analyzed for the first time the interaction potential of (*E*)-1-(4-aminophenyl)-3-phenylprop-2-en-1-one (C1), (*E*)-1-(4-aminophenyl)-3-(4-methoxyphenyl)-prop-2-en-1-one (C4), (*E*)-1-(4-aminophenyl)-3-(4ethoxyphenyl)-prop-2-en-1-one (C9) chalcones through *in silico* approach. The molecular docking and the molecular electrostatic potential results indicated that the chalcones analyzed presented a strong interaction with the *Leishmania* major receptor, with affinity energy similar to the ligand co-crystallized. Besides, the interaction potential energy analysis from molecular dynamics simulations indicated the C9 ligand interacted more strongly than the 4-bromo-2,6-dichloro-*N*-(1,3,5-trimethyl-1*H*-pyrazolyl) benzenesulfonamide ligand with the *Leishmania* major receptor, especially for the Phe 88, Tyr 217 and His 219 residues. Therefore, the C9 chalcone might potentially treat Leishmaniasis disease.

Bis-1,2,4-triazol derivatives: Synthesis, characterization, DFT, antileishmanial activity and molecular docking study.

Süleymanoğlu N, Ustabaş R, Güler Hİ, Direkel Ş, Çelik F, Ünver Y.
Août-Sept 2023
J Biomol Struct Dyn.
https://pubmed.ncbi.nlm.nih.gov/35850638/

Lèpre

[The rise and fall of the leprosy clinic in Ru Gao in the North of Jiangsu in the period of the Republic of China].

Xu CY, Peng W.
28-05-2023
Zhonghua Yi Shi Za Zhi.
https://pubmed.ncbi.nlm.nih.gov/37474336/

The efficacy of a whole foods, plant-based dietary lifestyle intervention for the treatment of peripheral neuropathic pain in leprosy: a randomized control trial protocol.

Klowak M, Boggild AK.
04-06-2023
Front Nutr.
https://pubmed.ncbi.nlm.nih.gov/37469546/

Introduction: Despite effective treatment of leprosy via WHO-approved multi-drug therapy (MDT), patients still suffer from debilitating neuropathic sequelae, including peripheral neuropathic pain (PNP), and continue to develop intercurrent etiologies (such as diabetes), and progressive existing neuropathy over time. Strategies seeking to improve physiological and metabolic wellness, including those that reduce systemic inflammation and enhance immune responsiveness to neurotoxic factors may influence underlying neuropathic etiologies. A whole food plant-based diet (WFPBD) has been shown to be effective in the management of neuropathic pain due to diabetes, limiting severity and relevant symptomology. Diabetes remains a significant sequela of leprosy, as up to 50% of patients in reaction requiring corticosteroids, may develop a biochemical diabetes. As nutritional interventions may modulate both leprosy and diabetes, a specific exploration of these relationships remains relevant. Objectives: (1) To demonstrate the effect of a WFPBD lifestyle intervention, on neuropathic pain variables in leprosy; and (2) To contextualize the significance of diet in the treatment of chronic sequelae in leprosy by evaluating tolerability and side effect profile. Methods: A prospective, randomized, controlled, single-blind, multicentre interventional trial is described. Weekly one-hour dietary counseling sessions promoting a WFPBD emphasizing vegetables, fruits, whole-grains, nuts, and legumes, omitting animal products, and limiting fat intake over a six-month duration will be implemented. Participants will be 70 age and sex-matched individuals experiencing active or treated "cured" leprosy and PNP, randomized to either intervention or control groups. Primary outcome measures include efficacy via visual analog scale, subjective questionnaire and objective quantitative sensory testing, as well as safety, tolerability, and harms of a WFPBD on PNP in leprosy. This study will be initiated after Research Ethics Board (REB) approval at all participating sites, and in advance of study initiation, the trial will be registered at ClinicalTrials.gov. Expected impact: It is hypothesized that WFPBDs will mitigate progression and severity of PNP and potentially reduce the adverse events related to standard corticosteroid treatment of leprosy reactions, thereby reducing disease severity. By examining the effects of WFPBDs on PNP in leprosy, we hope to illuminate data that will lead to the enhanced therapeutic management of this neglected tropical disease.

Erratum: Neves KVRN, Machado LMG, Lisboa MN, Steinmann P, Ignotti E. Self-reported clinical history of misdiagnosed leprosy cases in the State of Mato Grosso,

Brazil, 2016-2019. Cad Saúde Pública 2023; 39(5):e00279421.

[No authors listed]
17-07-2023
Cad Saude Publica.
https://pubmed.ncbi.nlm.nih.gov/37466549/

Hansen's disease and the first patient disease Registry.

Bardin P.
18-07-2023
Respirology.
https://pubmed.ncbi.nlm.nih.gov/37464271/

Efficacy and Safety of Naftifine Hydrochloride 2% Gel in Interdigital Tinea Pedis: A Phase III Randomised, Double-Blind, Parallel-Group, Active-Controlled Study in Indian Adult Patients.

Sinha SD, Rajamma A, Bandi MR, Sriramadasu SC, Sahu S, Kothiwala RK, Halder S, Sankerneni A, Panapakam M, Vemireddy VNR, Vattipalli R, Devireddy SR.
18-07-2023
Clin Drug Investig.
https://pubmed.ncbi.nlm.nih.gov/37462803/

Multifocal Lupus Vulgaris: A Rare Presentation.

Pugalia N, Madke B, Jawade S.
16-06-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37461762/

Lupus vulgaris (LV) is a common type of cutaneous tuberculosis and commonly presents as a single erythematous plaque either on the face or buttocks with scarring and an active spreading edge. Multiple lesions of LV are sparingly reported in the literature. We hereby report a case of LV in a male presenting with multiple lesions over the buttock, thigh, and trunk. The diagnosis was done on the basis of clinical findings, histopathology, positive tuberculin test, and response to a standard anti-tubercular regimen.

sTREM-1 and TNF-α levels are associated with the clinical outcome of leprosy patients.

Bezerra-Santos M, Bomfim LGS, Santos CNO, Cunha MWN, de Moraes EJR, Cazzaniga RA, Tenório MDL, Araujo JMS, Menezes-Silva L, Magalhães LS, Barreto AS, Reed SG, Duthie MS, Lipscomb MW, de Almeida RP, de Moura TR, de Jesus AR.
29-06-2023
Front Med (Lausanne).
https://pubmed.ncbi.nlm.nih.gov/37457576/

Leprosy reaction (LR) and physical disability (PD) are the most significant clinical complications of leprosy. Herein, we assessed the circulating serum-sTREM-1 and TNF-α levels and their genetic polymorphisms in leprosy. Serum-sTREM-1 and TNF-α levels were measured in leprosy patients (LP) before treatment (n = 51) and from their household contacts (HHCs; n = 25). DNA samples were genotyped using TREM-1 rs2234246 and TNF-α rs1800629-SNP in 210 LPs and 168 endemic controls. The circulating sTREM-1 and TNF-α levels are higher in the multibacillary form. The ROC curve of the serum-sTREM-1 levels was able to differentiate LR from non-LR and PD from non-PD. Similarly, LPs with serum-sTREM-1 levels >210 pg/ml have 3-fold and 6-fold higher chances of presenting with LR and PD, respectively. Genotypes CC+CT of the TREM-1 were associated with leprosy. Taken together, our analyses indicated that sTREM-1 and TNF-α play an important role in the pathogenesis of leprosy and provide promising biomarkers to assist in the diagnosis of leprosy complications.

Jarisch–Herxheimer reaction.

Gautam M, Sethi S, Nadkarni NJ.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457541/

Syphilis is caused by a spirochete, *Treponema pallidum*. Diagnosis of syphilis is made with a venereal disease research laboratory test. Treatment of choice is intramuscular injection benzathine Penicillin. The Jarisch–Herxheimer reaction (JHR) is a transient immunological phenomenon that can occur in patients during treatment for syphilis with penicillin. It is a rare phenomenon but can be a potentially severe one. It manifests clinically with short-term constitutional symptoms such as fever, chills, headache, and myalgia, besides exacerbation of existing cutaneous lesions. We report the case of a 24-year-old man presenting with JHR posttreatment with benzathine penicillin.

Penile ulcerative pyoderma gangrenosum: A rare entity.

Patel JK, Pillai DS, Bodar P, Nair PA.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457536/

Syphilis resurgence: Exploring the impact of COVID-19 pandemic.

Kaur T, Mahajan M, Mahajan BB.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457535

Clinicoetiological study on vaginal discharge among sexually active women attending a tertiary center in North Kerala, India.

John N, Rahima S, Raji TK, Santhosh P, Kidangazhiathmana A, Sukumarakurup S.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457531/

Clinicoepidemiological study of adverse cutaneous drug reactions among immunocompromised children at a tertiary care hospital.

Jarang T, Katakam BK, Bollepaka KK, Gindham H.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457520/

Introduction: Highly active antiretroviral therapy (HAART) is used to treat human immunodeficiency virus type 1 (HIV-1). Introduction of antiretroviral therapy (ART) has reduced the HIV/AIDS associated morbidity and mortality significantly. But 25% of all patients discontinue treatment because of adverse drug reactions (ADRs). Adverse cutaneous drug reactions (ACDR) are very common with ART regimens, which may range from mild pruritus, maculopapular rash to serious Steven Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). ACDRs comprise 10%-30% of all reported ADRs. Aims and objectives: To assess the different types of cutaneous adverse drug reactions in immunocompromised children of less than 18years. Materials and methods: This is a retrospective record-based study, conducted at department of Dermatology, Venereology and Leprosy, Government Medical College (GMC)/Government General Hospital (GGH), Suryapet, Telangana, India. Data was collected from the records available at ART centre, from November 2018 to October 2021 GGH, Suryapet. All the HIV infected children ≤18 years who were on ART, were included in this study. Patients of more than 18 years and on other medications were excluded. Demographic data, socio economic status, vaccination status, height, weight, complete blood analysis, complete urine analysis, erythrocyte sedimentation rate, liver and renal function tests and CD4 counts were recorded before initiation of ART. Results: A total of 330 children of less than 18 years were initiated for ART, at ART centre, Government General Hospital, Suraypet. Out of 330 children, 27.8% (92) children developed ACDRs. 58.7% (54) were males and 41.3% (38) were females. Maculopapular rash was seen in 65.2% (60) cases, urticaria was seen in 15.3% (14) cases, Steven Johnson Syndrome (SJS) was seen in 9.8% (9) cases, SJS/TEN overlap was seen in 6.5% (6) cases and toxic epidermal necrolysis (TEN) was seen in 3.2% (3) case. CD4 count was below 300 in 65.3% (60) cases above 300 in 34.7% (32) cases. Gap between initiation of the treatment and onset of reaction was less than one month in 65.3% (60) cases, and more than one month in 34.7% (32) cases.

Bilateral Tyson's abscess as a complication of acute gonorrhea.

Sankaranantham M.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457517/

Clinico-epidemiological profile of genital dermatoses in people living with HIV: A shifting paradigm from venereal to nonvenereal dermatoses.

Dhillon SK, Kura MM.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457512

Context: The protean mucocutaneous manifestations of HIV and the resultant opportunistic infections are well documented. Genital dermatoses can be either venereal or nonvenereal in origin. As the presence of HIV infection greatly increases the chances of acquiring another sexually transmitted pathogen, these are often presumed to be venereal in origin. Aims: The aims of the study were to record the different morphologies of genital skin lesions in seropositive patients and to classify them as venereal or nonvenereal in origin. Settings and design: This was an observational study undertaken in seropositive patients with genital skin lesions attending the outpatient department of dermatology at a tertiary health-care center. Subjects and methods: One hundred and seventy-seven seropositive patients with genital lesions were enrolled. A detailed history was taken; the genital and dermatological examination was performed. Statistical analysis used: None. Results: Males predominated the study population with the majority (79.1%) falling into the reproductive age group of 15-49 years. Nonvenereal genital dermatoses (59%) outnumbered sexually transmitted infections (STIs) (41%) out of which the most frequently encountered were dermatophytosis, scabies, and intertrigo. Other entities recorded were inflammatory dermatoses, cutaneous adverse drug reactions, and tumors. The most common STIs were herpes genitalis (55.4%) and anogenital warts (32.5%). Conclusion: This study showed that nonvenereal genital dermatoses are more common than STIs in people living with HIV. Our findings reiterate the fact that genital lesions should be approached with caution as a presumptive and hasty diagnosis of STI adds greatly to the morbidity of the patient in terms of guilt and shame, and adversely affects the quality of life.

"Lepromatous leprosy as a presenting feature of HIV:" Diagnostic and management dilemmas.

Hanumanthu V, Narang T, Dogra S, Kumar B.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457510

Pediculosis pubis presenting as pediculosis capitis, pediculosis corporis, and pediculosis ciliaris in a case of Alport syndrome.

Dave MD, Mehta HH, Gorasiya AR, Nimbark DN.
Jan-Juin 2023
Indian J Sex Transm Dis AIDS.
https://pubmed.ncbi.nlm.nih.gov/37457512/

Pediculosis is an infestation of lice on the human body. Pediculosis pubis is primarily found in the pubic region and is usually transmitted by sexual contact. Diagnosis is done by visualization of mites which can be aided by the use of dermoscope. Hereby, we report a case of an Alport syndrome patient having extensive pubic lice infestation

with no sexual history and probable transmission from cattle.

Definition of 'close contacts' in leprosy studies: protocol for a scoping review.

Ronse M, Nieto-Sanchez C, De Coninck S, Verdonck K, Peeters Grietens K.
20-07-2023
F1000Res.
https://pubmed.ncbi.nlm.nih.gov/37456573/

Usage of Dermoscopy as an Effective Diagnostic Tool in Pityriasis Alba: A Prospective Observational Study Among Children in a Suburban Hospital in South India.

Thomas IN, James JJ, Bala A, Mohan S, Dogiparthi S, Shanmugam NP Sr.
11-07-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37448397/

Culture circle with community health workers about (lack of) knowledge and stigma of leprosy.

Aquino DMC, Monteiro EMLM, Coutinho NPS, Soeiro VMDS, Santos TA, Oliveira EM, Pereira DLM, Caldas AJM.
10-07-2023
Rev Gaucha Enferm.
https://pubmed.ncbi.nlm.nih.gov/37436218/

Objective: To describe the construction aboutthe (lack of) knowledge and stigma of leprosy by Community Health Workers participating in the Culture Circle. Method: Qualitative, action-research type study supported by the Paulo Freire Culture Circle framework, carried out with 21 Community Health Workers. Data collected in November 2021, in the municipality of São Luís, Maranhão. The following categories were evidenced: knowledge about leprosy, signs and symptoms, stigma. Results: The participants had knowledge about the disease, but they verbalized people's disinformation about leprosy, disbelief in relation to the cure, and situations of prejudice and stigma that are still present today. Final considerations: The culture circle enabled the intertwining of scientific and empirical knowledge in the construction of a critical and reflective knowledge committed to welcoming and comprehensive care for people and families affected by leprosy.

Hi-plex deep amplicon sequencing for identification, high-resolution genotyping and multidrug resistance prediction of Mycobacterium leprae directly from patient biopsies by using Deeplex Myc-Lep.

Jouet A, Braet SM, Gaudin C, Bisch G, Vasconcellos S, Epaminondas Nicacio de Oliveira do Livramento RE, Prado Palacios YY, Fontes AB, Lucena N, Rosa P, Moraes M, La K, Badalato N, Lenoir E, Ferré A, Clément M, Hasker E, Grillone SH, Abdou W, Said A, Assoumani Y, Attoumani N, Laurent Y, Cambau E, de Jong BC, Suffys PN, Supply P.
Juil-2023
EBioMedicine.
https://pubmed.ncbi.nlm.nih.gov/37327675/

Background: Expansion of antimicrobial resistance monitoring and epidemiological surveillance are key components of the WHO strategy towards zero leprosy. The inability to grow Mycobacterium leprae in vitro precludes routine phenotypic drug susceptibility testing, and only limited molecular tests are available. We evaluated a culture-free targeted deep sequencing assay, for mycobacterial identification, genotyping based on 18 canonical SNPs and 11 core variable-number tandem-repeat (VNTR) markers, and detection of rifampicin, dapsone and fluoroquinolone resistance-associated mutations in rpoB/ctpC/ctpI, folP1, gyrA/gyrB, respectively, and hypermutation-associated mutations in nth. Methods: The limit of detection (LOD) was determined using DNA of M. leprae reference strains and from 246 skin biopsies and 74 slit skin smears of leprosy patients, with genome copies quantified by RLEP qPCR. Sequencing results were evaluated versus whole genome sequencing (WGS) data of 14 strains, and versus VNTR-fragment length analysis (FLA) results of 89 clinical specimens. Findings: The LOD for sequencing success ranged between 80 and 3000 genome copies, depending on the sample type. The LOD for minority variants was 10%. All SNPs detected in targets by WGS were identified except in a clinical sample where WGS revealed two dapsone resistance-conferring mutations instead of one by Deeplex Myc-Lep, due to partial duplication of the sulfamide-binding domain in folP1. SNPs detected uniquely by Deeplex Myc-Lep were missed by WGS due to insufficient coverage. Concordance with VNTR-FLA results was 99.4% (926/932 alleles). Interpretation: Deeplex Myc-Lep may help improve the diagnosis and surveillance of leprosy. Gene domain duplication is an original putative drug resistance-related genetic adaptation in M. leprae.
Funding: EDCTP2 programme supported by the European Union (grant number RIA2017NIM-1847 -PEOPLE). EDCTP, R2Stop: Effect:Hope, The Mission To End Leprosy, the Flemish Fonds Wetenschappelijk Onderzoek.

Morsures de serpent

Snakebite Advice and Counseling From Artificial Intelligence: An Acute Venomous Snakebite Consultation With ChatGPT.

Altamimi I, Altamimi A, Alhumimidi AS, Altamimi A, Temsah MH.
13-06-2023
Cureus.
https://pubmed.ncbi.nlm.nih.gov/37456381/

Urtica cannabina L. water extract exhibits anti-inflammatory activity by regulating inflammatory cytokines: In vitro and in vivo evidence.

Wujiamaiti Z, Kizaibek M, Bahetijian D, Li Y, Gui Y, Abula A.
13-07-2023
J Ethnopharmacol.
https://pubmed.ncbi.nlm.nih.gov/37453626/

Ethnopharmacological relevance: Urtica cannabina L. (U. cannabina) is a medicinal plant used in traditional Chinese and Kazakh medicine for treatment of various ailments such as rheumatoid arthritis, rheumatic pain, high blood pressure, and snake bites. However, very few studies have focused on the anti-inflammatory effects of U. cannabina and the mechanisms underlying these effects. Aim of the study: This study to investigate the in vitro and in vivo anti-inflammatory effect of U. cannabina, the underlying mechanisms, and its phytochemical profile. Materials and methods: We investigated the anti-inflammatory effects of the U. cannabina water extract on lipopolysaccharide-stimulated RAW264.7 macrophages and paw edema in rats and analyzed its chemical components using ultra-performance liquid chromatography-mass spectrometry (UPLC-MS). Results: U. cannabina water extract effectively inhibited the secretion of multiple inflammatory factors, and its corresponding mRNA expression in LPS-induced RAW264.7 cells ($p < 0.05$). Tincture of U. cannabina water extract significantly reduced carrageenan-induced rat paw edema and levels of inflammatory factors ($p < 0.05$). A total of 31 compounds, which mainly include organic acids, were tentatively identified based on the comparison of their mass spectrum profiles with those recorded in a mass spectra database. Conclusions: The results of this study elucidated the anti-inflammatory effect of U. cannabina water extract in vitro and in vivo and showed that the extract elicits the anti-inflammatory effects by regulating the activity of inflammatory cytokines. The results prove that U. cannabina is a valuable source of active compounds with anti-inflammatory activity.

Pharmacological Activity of Cepharanthine.

Liu K, Hong B, Wang S, Lou F, You Y, Hu R, Shafqat A, Fan H, Tong Y.
27-06-2023
Molecules.
https://pubmed.ncbi.nlm.nih.gov/37446681/

Cepharanthine, a natural bisbenzylisoquinoline (BBIQ) alkaloid isolated from the plant *Stephania Cephalantha Hayata*, is the only bisbenzylisoquinoline alkaloid approved for human use and has been used in the clinic for more than 70 years. Cepharanthine has a variety of medicinal properties, including signaling pathway inhibitory activities, immunomodulatory activities, and antiviral activities. Recently, cepharanthine has been confirmed to greatly inhibit SARS-CoV-2 infection. Therefore, we aimed to describe the pharmacological properties and mechanisms of cepharanthine, mainly including antitumor, anti-inflammatory, anti-pathogen activities, inhibition of bone resorption, treatment of alopecia, treatment of snake bite, and other activities. At the same time, we analyzed and summarized the potential antiviral mechanism of cepharanthine and concluded that one of the most important anti-viral mechanisms of cepharanthine may be the stability of plasma membrane fluidity. Additionally, we explained its safety and bioavailability, which provides evidence for cepharanthine as a potential drug for the treatment of a variety of diseases. Finally, we further discuss the potential new clinical applications of cepharanthine and provide direction for its future development.

Antiviral and Immunomodulatory Activities of Clinacanthus nutans (Burm. f.) Lindau.

Lin CM, Chen HH, Lung CW, Chen HJ.
28-06-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37445964/

Exotic (non-native) snakebite envenomation in Japan: A review of the literature between 2000 and 2022.

Aoki Y, Yoshimura K, Sakai A, Tachikawa A, Tsukamoto Y, Takahashi K, Yamano S, Smith C, Hayakawa K, Tasaki O, Ariyoshi K, Warrell DA.
11-07-2023
Toxicon.
https://pubmed.ncbi.nlm.nih.gov/37442298/

A limited number of studies have investigated the clinical characteristics of snakebite envenomation by exotic (non-native) snakes in Japan. This study reviewed the literature to determine the status and risk of bites by exotic pet snakes in Japan. We reviewed reports of snakebite due to exotic snakes in Japan published between 2000 and 2022, excluding reports of bites by snakes native to Japan, such as Gloydius blomhoffii, Rhabdophis tigrinus, and Protobothrops flavoviridis. During the study period, 11 exotic snakebites were recorded, involving 11 species. The majority of those bitten (10/11 cases) were male, all cases were hand injuries, and there were no fatalities. The snakes responsible belonged to the Colubridae (4/11 cases), Viperidae (4/11 cases), and Elapidae (3/11 cases) families. Cases of envenomation by G. brevicaudus, Bungarus candidus, and Dendroaspis angusticeps were of particular interest. Ten of the eleven patients developed local cytotoxic signs, and three developed "compartment syndrome," in which the surgeons performed decompressive incisions. Two bites from elapid snakes and one from a viperid snake resulted in respiratory failure. Antivenom was given in two cases. Complications were observed, such as acute kidney injury, rhabdomyolysis, coagulopathy, and residual dysfunction of the affected finger. Emergency rooms should be prepared to manage patients who have been bitten by exotic snakes, even though the number of reported cases is not high in Japan. Initial stabilization of patients is crucial, before a definitive diagnosis is made, as with native snakebite envenomation. Finger bites are reported in most cases, which may result in functional impairment of the fingers. In order to collect more comprehensive patient data in Japan, a reporting system for all snakebite envenomations should be considered.

Evaluation of three different ^{99m}Tc-based mock-venom agents for

lymphoscintigraphy studies in preclinical models of peripheral snakebite envenomation.

Tiwari N, Jaimini A, Jain GK, Aggarwal G, Mittal G.
Juil-Août-2023
J Pharmacol Toxicol Methods.
https://pubmed.ncbi.nlm.nih.gov/37295617/

Rage

Integrating full and partial genome sequences to decipher the global spread of canine rabies virus.

Holtz A, Baele G, Bourhy H, Zhukova A.
Nat Commun. 2023 Jul 17;
https://pubmed.ncbi.nlm.nih.gov/37460566/

Despite the rapid growth in viral genome sequencing, statistical methods face challenges in handling historical viral endemic diseases with large amounts of underutilized partial sequence data. We propose a phylogenetic pipeline that harnesses both full and partial viral genome sequences to investigate historical pathogen spread between countries. Its application to rabies virus (RABV) yields precise dating and confident estimates of its geographic dispersal. By using full genomes and partial sequences, we reduce both geographic and genetic biases that often hinder studies that focus on specific genes. Our pipeline reveals an emergence of the present canine-mediated RABV between years 1301 and 1403 and reveals regional introductions over a 700-year period. This geographic reconstruction enables us to locate episodes of human-mediated introductions of RABV and examine the role that European colonization played in its spread. Our approach enables phylogeographic analysis of large and genetically diverse data sets for many viral pathogens.

Scalable Bayesian divergence time estimation with ratio transformations.

Ji X, Fisher AA, Su S, Thorne JL, Potter B, Lemey P, Baele G, Suchard MA.
17-07-2023
Syst Biol.
https://pubmed.ncbi.nlm.nih.gov/37458991/

Divergence time estimation is crucial to provide temporal signals for dating biologically important events, from species divergence to viral transmissions in space and time. With the advent of high-throughput sequencing, recent Bayesian phylogenetic studies have analyzed hundreds to thousands of sequences. Such large-scale analyses challenge divergence time reconstruction by requiring inference on highly-correlated internal node heights that often become computationally infeasible. To overcome this limitation, we explore a ratio transformation that maps the original N-1 internal node heights into a space of one height parameter and N-2 ratio parameters. To make the analyses scalable, we develop a collection of linear-time algorithms to compute the gradient and Jacobian-associated terms of the log-likelihood with respect to these ratios. We then apply Hamiltonian Monte Carlo sampling with the ratio transform in a Bayesian framework to learn the divergence times in four pathogenic viruses (West Nile virus, rabies virus, Lassa virus and Ebola virus) and the coralline red algae. Our method both resolves a mixing issue in the West Nile virus example and improves inference efficiency by at least 5-fold for the Lassa and rabies virus examples as well as for the algae example. Our method now also makes it computationally feasible to incorporate mixed-effects molecular clock models for the Ebola virus example, confirms the findings from the original study and reveals clearer multimodal distributions of the divergence times of some clades of interest. [Divergence time estimation, Bayesian inference, Hamiltonian Monte Carlo, ratio transformation, effective sample size, phylogenetics, pathogens.

Breed, smaller weight, and multiple injections are associated with increased adverse event reports within three days following canine vaccine administration.

Moore GE, Morrison J, Saito EK, Spofford N, Yang M.
14-07-2023
J Am Vet Med Assoc.
https://pubmed.ncbi.nlm.nih.gov/37451674/

TRIM21 Promotes Rabies Virus Production by Degrading IRF7 through Ubiquitination.

Zhang B, Cai T, He H, Huang X, Chen G, Lai Y, Luo Y, Huang S, Luo J, Guo X.
30-06-2023
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/37446070/

Schistosomiase

Single-Cell Analysis of CX3CR1+ Cells Reveals a Pathogenic Role for BIRC5+ Myeloid Proliferating Cells Driven by Staphylococcus aureus Leukotoxins.

Loredan DG, Devlin JC, Lacey KA, Howard N, Chen Z, Zwack EE, Lin JD, Ruggles KV, Khanna KM, Torres VJ, Loke P.
19-07-2023
J Immunol.
https://pubmed.ncbi.nlm.nih.gov/37466391

Our previous studies identified a population of stem cell-like proliferating myeloid cells within inflamed tissues that could serve as a reservoir for tissue macrophages to adopt different activation states depending on the microenvironment. By lineage-tracing cells derived from CX3CR1+ precursors in mice during infection and profiling by single-cell RNA sequencing, in this study, we identify a cluster of BIRC5+ myeloid cells that expanded in the liver during chronic infection with either the parasite Schistosoma mansoni or the bacterial pathogen Staphylococcus aureus. In the absence of tissue-damaging toxins, S. aureus infection does not elicit these BIRC5+ cells. Moreover, deletion of BIRC5 from CX3CR1-

expressing cells results in improved survival during S. aureus infection. Hence the combination of single-cell RNA sequencing and genetic fate-mapping CX3CR1+ cells revealed a toxin-dependent pathogenic role for BIRC5 in myeloid cells during S. aureus infection.

Prevalence and risk factors of schistosomiasis and hookworm infection in seasonal transmission settings in northern Côte d'Ivoire: A cross-sectional study.

Kouadio JN, Giovanoli Evack J, Sékré JK, Achi LY, Ouattara M, Hattendorf J, Balmer O, Bonfoh B, Zinsstag J, Utzinger J, N'Goran EK.
17-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37459286/

[Progress of schistosomiasis control in People's Republic of China in 2022].

Zhang L, He J, Yang F, Dang H, Li Y, Guo S, Li S, Cao C, Xu J, Li S, Zhou X.
13-06-2023
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
https://pubmed.ncbi.nlm.nih.gov/37455091/

This report presented the endemic status of schistosomiasis and analyzed the data collected from the national schistosomiasis prevention and control system and national schistosomiasis surveillance program in the People's Republic of China in 2022. Among the 12 provinces (municipality and autonomous region) endemic for schistosomiasis, Shanghai Municipality, Zhejiang Province, Fujian Province, Guangdong Province and Guangxi Zhuang Autonomous Region continued to maintain the achievements of schistosomiasis elimination, and Sichuan and Jiangsu provinces maintained the criteria of transmission interruption, while Yunnan, Hubei, Anhui, Jiangxi and Hunan provinces maintained the criteria of transmission control by the end of 2022. A total of 452 counties (cites, districts) were found to be endemic for schistosomiasis in China in 2022, with 27 434 endemic villages covering 73 424 400 people at risk of infections. Among the 452 endemic counties (cities, districts), 75.89% (343/452), 23.45% (106/452) and 0.66% (3/452) achieved the criteria of elimination, transmission interruption and transmission control of schistosomiasis, respectively. In 2022, 4 317 356 individuals received serological tests for schistosomiasis, and 62 228 were sero-positive. A total of 208 646 individuals received stool examinations for schistosomiasis, with one positive and another two cases positive for urine microscopy, and these three 3 cases were imported schistosomiasis patients from Africa. There were 28 565 cases with advanced schistosomiasis documented in China by the end of 2022. *Oncomelania hupensis* snail survey was performed in 18 891 endemic villages in China in 2022 and *O. hupensis* snails were found in 6 917 villages (36.62% of all surveyed villages), with 8 villages identified with emerging snail habitats. Snail survey was performed at an area of 655 703.01 hm^2 and 183 888.60 hm^2 snail habitats were found, including 110.58 hm^2 emerging snail habitats and 844.35 hm^2 re-emerging snail habitats. There were 477 200 bovines raised in the schistosomiasis endemic areas of China in 2022, and 113 946 bovines received serological examinations for schistosomiasis, with 204 sero-positives detected. Among the 131 715 bovines received stool examinations, no positives were identified. In 2022, there were 19 726 schistosomiasis patients receiving praziquantel chemotherapy, and expanded chemotherapy was performed in 714 465 person-time for humans and 234 737 herd-time for bovines in China. In 2022, snail control with chemical treatment was performed at an area of 119 134.07 hm^2, and the actual area of chemical treatment was 65 825.27 hm^2, while environmental improvements were performed at an area of 1 163.96 hm^2. Data from the national schistosomiasis surveillance program of China showed that the mean prevalence of *Schistosoma japonicum* infections was both zero in humans and bovines in 2022, and no *S. japonicum* infection was detected in *O. hupensis* snails. These data demonstrated that the endemic status of schistosomiasis continued to decline in China in 2022, with 3 confirmed schistosomiasis patients that had a foreign nationality and all imported from Africa, and the areas of snail habitats remained high. Further improvements in the construction of the schistosomaisis surveillance and forecast system, and reinforcement of *O. hupensis* survey and control are required to prevent the re-emerging schistosomiasis.

Design, Synthesis and Evaluation of Praziquantel Analogues and New Molecular Hybrids as Potential Antimalarial and Anti-Schistosomal Agents.

Kasago FM, Häberli C, Keiser J, Masamba W.
03-07-2023
Molecules.
https://pubmed.ncbi.nlm.nih.gov/37446846/

Malaria and schistosomiasis are two of the neglected tropical diseases that persistently wreak havoc worldwide. Although many antimalarial drugs such as chloroquine are readily available, the emergence of drug resistance necessitates the development of new therapies to combat this disease. Conversely, Praziquantel (PZQ) remains the sole effective drug against schistosomiasis, but its extensive use raises concerns about the potential for drug resistance to develop. In this project, the concept of molecular hybridization was used as a strategy to design the synthesis of new molecular hybrids with potential antimalarial and antischistosomal activity. A total of seventeen molecular hybrids and two PZQ analogues were prepared by coupling 6-alkylpraziquanamines with cinnamic acids and cyclohexane carboxylic acid, respectively. The synthesised compounds were evaluated for their antimalarial and antischistosomal activity; while all of the above compounds were inactive against *Plasmodium falciparum* (IC_{50} > 6 µM), many were active against schistosomiasis with four particular compounds exhibiting up to 100% activity against newly transformed schistosomula and adult worms at 50 µM. Compared to PZQ, the reference drug, the activity of which is 91.7% at 1 µM, one particular molecular hybrid, compound **32**, which bears a para-isopropyl group on the cinnamic acid

moiety, exhibited a notable activity at 10 µM (78.2% activity). This compound has emerged as the front runner candidate that might, after further optimization, hold promise as a potential lead compound in the fight against schistosomiasis.

Bridged 1,2,4-Trioxolanes: $SnCl_4$-Catalyzed Synthesis and an In Vitro Study against S. mansoni.

Radulov PS, Yaremenko IA, Keiser J, Terent'ev AO.
22-06-2023
Molecules.
https://pubmed.ncbi.nlm.nih.gov/37446575/

A synthesis of bridged 1,2,4-trioxolanes (bridged ozonides) from 1,5-diketones and hydrogen peroxide catalyzed by $SnCl_4$ was developed. It was shown that the ratio of target ozonides can be affected by the application of $SnCl_4$ as a catalyst and varying the solvent. A wide range of bridged 1,2,4-trioxolanes (ozonides) was obtained in yields from 50 to 84%. The ozonide cycle was moderately resistant to the reduction of the ester group near the peroxide cycle to alcohol with $LiAlH_4$. The bridged ozonides were evaluated for their antischistosomal activity**.** These ozonides exhibited a very high activity against newly transformed schistosomula and adult *Schistosoma mansoni*.

Small change, big difference: A promising praziquantel derivative designated P96 with broad-spectrum antischistosomal activity for chemotherapy of schistosomiasis japonica.

Xu J, Dong LL, Sun H, Huang P, Zhang RZ, Wang XY, Sun DQ, Xia CM.
06-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37410790/

Assessing the prevalence of Female Genital Schistosomiasis and comparing the acceptability and performance of health worker-collected and self-collected cervical-vaginal swabs using PCR testing among women in North-Western Tanzania: The ShWAB study.

Ursini T, Scarso S, Mugassa S, Othman JB, Yussuph AJ, Ndaboine E, Mbwanji G, Mazzi C, Leonardi M, Prato M, Pomari E, Mazigo HD, Tamarozzi F.
06-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37410782/

Schistosoma mansoni infection alters the host pre-vaccination environment resulting in blunted Hepatitis B vaccination immune responses.

Muir R, Metcalf T, Fourati S, Bartsch Y, Kyosiimire-Lugemwa J, Canderan G, Alter G, Muyanja E, Okech B, Namatovu T, Namara I, Namuniina A, Ssetaala A, Mpendo J, Nanvubya A, Kitandwe PK, Bagaya BS, Kiwanuka N, Nassuna J, Biribawa VM, Elliott AM, de Dood CJ, Senyonga W, Balungi P, Kaleebu P, Mayanja Y, Odongo M, Connors J, Fast P, Price MA, Corstjens PLAM, van Dam GJ, Kamali A, Sekaly RP, Haddad EK.
05-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37406029/

Schistosomiasis is a disease caused by parasitic flatworms of the Schistosoma spp., and is increasingly recognized to alter the immune system, and the potential to respond to vaccines. The impact of endemic infections on protective immunity is critical to inform vaccination strategies globally. We assessed the influence of Schistosoma mansoni worm burden on multiple host vaccine-related immune parameters in a Ugandan fishing cohort (n = 75) given three doses of a Hepatitis B (HepB) vaccine at baseline and multiple timepoints post-vaccination. We observed distinct differences in immune responses in instances of higher worm burden, compared to low worm burden or non-infected. Concentrations of pre-vaccination serum schistosome-specific circulating anodic antigen (CAA), linked to worm burden, showed a significant bimodal distribution associated with HepB titers, which was lower in individuals with higher CAA values at month 7 post-vaccination (M7). Comparative chemokine/cytokine responses revealed significant upregulation of CCL19, CXCL9 and CCL17 known to be involved in T cell activation and recruitment, in higher CAA individuals, and CCL17 correlated negatively with HepB titers at month 12 post-vaccination. We show that HepB-specific CD4+ T cell memory responses correlated positively with HepB titers at M7. We further established that those participants with high CAA had significantly lower frequencies of circulating T follicular helper (cTfh) subpopulations pre- and post-vaccination, but higher regulatory T cells (Tregs) post-vaccination, suggesting changes in the immune microenvironment in high CAA could favor Treg recruitment and activation. Additionally, we found that changes in the levels of innate-related cytokines/chemokines CXCL10, IL-1β, and CCL26, involved in driving T helper responses, were associated with increasing CAA concentration. This study provides further insight on pre-vaccination host responses to Schistosoma worm burden which will support our understanding of vaccine responses altered by pathogenic host immune mechanisms and memory function and explain abrogated vaccine responses in communities with endemic infections.

Loading praziquantel within solid lipid nanoparticles improved its schistosomicidal efficacy against the juvenile stage.

Mogahed NMFH, El-Temsahy MM, Abou-El-Naga IF, Makled S, Sheta E, Ibrahim EI.
Août-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37285898/

Trachome

Individual longitudinal compliance to neglected tropical disease mass drug administration programmes, a systematic review.

Maddren R, Phillips A, Rayment Gomez S, Forbes K, Collyer BS, Kura K, Anderson R.
17-07-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37459369/

Repeated distribution of preventative chemotherapy (PC) by mass drug administration forms the mainstay of transmission control for five of the 20 recognised neglected tropical diseases (NTDs); soil-transmitted helminths, schistosomiasis, lymphatic filariasis, onchocerciasis and trachoma. The efficiency of such programmes is reliant upon participants swallowing the offered treatment consistently at each round. This is measured by compliance, defined as the proportion of eligible participants swallowing treatment. Individually linked longitudinal compliance data is important for assessing the potential impact of MDA-based control programmes, yet this accurate monitoring is rarely implemented in those for NTDs. Longitudinal compliance data reported by control programmes globally for the five (PC)-NTDs since 2016 is examined, focusing on key associations of compliance with age and gender. PubMed and Web of Science was searched in January 2022 for articles written in English and Spanish, and the subsequent extraction adhered to PRISMA guidelines. Study title screening was aided by Rayyan, a machine learning software package. Studies were considered for inclusion if primary compliance data was recorded for more than one time point, in a population larger than 100 participants. All data analysis was conducted in R. A total of 89 studies were identified containing compliance data, 57 were longitudinal studies, of which 25 reported individually linked data reported by varying methods. The association of increasing age with the degree of systematic treatment was commonly reported. The review is limited by the paucity of data published on this topic. The varying and overlapping terminologies used to describe coverage (receiving treatment) and compliance (swallowing treatment) is reviewed. Consequently, it is recommended that WHO considers clearly defining the terms for coverage, compliance, and longitudinal compliance which are currently contradictory across their NTD treatment guidelines. This review is registered with PROSPERO (number: CRD42022301991).

Synthesis and biological evaluation of sulfonylpyridine derivatives as potential anti-chlamydia agents.

Feng J, Janaína de Campos L, Seleem MA, Conda-Sheridan M.
30-06-2023
Bioorg Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37453189/

Trématodoses d'origine alimentaire (clonorchiase, opisthorchiase, fasciolase et paragonimose

Survey of intestinal parasites in swine farms raised in Western Nepal.

Chaudhary B, Parajuli RP, Dhakal P.
18-07-2023
Vet Med Sci.
https://pubmed.ncbi.nlm.nih.gov/37463607/

Background: Pigs (Sus scrofa domesticus), an important domestic livestock, are generally affected by helminth and protozoan parasites. Rearing pigs in rural regions in Nepal is a common practice for subsistence farming. A cross-sectional survey was conducted to determine the occurrence of gastrointestinal parasites (GIPs) in pigs raised in Western Nepal. Methods: A total of 200 faecal samples from commercial and smallholder farms were examined by wet mounts, flotation, sedimentation and staining techniques. Results: The results revealed that overall 86.5% of samples were found shedding oocysts or eggs of one or more GIPs. Three species of protozoa [Eimeria sp. (26%), Entamoeba coli (25.5%) and Coccidia (29%)] and nine species of helminths parasites (Ascaris suum (32.5%), Trichuris suis (30%), strongyle-type nematode (27.5%), hookworm (26%), Fasciola sp. (17.5%), Physaloptera sp. (17.5%), Strongyloides sp. (17.5%), Metastrongylus sp. (8%) and Oesophagostomum sp. (5.5%)] were identified. Female pigs were found to have higher protozoan infection than males, but such a difference was not noticed with regard to helminth parasites. Strongyles and Oesophagostomum infection were higher in commercial farms compared to smallholder farms, whereas the prevalences of E. coli and other protozoans were higher in smallholder farms. Among the contextual factors evaluated for association, weight and gender of pigs, and annual income and gender of managers/caretakers were significantly ($p < 0.05$) associated with the prevalence of GIPs in pigs. The overall prevalence of certain helminths such as strongyle-type nematode and A. suum was significantly ($p < 0.05$) associated with the weight of pigs after adjusting other contextual factors. Conclusions: This study detected relatively high prevalence of intestinal parasites in domestic pig facilities. Molecular epidemiological studies are essential to verify the exact zoonotic potential of parasites carried by pigs in the region. An effective periodic monitoring of GIPs of pigs needs to be carried out to minimize their further dissemination.

Genetic variation and population structure of Fasciola hepatica: an in silico analysis.

Alvi MA, Khalid A, Ali RMA, Saqib M, Qamar W, Li L, Ahmad B, Fu BQ, Yan HB, Jia WZ.
17-07-2023
Parasitol Res.
https://pubmed.ncbi.nlm.nih.gov/37458821/

Activity of cumin essential oil to control fascioliasis: Efficacy and changes in the tegument of Fasciola hepatica.

Brauner de Mello A, Baccega B, Obelar Martins F, Ignês de Santi I, Islabão YW, de Giacometi M, Pereira Soares M, da Rosa Farias NA, Belmonte de Oliveira C.
14-07-2023
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37454922/

Fasciola hepatica, the liver trematode, infects ruminants and causes economic loss. Because parasites are developing resistance to commercial drugs, the negative effects of parasitism are increasing. In this study, we aimed to evaluate the efficacy of cumin (Cuminum cyminum) essential oil against F. hepatica eggs and adults. The eggs were incubated with eight concentrations of the essential oil (0.031125-4.15 mg/mL), and viable eggs were counted after 14 days and classified as embryonated or non-embryonated. Adult flukes were incubated in Roswell Park Memorial Institute medium to ensure their viability and then incubated in essential oil. They were observed for 24 h after treatment. The adults were assessed with the two lowest effective oil concentrations used in the ovicidal test. Three controls were used for both tests: nitroxynil, a negative control, and Tween®80. After incubation in oil, the adult specimens were processed for histological analysis and stained with hematoxylin-eosin. In addition, the oil was tested for cytotoxicity using Madin-Darby bovine kidney cells to assess any possible effect on them. The oil was effective in ovicidal and adulticidal inhibition of the trematode, with statistically significant results. All concentrations assessed in the ovicidal test were 100% effective. The adult test was effective within 15 h and inactivated all the specimens at the highest concentration evaluated (0.06225 mg/mL). Histological analysis showed that cumin essential oil resulted in marked areas of vacuolization. The spines showed no structural changes but were surrounded by microvesicles. These findings indicated that cumin oil could be a potential compound in the control of fasciolosis.

Study of the cross-talk between Fasciola hepatica juveniles and the intestinal epithelial cells of the host by transcriptomics in an in vitro model.

Becerro-Recio D, Serrat J, López-García M, Torres-Valle M, Colina F, Fernández IM, González-Miguel J, Siles-Lucas M.
01-07-2023
Vet Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37450963/

Fasciolosis is a globally widespread trematodiasis with a major economic and veterinary impact. Therefore, this disease is responsible for millions of dollars in losses to the livestock industry, and also constitutes an emerging human health problem in endemic areas. The ubiquitous nature of Fasciola hepatica, the main causative agent, is one of the key factors for the success of fasciolosis. Accordingly, this parasite is able to subsist in a wide variety of ecosystems and hosts, thanks to the development of a plethora of strategies for adaption and immune evasion. Fasciolosis comprises a growing concern due to its high prevalence rates, together with the emergence of strains of the parasite resistant to the treatment of choice (triclabendazole). These facts highlight the importance of developing novel control measures which allow for an effective protection against the disease before F. hepatica settles in a niche inaccessible to the immune system. However, knowledge about the initial phases of the infection, including the migration mechanisms of the parasite and the early innate host response, is still scarce. Recently, our group developed an in vitro host-parasite interaction model that allowed the early events to be unveiled after the first contact between the both actors. This occurs shortly upon ingestion of F. hepatica metacercariae and the emergence of the newly excysted juveniles (FhNEJ) in the host duodenum. Here, we present a transcriptomic analysis of such model using an approach based on RNA sequencing (RNA-Seq), which reveals changes in gene expression related to proteolysis and uptake of metabolites in FhNEJ. Additionally, contact with the parasite triggered changes in host intestinal cells related to pseudogenes expression and host defence mechanisms, including immune response, among others. In sum, these results provide a better understanding of the early stages of fasciolosis at molecular level, and a pool of targets that could be used in future therapeutic strategies against the disease.

Diversity, prevalence and risk factors associated to gastrointestinal tract parasites in wild and domestic animals from Pakistan.

Khattak I, Akhtar A, Shams S, Usman T, Haider J, Nasreen N, Khan A, Ben Said M.
11-07-2023
Parasitol Int.
https://pubmed.ncbi.nlm.nih.gov/37442336/

One Health for fascioliasis control in human endemic areas.

Mas-Coma S, Valero MA, Bargues MD.
Août-2023
Trends Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37385922/

Fasciola hepatica and F. gigantica are liver flukes causing fascioliasis, a worldwide zoonotic, complex disease. Human infection/reinfection occurs in endemic areas where preventive chemotherapy is applied, because of fasciolid transmission ensured by livestock and lymnaeid snail vectors. A One Health control action is the best complement to decrease infection risk. The multidisciplinary framework needs to focus on freshwater transmission foci and their environment, lymnaeids, mammal reservoirs, and inhabitant infection, ethnography and housing. Local epidemiological and transmission

knowledge furnished by previous field and experimental research offers the baseline for control design. A One Health intervention should be adapted to the endemic area characteristics. Long-term control sustainability may be achieved by prioritizing measures according to impact depending on available funds.

Trypanosomes (trypanosomiase et maladie de Chagas)

Identification of a small-molecule inhibitor that selectively blocks DNA-binding by Trypanosoma brucei replication protein A1.

Mukherjee A, Hossain Z, Erben E, Ma S, Choi JY, Kim HS.
20-07-2023
Nat Commun.
https://pubmed.ncbi.nlm.nih.gov/37474515/

Balancing the functions of DNA extracellular traps in intracellular parasite infections: implications for host defense, disease pathology and therapy.

Koh CC, Gollob KJ, Dutra WO.
20-07-2023
Cell Death Dis.
https://pubmed.ncbi.nlm.nih.gov/37474501/

The release of DNA to the extracellular milieu is a biological process referred to as etosis, which is involved in both physiological and pathological functions. Although the release of DNA extracellular traps (ETs) was initially attributed to innate immune cells such as neutrophils, eosinophils, and macrophages, recent studies have shown that T cells, as well as non-immune cells, are capable of releasing ETs. These structures were described primarily for their potential to trap and kill pathogens, presenting an important strategy of host defense. Intriguingly, these functions have been associated with intracellular pathogens such as the parasites Leishmania sp. and Trypanosoma cruzi, causative agents of leishmaniasis and Chagas disease, respectively. These are two devastating tropical diseases that lead to thousands of deaths every year. In an apparent contradiction, ETs can also induce and amplify inflammation, which may lead to worsening disease pathology. This has prompted the concept of targeting ETs' release as a means of controlling tissue destruction to treat human diseases. What is the best approach to prevent disease severity: inducing ETs to kill pathogens or preventing their release? In this Perspective article, we will discuss the importance of understanding ETs released by different cell types and the need to balance their potentially complementary functions. In addition, we will explore other functions of ETs and their translational applications to benefit individuals infected with intracellular parasites and other pathogens. Ultimately, a better understanding of the role of ETs in disease pathogenesis will provide valuable insights into developing novel therapies for human diseases.

Multiple domains of the integral KREPA3 protein are critical for the structure and precise functions of RNA Editing Catalytic Complexes in Trypanosoma brucei.

Davidge B, McDermott SM, Carnes J, Lewis I, Tracy M, Stuart K.
20-07-2023
RNA.
https://pubmed.ncbi.nlm.nih.gov/37474258/

Discovery of 5-Phenylpyrazolopyrimidinone Analogs as Potent Antitrypanosomal Agents with In Vivo Efficacy.

Zheng Y, van den Kerkhof M, van der Meer T, Gul S, Kuzikov M, Ellinger B, de Esch IJP, Siderius M, Matheeussen A, Maes L, Sterk GJ, Caljon G, Leurs R.
20-07-2023
J Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37471520/

Current Prospects of Saponins as Promising Anti-Trypanosoma Brucei Compounds: Insight into the Mechanisms of Action.

Pone Kamdem B, Fekam Boyom F.
19-07-2023
Curr Drug Targets.
https://pubmed.ncbi.nlm.nih.gov/37469154/

Background: Human African trypanosomiasis (HAT) is a parasitic infection that may lead to death if left untreated. This disease is caused by a protozoan parasite of the genus Trypanosoma and is transmitted to humans through tsetse fly bites. The disease is widespread across Sub-Saharan Africa, with 70% of cases in recent reports in the Democratic Republic of the Congo and an average of less than 1000 cases are declared annually. Since there is no appropriate treatment for HAT, steroidal and triterpenoid saponins have been reported to be effective in in vitro studies and might serve as scaffolds for the discovery of new treatments against this disease. Aim of the study: The present study aimed to summarize up-to-date information on the anti-Trypanosoma brucei activity of steroidal and triterpenoid saponins. The mechanisms of action of in vitro bioactive compounds were also discussed. Methods: Information on the anti-Trypanosoma brucei activity of plant saponins was obtained from published articles, dissertations, theses, and textbooks through a variety of libraries and electronic databases. Results: There has been incredible progress in the identification of steroidal and triterpenoid saponins with pronounced in vitro activity against Trypanosoma brucei. Indeed, more than forty saponins were identified as having anti-T. brucei effect with activity ranging from moderate to highly active. The mechanisms of action of most of these saponins included DNA damage, cell cycle arrest, induction of apoptosis through downregulation of bcl-2 and MDM2, and upregulation of Bax and Bak, among others. Conclusion: Referring to in vitro studies, plant saponins have shown anti-Trypanosoma brucei activity; however, more

cytotoxic and in vivo studies and detailed mechanisms of action of the bioactive saponins should be further considered.

Comparative pathogenicity of single and mixed drug-resistant Trypanosoma brucei brucei and Trypanosoma congolense infections in rats.

Obi CF, Okpala MI, Anyogu DC, Onyeabo A, Aneru GE, Ezeh IO, Ezeokonkwo RC.
07-07-2023
Res Vet Sci.
https://pubmed.ncbi.nlm.nih.gov/37467559/

Drug-resistant trypanosomes are widespread in sub-Saharan Africa and in conjunction with the drug-sensitive phenotypes cause a serious endemic wasting disease in animals. We evaluated the pathogenicity of single and mixed drug-resistant Trypanosoma brucei brucei and T. congolense isolates in 35 female rats, randomly divided into seven groups (1-7) of five rats. Group 1 was the uninfected control. Groups 2 and 3 were infected with drug-sensitive T. brucei brucei and T. congolense, respectively, whereas groups 4 and 5 were infected with multidrug-resistant T. brucei brucei and T. congolense respectively. Group 6 were infected with drug-sensitive T. brucei brucei and T. congolense while group 7 were infected with multidrug-resistant T. brucei brucei and T. congolense. Parasitaemia kinetics, haematological parameters, body weight, clinical signs, survival time, gross and histopathological changes in the spleen were evaluated. Parasitaemia occurred between day 3-9 post-infection in all the infected groups. Rats in groups 4 and 7 had markedly prolonged ($p < 0.05$) pre-patent period, days to first peak parasitaemia, survival time, and lower ($p < 0.05$) parasitaemia level than groups 2 and 6 rats while these parameters were comparable for groups 3 and 5 rats. Anaemia was noted in the infected groups but the severity did not vary amongst the infected groups. Severe clinical signs and splenic lesions were noted in rats infected with drug-sensitive trypanosome species compared to the multidrug-resistant species. Therefore, we conclude that the trypanosome isolates were pathogenic. However, the drug-sensitive T. brucei brucei and mixed drug-sensitive trypanosome infections were more pathogenic than their multidrug-resistant counterparts.

Ursolic acid-rich extract presents trypanocidal action in vitro but worsens mice under experimental acute Chagas disease.

Daga MA, Nicolau ST, Jurumenha-Barreto J, Lima LBS, Cabral IL, Pivotto AP, Stefanello A, Amorim JPA, Hoscheid J, Silva EA, Ayala TS, Menolli RA.
19-07-2023
Parasite Immunol.
https://pubmed.ncbi.nlm.nih.gov/37467029/

Chagas disease is a neglected tropical disease with only two drugs available for treatment and the plant Cecropia pachystachya has several compounds with antimicrobial and anti-inflammatory activities. This study aimed to evaluate a supercritical extract from C. pachystachya leaves in vitro and in vivo against Trypanosoma cruzi. A supercritical CO_2 extraction was used to obtain the extract (CPE). Cytotoxicity and immunostimulation ability were evaluated in macrophages, and the in vitro trypanocidal activity was evaluated against epimastigotes and trypomastigotes forms. In vivo tests were done by infecting BALB/c mice with blood trypomastigotes forms and treating animals orally with CPE for 10 days. The parasitemia, survival rate, weight, cytokines and nitric oxide dosage were evaluated. CPE demonstrated an effect on the epi and trypomastigotes forms of the parasite (IC_{50} 17.90 ± 1.2 µg/mL; LC_{50} 26.73 ± 1.2 µg/mL) and no changes in macrophages viability, resulting in a selectivity index similar to the reference drug. CPE-treated animals had a worsening compared to non-treated, demonstrated by higher parasitemia and lower survival rate. This result was attributed to the anti-inflammatory effect of CPE, demonstrated by the higher IL-10 and IL-4 values observed in the treated mice compared to the control ones. CPE demonstrated a trypanocidal effect in vitro and a worsening in the in vivo infection due to its anti-inflammatory activity.

Trypanosoma brucei Invariant Surface gp65 Inhibits the Alternative Pathway of Complement by Accelerating C3b Degradation.

Lorentzen J, Olesen HG, Hansen AG, Thiel S, Birkelund S, Andersen CBF, Andersen GR.
17-07-2023
J Immunol.
https://pubmed.ncbi.nlm.nih.gov/37466368/

Ferrocene-based nitroheterocyclic sulfonylhydrazones: design, synthesis, characterization and trypanocidal properties.

Gallardo M, Arancibia R, Jiménez C, Wilkinson S, Toro PM, Roussel P, Henry N.
18-07-2023
J Biol Inorg Chem.
https://pubmed.ncbi.nlm.nih.gov/37462740/

A series of new ferrocenyl nitroheterocyclic sulfonylhydrazones (1a-4a and 1b-2b) were prepared by the reaction between formyl (R = H) or acetyl (R = CH_3) nitroheterocyclic precursors [4/5-NO_2(C_5H_2XCOR), where X = O, S)] and ferrocenyl tosyl hydrazine [(η^5-C_5H_5)Fe(η^5-$C_5H_4SO_2$-NH-NH_2)]. All compounds were characterized by conventional spectroscopic techniques. In the solid state, the molecular structures of compounds 1a, 2b, and 3a were determined by single-crystal X-ray diffraction. The compounds showed an E-configuration around the C=N moiety. Evaluation of trypanocidal activity, measured in vitro against the Trypanosoma cruzi and Trypanosoma brucei strains, indicated that all organometallic tosyl hydrazones displayed activity against both parasite species with a higher level of potency toward T. brucei than T. cruzi. Moreover, the biological evaluation showed that the 5-nitroheterocyclic derivatives were more efficient

trypanocidal agents than their 4-nitroheterocyclic counterparts.

Distinct structural motifs are necessary for targeting and import of Tim17 in Trypanosoma brucei mitochondrion.

Darden C, Donkor J, Korolkova O, Khan Barozai MY, Chaudhuri M.
07-07-2023
bioRxiv.
https://pubmed.ncbi.nlm.nih.gov/37461662/

Seroprevalence of Chagas Disease among People of Latin American Descent Living in Suffolk County, Long Island, New York.

Saldivar MA, Michelen YE, Milla L, Kalogeropoulos AP, Sin E, Hellman HL, Gilman RH, Marcos LA.
17-07-2023
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/37460089/

This cross-sectional study estimated a one-time point seroprevalence rate of Chagas disease among people of Latin American descent in Suffolk County, Long Island, New York. Subjects who met the inclusion criteria were screened using the Chagas Detect Plus Rapid Test (InBios, Seattle, WA) with confirmation via Trypanosoma cruzi enzyme immunoassay and T. cruzi immunoblot assay. Administration of a questionnaire regarding demographics and risk factors followed. A seroprevalence rate of 10.74% was found. Identified risk factors included prior residence in a palm leaf house (odds ratio [OR], 10.42; P = 0.003; 95% CI, 2.18-49.76), residence in a house with triatomines (OR, 9.03; P = 0.006; 95% CI, 1.90-42.88), and history of triatomine bite (OR, 9.52; P = 0.009; 95% CI, 1.75-51.77). Our findings emphasize the importance of this frequently underdiagnosed disease and help highlight the importance of early screening among high-risk populations.

Characterization of two novel proteins involved in mitochondrial DNA anchoring in Trypanosoma brucei.

Amodeo S, Bregy I, Hoffmann A, Fradera-Sola A, Kern M, Baudouin H, Zuber B, Butter F, Ochsenreiter T.
17-07-2023
PLoS Pathog.
https://pubmed.ncbi.nlm.nih.gov/37459364/

Trypanosoma brucei is a single celled eukaryotic parasite in the group of the Kinetoplastea. The parasite harbors a single mitochondrion with a singular mitochondrial genome that is known as the kinetoplast DNA (kDNA). The kDNA consists of a unique network of thousands of interlocked circular DNA molecules. To ensure proper inheritance of the kDNA to the daughter cells, the genome is physically linked to the basal body, the master organizer of the cell cycle in trypanosomes. The connection that spans, cytoplasm, mitochondrial membranes and the mitochondrial matrix is mediated by the Tripartite Attachment Complex (TAC). Using a combination of proteomics and RNAi we test the current model of hierarchical TAC assembly and identify TbmtHMG44 and TbKAP68 as novel candidates of a complex that connects the TAC to the kDNA. Depletion of TbmtHMG44 or TbKAP68 each leads to a strong kDNA loss but not missegregation phenotype as previously defined for TAC components. We demonstrate that the proteins rely on both the TAC and the kDNA for stable localization to the interface between these two structures. In vitro experiments suggest a direct interaction between TbmtHMG44 and TbKAP68 and that recombinant TbKAP68 is a DNA binding protein. We thus propose that TbmtHMG44 and TbKAP68 are part of a distinct complex connecting the kDNA to the TAC.

Competition among variants is predictable and contributes to the antigenic variation dynamics of African trypanosomes.

Escrivani DO, Scheidt V, Tinti M, Faria J, Horn D.
17-07-2023
PLoS Pathog.
https://pubmed.ncbi.nlm.nih.gov/37459347/

Crossing experiments detect partial reproductive isolation among populations of Triatoma longipennis (Hemiptera: Reduviidae: Triatominae).

Martínez-Ibarra JA, Nogueda-Torres B, Meraz-Medina T, Goicochea Del Rosal G.
17-07-2023
J Med Entomol.
https://pubmed.ncbi.nlm.nih.gov/37459050/

Structure-based design, optimization of lead, synthesis, and biological evaluation of compounds active against Trypanosoma cruzi.

de Almeida GC, de Oliveira GB, da Silva Monte Z, Costa ÉCS, da Silva Falcão EP, Scotti L, Scotti MT, Oliveira Silva R, Pereira VRA, da Silva ED, Junior PAS, de Andrade Cavalcante MK, de Melo SJ.
16-07-2023
Chem Biol Drug Des.
https://pubmed.ncbi.nlm.nih.gov/37455325/

Chagas' disease affects approximately eight million people throughout the world, especially the poorest individuals. The protozoan that causes this disease-Trypanosoma cruzi-has the enzyme cruzipain, which is the main therapeutic target. As no available medications have satisfactory effectiveness and safety, it is of fundamental importance to design and synthesize novel analogues that are more active and selective. In the present study, molecular docking and the in silico prediction of ADMET properties were used as strategies to optimize the trypanocidal activity of the pyrimidine compound ZN3F based on interactions with the target site in cruzipain. From the computational results, eight 4-amino-5-carbonitrile-pyrimidine analogues were proposed, synthesized (5a-f and 7g-h) and, tested in vitro on the trypomastigote form of the Tulahuen strain of T. cruzi. The

in silico study showed that the designed analogues bond favorably to important amino acid residues of the active site in cruzipain. An in vitro evaluation of cytotoxicity was performed on L929 mammal cell lines. All derivatives inhibited the Tulahuen strain of T. cruzi and also exhibited lower toxicity to L929 cells. The 5e product, in particular, proved to be a potent, selective (IC_{50} = 2.79 ± 0.00 µM, selectivity index = 31.3) inhibitor of T. cruzi. The present results indicated the effectiveness of drugs based on the structure of the receptor, revealing the potential trypanocidal of pyrimidines. This study also provides information on molecular aspects for the inhibition of cruzipain.

Emerging Infectious Diseases of the Skin: A Review of Clinical and Histologic Findings.

McMahon DE, Schuetz AN, Kovarik CL.
14-07-2023
Hum Pathol.
https://pubmed.ncbi.nlm.nih.gov/37454994/

Inclusion complex of O-allyl-lawsone with 2-hydroxypropyl-β-cyclodextrin: Preparation, physical characterization, antiparasitic and antifungal activity.

Nicoletti CD, Dos Santos Galvão RM, de Sá Haddad Queiroz M, Barboclher L, Faria AFM, Teixeira GP, Souza ALA, de Carvalho da Silva F, Ferreira VF, da Silva Lima CH, Borba-Santos LP, Rozental S, Futuro DO, Faria RX.
14-07-2023
J Bioenerg Biomembr.
https://pubmed.ncbi.nlm.nih.gov/37442875/

The subclass naphthoquinone represents a substance group containing several compounds with important activities against various pathogenic microorganisms. Accordingly, we evaluated O-allyl-lawsone (OAL) antiparasitic and antifungal activity free and encapsulated in 2-hydroxypropyl-β-cyclodextrin (OAL MKN) against Trypanosoma cruzi and Sporothrix spp. OAL and OAL MKN were synthesized and characterized by physicochemical methods. The IC_{50} values of OAL against T. cruzi were 2.4 µM and 96.8 µM, considering epimastigotes and trypomastigotes, respectively. At the same time, OAL MKN exhibited a lower IC_{50} value (0.5 µM) for both trypanosome forms and low toxicity for mammalian cells. Additionally, the encapsulation showed a selectivity index approximately 240 times higher than that of benznidazole. Regarding antifungal activity, OAL and OAL MKN inhibited Sporothrix brasiliensis growth at 16 µM, while Sporothrix schenckii was inhibited at 32 µM. OAL MKN also exhibited higher selectivity toward fungus than mammalian cells. In conclusion, we described the encapsulation of O-allyl-lawsone in 2-hydroxypropyl-β-cyclodextrin, increasing the antiparasitic activity compared with the free form and reducing the cytotoxicity and increasing the selectivity towardSporothrix yeasts and the T. cruzi trypomastigote form. This study highlights the potential development of this inclusion complex as an antiparasitic and antifungal agent to treat neglected diseases.

Design and synthesis of new 1,2,3-triazoles derived from eugenol and analogues with in vitro and in vivo activity against Trypanosoma cruzi.

Reis RCFM, Dos Santos EG, Benedetti MD, Reis ACC, Brandão GC, Silva GND, Diniz LA, Ferreira RS, Caldas IS, Braga SFP, Souza TB.
05-10-2023
Eur J Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37441850/

Chagas disease (CD) is a neglected tropical disease endemic in 21 countries and affects about 8 million people around the world. The pharmacotherapy for this disease is limited to two drugs (Benznidazole and Nifurtimox) and both are associated with important limitations, as low cure rate in the chronic phase of the disease, high toxicity and increasing resistance by Trypanosoma cruzi. Recently, we reported a bioactive 1,2,3-triazole (compound 35) active in vitro (IC_{50} 42.8 µM) and in vivo (100 mg/kg) against T. cruzi Y strains and preliminary in silico studies suggested the cysteine protease cruzain as a possible target. Considering these initial findings, we describe here the design and synthesis of new 1,2,3-triazoles derivatives of our hit compound (35). The triazoles were initially evaluated against healthy cells derived from neonatal rat cardiomyoblasts (H9c2 cells) to determine their cytotoxicity and against epimastigotes forms of T. cruzi Y strain. The most active triazoles were compounds 26 (IC_{50} 19.7 µM) and 27 (IC_{50} 7.3 µM), while benznidazole was active at 21.6 µM. Derivative 27 showed an interesting selectivity index considering healthy H9c2 cells (>77). Promising activities against trypomastigotes forms of the parasite were also observed for triazoles 26 (IC_{50} 20.74 µM) and 27 (IC_{50} 8.41 µM), mainly 27 which showed activity once again higher than that observed for benznidazole (IC_{50} 12.72 µM). While docking results suggested cruzain as a potential target for these compounds, no significant enzyme inhibition was observed in vitro, indicating that their trypanocidal activity is related to another mode of action. Considering the promising in vitro results of triazoles 26 and 27, the in vivo toxicity was initially verified based on the evaluation of behavioral and physiological parameters, mortality, effect in body weight gain, and through the measurement of AST/ALT enzymes, which are markers of liver toxicity. All these evaluations pointed to a good tolerability of the animals, especially considering triazole 27. A reduction in parasitemia was observed among animals treated with triazole 27, but not among those treated with derivative 26. Regarding the dosage, derivative 27 (100 mg/kg) was the most active sample against T. cruzi infection, showing a 99.4% reduction in parasitemia peak. Triazole 27 at a dosage of 100 mg/kg influenced the humoral immune response and reduced myocarditis in the animals, bringing antibody levels closer to those observed among healthy mice. Altogether, our results indicate compound 27 as a new lead for the development of drug candidates to treat Chagas disease.

Navigating the boundaries between metabolism and epigenetics in trypanosomes.

Menezes AP, Murillo AM, de Castro CG, Bellini NK, Tosi LRO, Thiemann OH, Elias MC, Silber AM, da Cunha JPC.
Août-2023
Trends Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37349193/

Diversity of trypanosome species in small ruminants, dogs and pigs from three sleeping sickness foci of the south of Chad.

Vourchakbe J, Tiofack Zebaze AA, Kante Tagueu S, Demba Kodindo I, Barka Padja A, Simo G.
Oct-2023
Parasitol Int.
https://pubmed.ncbi.nlm.nih.gov/37330040/

Ulcère de Buruli

Buruli ulcer - A neglected tropical disease in the Barwon region of Victoria, Australia: An emerging public health threat with local and national ramifications.

Bartley B, O'Brien D.
Août-2023
Emerg Med Australas.
https://pubmed.ncbi.nlm.nih.gov/37474501

The release of DNA to the extracellular milieu is a biological process referred to as etosis, which is involved in both physiological and pathological functions. Although the release of DNA extracellular traps (ETs) was initially attributed to innate immune cells such as neutrophils, eosinophils, and macrophages, recent studies have shown that T cells, as well as non-immune cells, are capable of releasing ETs. These structures were described primarily for their potential to trap and kill pathogens, presenting an important strategy of host defense. Intriguingly, these functions have been associated with intracellular pathogens such as the parasites Leishmania sp. and Trypanosoma cruzi, causative agents of leishmaniasis and Chagas disease, respectively. These are two devastating tropical diseases that lead to thousands of deaths every year. In an apparent contradiction, ETs can also induce and amplify inflammation, which may lead to worsening disease pathology. This has prompted the concept of targeting ETs' release as a means of controlling tissue destruction to treat human diseases. What is the best approach to prevent disease severity: inducing ETs to kill pathogens or preventing their release? In this Perspective article, we will discuss the importance of understanding ETs released by different cell types and the need to balance their potentially complementary functions. In addition, we will explore other functions of ETs and their translational applications to benefit individuals infected with intracellular parasites and other pathogens. Ultimately, a better understanding of the role of ETs in disease pathogenesis will provide valuable insights into developing novel therapies for human diseases.

Buruli ulcer: application of thermography for remote diagnosis of a neglected tropical disease.

Yotsu RR, Vagamon B, Almamy D, Aka N, Yeboue LKG, Yao A, Blanton RE.
17-07-2023
Br J Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37071786/