



Veille scientifique

Maladies tropicales négligées

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Dengue, chikungunya et maladie à virus Zika

Identification and validation of ferroptosis-related genes in patients infected with dengue virus: implication in the pathogenesis of DENV.

Li J, Yan X, Li B, Huang L, Wang X, He B, Xie H, Wu Q, Chen L.

27-03-2023

Virus Genes.

<https://pubmed.ncbi.nlm.nih.gov/36973608/>

Ferroptosis, an iron-dependent form of regulated cell death, has been associated with many virus infections. However, the role of ferroptosis in dengue virus (DENV) infection remains to be clarified. In our study, a dengue fever microarray dataset (GSE51808) of whole blood samples was downloaded from the Gene Expression Omnibus (GEO), and a list of ferroptosis related genes (FRGs) was extracted from the FerrDb. We identified 37 ferroptosis-related differentially expressed genes (FR-DEGs) in DENV-infected patient blood samples compared to healthy individuals. Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses as well as protein-protein interaction (PPI) network of FR-DEGs revealed that these 37 FR-DEGs were mainly related to the C-type lectin receptor and p53 signaling pathway. Nine out of the 37 FR-DEGs (HSPA5, CAV1, HRAS, PTGS2, JUN, IL6, ATF3, XBP1, and CDKN2A) were hub genes, of which 5 were validated by qRT-PCR in DENV-infected HepG2 cells. Finally, using miRNA-mRNA regulatory network, we identified has-miR-124-3p and has-miR-16-5p as the most critical miRNAs in regulating the expression of these hub genes. In conclusion, our findings demonstrated that 5 FR-DEGs, JUN, IL6, ATF3, XBP1, and CDKN2A, and two miRNAs, has-miR-124-3p and has-miR-16-5p may implicate an essential role of ferroptosis in DENV infection, and further studies are warranted to explore the underlying mechanisms.

Dengue and chikungunya cases surge as climate change spreads arboviral diseases to new regions.

Taylor L.

27-03-2023

BMJ.

<https://pubmed.ncbi.nlm.nih.gov/36972905/>

Epidemiological Investigation of the 2019 Dengue Outbreak in Dhaka, Bangladesh.

Yesmin S, Sarmin S, Ahammad AM, Rafi MA, Hasan MJ.

16-03-2023

J Trop Med.

<https://pubmed.ncbi.nlm.nih.gov/36968192/>

Fabrication of Rapid Electrical Pulse-Based Biosensor Consisting of Truncated

DNA Aptamer for Zika Virus Envelope Protein Detection in Clinical Samples.

Jang M, Lee M, Sohn H, Park C, Lee T.

15-03-2023

Materials (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36984234/>

Zika virus (ZV) infection causes fatal hemorrhagic fever. Most patients are unaware of their symptoms; therefore, a rapid diagnostic tool is required to detect ZV infection. To solve this problem, we developed a rapid electrical biosensor composed of a truncated DNA aptamer immobilized on an interdigitated gold micro-gap electrode and alternating current electrothermal flow (ACEF) technique. The truncated ZV aptamer (T-ZV apt) was prepared to reduce the manufacturing cost for biosensor fabrication, and it showed binding affinity similar to that of the original ZV aptamer. This pulse-voltammetry-based biosensor was composed of a T-ZV apt immobilized on an interdigitated micro-gap electrode. Atomic force microscopy was used to confirm the biosensor fabrication. In addition, the optimal biosensor performance conditions were investigated using pulse voltammetry. ACEF promoted aptamer-target binding, and the target virus envelope protein was detected in the diluted serum within 10 min. The biosensor waveform increased linearly as the concentration of the Zika envelope in the serum increased, and the detection limit was 90.1 pM. Our results suggest that the fabricated biosensor is a significant milestone for rapid virus detection.

RVG Peptide-Functionalized Favipiravir Nanoparticle Delivery System Facilitates Antiviral Therapy of Neurotropic Virus Infection in a Mouse Model.

Ren M, Zhou Y, Tu T, Jiang D, Pang M, Li Y, Luo Y, Yao X, Yang Z, Wang Y.

19-03-2023

Int J Mol Sci.

<https://pubmed.ncbi.nlm.nih.gov/36982925/>

Neurotropic viruses severely damage the central nervous system (CNS) and human health. Common neurotropic viruses include rabies virus (RABV), Zika virus, and poliovirus. When treating neurotropic virus infection, obstruction of the blood-brain barrier (BBB) reduces the efficiency of drug delivery to the CNS. An efficient intracerebral delivery system can significantly increase intracerebral delivery efficiency and facilitate antiviral therapy. In this study, a rabies virus glycopeptide (RVG) functionalized mesoporous silica nanoparticle (MSN) packaging favipiravir (T-705) was developed to generate T-705@MSN-RVG. It was further evaluated for drug delivery and antiviral treatment in a VSV-infected mouse model. The RVG, a polypeptide consisting of 29 amino acids, was conjugated on the nanoparticle to enhance CNS delivery. The T-705@MSN-RVG caused a significant decrease in virus titers and virus proliferation without inducing substantial cell damage in vitro. By releasing T-705, the nanoparticle promoted viral inhibition in the brain during infection. At 21 days post-infection (dpi), a significantly enhanced survival ratio (77%) was observed in the group inoculated with nanoparticle compared with the non-

treated group (23%). The viral RNA levels were also decreased in the therapy group at 4 and 6 dpi compared with that of the control group. The T-705@MSN-RVG could be considered a promising system for CNS delivery for treating neurotropic virus infection.

Inter- and Intramolecular RNA-RNA Interactions Modulate the Regulation of Translation Mediated by the 3' UTR in West Nile Virus.

Romero-López C, Roda-Herreros M, Berzal-Herranz B, Ramos-Lorente SE, Berzal-Herranz A.

10-03-2023

Int J Mol Sci.

<https://pubmed.ncbi.nlm.nih.gov/36982407/>

Correlation of Dengue and Meteorological Factors in Bangladesh: A Public Health Concern.

Islam MA, Hasan MN, Tiwari A, Raju MAW, Jannat F, Sangkham S, Shammas MI, Sharma P, Bhattacharya P, Kumar M.

15-03-2023

Int J Environ Res Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36982061/>

Dengue virus (DENV) is an enveloped, single-stranded RNA virus, a member of the *Flaviviridae* family (which causes Dengue fever), and an arthropod-transmitted human viral infection. Bangladesh is well known for having some of Asia's most vulnerable Dengue outbreaks, with climate change, its location, and its dense population serving as the main contributors. For speculation about DENV outbreak characteristics, it is crucial to determine how meteorological factors correlate with the number of cases. This study used five time series models to observe the trend and forecast Dengue cases. Current data-based research has also applied four statistical models to test the relationship between Dengue-positive cases and meteorological parameters. Datasets were used from NASA for meteorological parameters, and daily DENV cases were obtained from the Directorate General of Health Service (DGHS) open-access websites. During the study period, the mean of DENV cases was 882.26 ± 3993.18 , ranging between a minimum of 0 to a maximum of 52,636 daily confirmed cases. The Spearman's rank correlation coefficient between climatic variables and Dengue incidence indicated that no substantial relationship exists between daily Dengue cases and wind speed, temperature, and surface pressure (Spearman's rho; $r = -0.007, p > 0.05$; $r = 0.085, p > 0.05$; and $r = -0.086, p > 0.05$, respectively). Still, a significant relationship exists between daily Dengue cases and dew point, relative humidity, and rainfall ($r = 0.158, p < 0.05$; $r = 0.175, p < 0.05$; and $r = 0.138, p < 0.05$, respectively). Using the ARIMAX and GA models, the relationship for Dengue cases with wind speed is -666.50 [95% CI: -1711.86 to 378.86] and -953.05 [-2403.46 to 497.36], respectively. A similar negative relation between Dengue cases and wind speed was also determined in the GLM model (IRR = 0.98). Dew point and surface pressure also represented a negative correlation in both ARIMAX and GA models, respectively,

but the GLM model showed a positive association. Additionally, temperature and relative humidity showed a positive correlation with Dengue cases (105.71 and 57.39, respectively, in the ARIMAX, 633.86, and 200.03 in the GA model). In contrast, both temperature and relative humidity showed negative relation with Dengue cases in the GLM model. In the Poisson regression model, windspeed has a substantial significant negative connection with Dengue cases in all seasons. Temperature and rainfall are significantly and positively associated with Dengue cases in all seasons. The association between meteorological factors and recent outbreak data is the first study where we are aware of the use of maximum time series models in Bangladesh. Taking comprehensive measures against DENV outbreaks in the future can be possible through these findings, which can help fellow researchers and policymakers.

Performance of VIDAS® Diagnostic Tests for the Automated Detection of Dengue Virus NS1 Antigen and of Anti-Dengue Virus IgM and IgG Antibodies: A Multicentre, International Study.

Versiani AF, Kaboré A, Brossault L, Dromenq L, Dos Santos TMIL, Milhim BHGA, Estofotele CF, Cissé A, Sorgho PA, Senot F, Tessonneau M, Diabougba S, Nogueira ML.

16-03-2023

Diagnostics (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36980445/>

DDPM: A Dengue Disease Prediction and Diagnosis Model Using Sentiment Analysis and Machine Learning Algorithms.

Gupta G, Khan S, Guleria V, Almjaljly A, Alabdullah BI, Siddiqui T, Albahlal BM, Alajlan SA, Al-Subaie M.

14-03-2023

Diagnostics (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36980401/>

Use of Graphene and Its Derivatives for the Detection of Dengue Virus.

Dutta R, Rajendran K, Jana SK, Saleena LM, Ghorai S.

06-03-2023

Biosensors (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36979561/>

Every year, the dengue virus and its principal mosquito vector, *Aedes* sp., have caused massive outbreaks, primarily in equatorial countries. The pre-existing techniques available for dengue detection are expensive and require trained personnel. Graphene and its derivatives have remarkable properties of electrical and thermal conductivity, and are flexible, light, and biocompatible, making them ideal platforms for biosensor development. The incorporation of these materials, along with appropriate nanomaterials, improves the quality of detection methods. Graphene can help overcome the difficulties associated with conventional techniques. In this review, we have given comprehensive details on current graphene-based diagnostics for dengue virus

detection. We have also discussed state-of-the-art biosensing technologies and evaluated the advantages and disadvantages of the same.

Nanobodies Selectively Binding to the Idiotypic of a Dengue Virus Neutralizing Antibody Do Not Necessarily Mimic the Viral Epitope.

Poggianella M, Bernedo R, Oloketuyi S, de Marco A.
17-03-2023

Biomolecules.

<https://pubmed.ncbi.nlm.nih.gov/36979486/>

Vaccination against dengue virus is challenged by the fact that a generic immune response can induce antibody-dependent-enhancement (ADE) in secondary infections. Only some antibodies targeting a quaternary epitope formed by the dimerization of the virus protein E possess sufficient neutralizing capacity. Therefore, the immunization with anti-idiotypic antibodies of neutralizing antibodies might represent a safe vaccination strategy. Starting from a large pre-immune library, we succeeded in isolating a wide set of anti-idiotypic nanobodies characterized by selective and strong binding to the paratope of the neutralizing antibody 1C10. However, the mice immunized with such constructs did not produce effective antibodies, despite at least some of them eliciting an immune response selective for the nanobody variable regions. The results suggest that complex conformational epitopes might be difficult to be recreated by anti-idiotypic structures. The selection process of the anti-idiotypic candidates might be optimized by applying epitope mapping and modeling approaches aimed at identifying the key residues that is necessary to bind to trigger selective immune response.

Compounds Inhibiting Noppera-bo, a Glutathione S-transferase Involved in Insect Ecdysteroid Biosynthesis: Novel Insect Growth Regulators.

Ebihara K, Niwa R.
02-03-2023

Biomolecules.

<https://pubmed.ncbi.nlm.nih.gov/36979396/>

Roles and mechanisms of exosomal microRNAs in viral infections.

Mao L, Chen Y, Gu J, Zhao Y, Chen Q.
28-03-2023

Arch Virol.

<https://pubmed.ncbi.nlm.nih.gov/36977948/>

Exosomes are small extracellular vesicles with a diameter of 30-150 nm that originate from endosomes and fuse with the plasma membrane. They are secreted by almost all kinds of cells and can stably transfer different kinds of cargo from donor to recipient cells, thereby altering cellular functions for assisting cell-to-cell communication. Exosomes derived from virus-infected cells during viral infections are likely to contain different microRNAs (miRNAs) that can be transferred to recipient cells. Exosomes can either promote or suppress viral infections

and therefore play a dual role in viral infection. In this review, we summarize the current knowledge about the role of exosomal miRNAs during infection by six important viruses (hepatitis C virus, enterovirus A71, Epstein-Barr virus, human immunodeficiency virus, severe acute respiratory syndrome coronavirus 2, and Zika virus), each of which causes a significant global public health problem. We describe how these exosomal miRNAs, including both donor-cell-derived and virus-encoded miRNAs, modulate the functions of the recipient cell. Lastly, we briefly discuss their potential value for the diagnosis and treatment of viral infections.

Zika, Flavivirus and Malaria Antibody Cocirculation in Nigeria.

Mac PA, Kroeger A, Daehne T, Anyaike C, Velayudhan R, Panning M.

14-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977172/>

Molecular Mechanisms of Antibiotic Resistance and Novel Treatment Strategies for *Helicobacter pylori* Infections.

Srisuphanunt M, Wilairatana P, Kooltheat N, Duangchan T, Katzenmeier G, Rose JB.

11-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977164/>

Helicobacter pylori infects approximately 50% of the world's population and is considered the major etiological agent of severe gastric diseases, such as peptic ulcers and gastric carcinoma. Increasing resistance to standard antibiotics has now led to an ever-decreasing efficacy of eradication therapies and the development of novel and improved regimens for treatment is urgently required. Substantial progress has been made over the past few years in the identification of molecular mechanisms which are conducive to resistant phenotypes as well as for efficient strategies to counteract strain resistance and to avoid the use of ineffective antibiotics. These involve molecular testing methods, improved salvage therapies, and the discovery of novel and potent antimicrobial compounds. High rates of prevalence and gastric cancer are currently observed in Asian countries, including Japan, China, Korea, and Taiwan, where concomitantly intensive research efforts were initiated to explore advanced eradication regimens aimed at reducing the risk of gastric cancer. In this review, we present an overview of the known molecular mechanisms of antibiotic resistance and discuss recent intervention strategies for *H. pylori* diseases, with a view of the research progress in Asian countries.

Serum Cortisol as a Biomarker of Severe Dengue.

Bongsebandhu-Phubhakdi C, Supornsilchai V, Aroonparkmongkol S, Limothai U, Tachaboon S, Dinhuzen J, Chaisuriyong W, Trongkamolchai S,

Wanpaisitkul M, Chulapornsiri C, Tiawilai A, Tiawilai T, Tantawichien T, Thisyakorn U, Srisawat N.
27-02-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/36977147/>

Bacillus thuringiensis Cyt Proteins as Enablers of Activity of Cry and Tpp Toxins against Aedes albopictus.

Lai L, Villanueva M, Muruzabal-Galarza A, Fernández AB, Unzue A, Toledo-Arana A, Caballero P, Caballero CJ.
10-03-2023
Toxins (Basel).
<https://pubmed.ncbi.nlm.nih.gov/36977103/>

Aedes albopictus is a species of mosquito, originally from Southeast Asia, that belongs to the Culicidae family and the Dipteran insect order. The distribution of this vector has rapidly changed over the past decade, making most of the temperate territories in the world vulnerable to important human vector-borne diseases such as dengue, yellow fever, Zika or chikungunya. *Bacillus thuringiensis* var. *israeliensis* (Bti)-based insecticides represent a realistic alternative to the most common synthetic insecticides for the control of mosquito larvae. However, several studies have revealed emerging resistances to the major Bti Crystal proteins such as Cry4Aa, Cry4Ba and Cry11Aa, making the finding of new toxins necessary to diminish the exposure to the same toxicity factors overtime. Here, we characterized the individual activity of Cyt1Aa, Cry4Aa, Cry4Ba and Cry11Aa against *A. albopictus* and found a new protein, Cyt1A-like, that increases the activity of Cry11Aa more than 20-fold. Additionally, we demonstrated that Cyt1A-like facilitates the activity three new Bti toxins: Cry53-like, Cry56A-like and Tpp36-like. All in all, these results provide alternatives to the currently available Bti products for the control of mosquito populations and position Cyt proteins as enablers of activity for otherwise non-active crystal proteins.

Frequent first-trimester pregnancy loss in rhesus macaques infected with African-lineage Zika virus.

Rosinski JR, Raasch LE, Barros Tiburcio P, Breitbart ME, Shepherd PM, Yamamoto K, Razo E, Krabbe NP, Bliss MI, Richardson AD, Einwalter MA, Weiler AM, Sneed EL, Fuchs KB, Zeng X, Noguchi KK, Morgan TK, Alberts AJ, Antony KM, Kabakov S, Ausderau KK, Bohm EK, Pritchard JC, Spanton RV, Ver Hoove JN, Kim CBY, Nork TM, Katz AW, Rasmussen CA, Hartman A, Mejia A, Basu P, Simmons HA, Eickhoff JC, Friedrich TC, Aliota MT, Mohr EL, Dudley DM, O'Connor DH, Newman CM.
28-03-2023
PLoS Pathog.
<https://pubmed.ncbi.nlm.nih.gov/36976812/>

In the 2016 Zika virus (ZIKV) pandemic, a previously unrecognized risk of birth defects surfaced in babies whose mothers were infected with Asian-lineage ZIKV during pregnancy. Less is known about the impacts of gestational African-lineage ZIKV infections. Given high human immunodeficiency virus (HIV) burdens in regions where African-lineage ZIKV circulates, we evaluated

whether pregnant rhesus macaques infected with simian immunodeficiency virus (SIV) have a higher risk of African-lineage ZIKV-associated birth defects. Remarkably, in both SIV+ and SIV- animals, ZIKV infection early in the first trimester caused a high incidence (78%) of spontaneous pregnancy loss within 20 days. These findings suggest a significant risk for early pregnancy loss associated with African-lineage ZIKV infection and provide the first consistent ZIKV-associated phenotype in macaques for testing medical countermeasures.

Genetic Diversity of Dengue Vector Aedes albopictus Collected from South Korea, Japan, and Laos.

Shin J, Rahman MM, Kim J, Marcombe S, Jung J.
20-03-2023
Insects.
<https://pubmed.ncbi.nlm.nih.gov/36975982/>

Vertical Transmission of Zika Virus by Florida Aedes aegypti and Ae. albopictus.

Zimler RA, Alto BW.
16-02-2023
Insects.
<https://pubmed.ncbi.nlm.nih.gov/36975974/>

Mosquito-Borne Diseases and Their Control Strategies: An Overview Focused on Green Synthesized Plant-Based Metallic Nanoparticles.

Onen H, Luzala MM, Kigozi S, Sikumbili RM, Muanga CK, Zola EN, Wendji SN, Buya AB, Balciunaitiene A, Viškelis J, Kaddumukasa MA, Memvanga PB.
23-02-2023
Insects.
<https://pubmed.ncbi.nlm.nih.gov/36975906/>

Mosquitoes act as vectors of pathogens that cause most life-threatening diseases, such as malaria, Dengue, Chikungunya, Yellow fever, Zika, West Nile, *Lymphatic filariasis*, etc. To reduce the transmission of these mosquito-borne diseases in humans, several chemical, biological, mechanical, and pharmaceutical methods of control are used. However, these different strategies are facing important and timely challenges that include the rapid spread of highly invasive mosquitoes worldwide, the development of resistance in several mosquito species, and the recent outbreaks of novel arthropod-borne viruses (e.g., Dengue, Rift Valley fever, tick-borne encephalitis, West Nile, yellow fever, etc.). Therefore, the development of novel and effective methods of control is urgently needed to manage mosquito vectors. Adapting the principles of nanobiotechnology to mosquito vector control is one of the current approaches. As a single-step, eco-friendly, and biodegradable method that does not require the use of toxic chemicals, the green synthesis of nanoparticles using active toxic agents from plant extracts available since ancient times exhibits antagonistic responses and broad-spectrum target-specific activities against different species of vector mosquitoes. In this article, the current state of knowledge on the different mosquito control strategies in general, and on repellent

and mosquitocidal plant-mediated synthesis of nanoparticles in particular, has been reviewed. By doing so, this review may open new doors for research on mosquito-borne diseases.

Serological Cross-Reactivity in Zoonotic Flaviviral Infections of Medical Importance.

Gomes da Silva P, Seixas Dos Reis JA, Nogueira Rodrigues M, da Silva Ardaya Q, Mesquita JR.

24-02-2023

Antibodies (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36975365/>

Dengue serotype characterization during the 2022 dengue epidemic in Kathmandu, Nepal.

Amatya B, Schwartz E, Biber A, Erster O, Lustig Y, Pradhan R, Khadka B, Pandey P.

27-03-2023

J Travel Med.

<https://pubmed.ncbi.nlm.nih.gov/36971480/>

Strong positive selection in *Aedes aegypti* and the rapid evolution of insecticide resistance.

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

27-03-2023

Mol Biol Evol.

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

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

Integrative bulk and single-cell transcriptome profiling analysis reveals

IFI27 as a novel interferon-stimulated gene in dengue.

Jiang C, He C, Kan J, Guan H, Zhou T, Yang Y.

27-03-2023

J Med Virol.

<https://pubmed.ncbi.nlm.nih.gov/36971141/>

Identification and validation of novel non-nucleoside class of molecules inhibiting the dengue virus replication.

Roy KK, Jyothi D, Paul U, Sukla S.

27-03-2023

J Biomol Struct Dyn.

<https://pubmed.ncbi.nlm.nih.gov/36970872/>

There is currently no drug available to treat mosquito-borne dengue. The C-terminal RNA-dependent RNA polymerase (RdRp) domain in the non-structural type 5 (NS5) protein of the dengue virus (DENV) is essential for viral RNA synthesis and replication, and therefore, it is an attractive target for the anti-dengue drug development. We report herein the discovery and validation of two novel non-nucleoside classes of small molecules as DENV RdRp inhibitors. Firstly, using the refined X-ray structure of the DENV NS5 RdRp domain (PDB-ID: 4VOR), we conducted docking, binding free-energy studies, and short-scale molecular dynamics simulation to investigate the binding sites of known small molecules that led to the optimized protein-ligand complex. Subsequently, protein structure-based screening of a commercial database (~500,000 synthetic compounds), pre-filtered for the drug-likeness, led to the top-ranked 171 molecules, which was then subjected to structural diversity analysis and clustering. This process led to six structurally distinct and best-scored compounds that were procured from the commercial vendor, and then subjected to the *in vitro* testing in the MTT and dengue infection assays. It revealed two unique and structurally unique compounds, KKR-D-02 and KKR-D-03, exhibiting 84 and 81% reductions, respectively, in DENV copy number in repeated assays in comparison to the virus-infected cell controls. These active compounds represent novel scaffolds for further structure-based discovery of novel candidate molecules for the intervention of dengue. Communicated by Ramaswamy H. Sarma.

Handheld virus concentration method using a hollow fiber filter module.

Higuchi S, Satou T, Uchida Y.

11-03-2032

MethodsX.

<https://pubmed.ncbi.nlm.nih.gov/36970019/>

Pakistan's healthcare preparedness after the NIH warned of a new diphtheria strain and Covid-19 variation.

Muzzamil M, Naz S, Mumtaz H, Omair W.

12-03-2023

J Taibah Univ Med Sci.

<https://pubmed.ncbi.nlm.nih.gov/36969319/>

Objective: In this paper, we examine the current crisis of regarding preparedness of healthcare industries in Pakistan, analyzing the causes, effects, and potential recommendations to this problem. **Methods:** Highlighting the efforts and issues surrounding this topic is necessary for developing and implementing research-based solutions that accurately reflect the current state of the healthcare industry. This short overview is prepared in accordance with accepted practices in published studies around the world. Our findings were based on a search of the literature databases PubMed, Google Scholar, Journals Online, and the Internet Library. **Results:** Searching for "Healthcare Preparedness in Pakistan" yielded the expected results. Particularly of interest to the researchers was the question of why, despite efforts to boost vaccination rates and emergency immunization response capacities in the event of epidemics, progress on SDG3 immunization indicators has been minimal. Immunization is critically important because vaccine-preventable diseases pose a significant risk to the general population. Pakistan's authorities and government should take deliberate action to increase immunization rates. **Conclusion:** Particularly disadvantaged countries and regions are hit the worst by climate change. Pakistan continues to be hit hard by diseases like acute watery diarrhea, dengue fever, malaria, and COVID-19 are on the rise as a result of the flooding, especially in shelters and areas where water and sanitation systems have been affected. After devastating floods in KP, Sindh, and Punjab, over 70 suspected cases of diphtheria were reported. Diphtheria epidemics illustrate the precarious position of flood victims. It would be catastrophic if the newly found diphtheria strain or the covid-19 variation reached the underserved flood victims. Immunization protects against life-threatening illnesses so its government responsibility to improve immunization rates in Pakistan.

Population genetic characteristics of *Aedes aegypti* in 2019 and 2020 under the distinct circumstances of dengue outbreak and the COVID-19 pandemic in Yunnan Province, China.

Wang G, Gao J, Ma Z, Liu Y, Wang M, Xing D, Li C, Guo X, Zhao T, Jiang Y, Dong Y, Zhang H, Zhao T.

09-03-2023

Front Genet.

<https://pubmed.ncbi.nlm.nih.gov/36968606/>

Antibody seropositivity and endemicity of chikungunya and Zika viruses in Nigeria.

Mac PA, Airiohuodion PE, Zubair S, Tadele M, Aighobahi JO, Anyaie C, Kroeger A, Panning M.

2023

Anim Dis.

<https://pubmed.ncbi.nlm.nih.gov/36968287/>

Mosquito-borne infections are of global health concern because of their rapid spread and upsurge, which creates a risk for coinfections. chikungunya virus (CHIKV), an arbovirus disease transmitted by *Aedes aegypti* or *A. albopictus*, and malaria, a parasitic disease transmitted by

Anopheles gambiae, are prevalent in Nigeria and neighbouring countries, but their burden and possible coinfections are poorly understood. In this study, we investigated the antibody seropositivity and endemicity of chikungunya and Zika viruses (ZIKV) in three regions of Nigeria. A cross-sectional sero-survey was conducted on 871 participants. Samples were collected from outpatients by simple random sampling. Analyses of the samples were performed using recomLine Tropical Fever for the presence of antibody serological marker IgG immunoblot with CHIKV VLP (virus like particle), ZIKV NS1 and ZIKV Equad according to manufacturers' instructions and malaria RDT for malaria parasite. There was a significantly higher antibody seropositivity against CHIKV in the central region than in the northern and southern regions (69.5%, 291/419), while ZIKV-seropositivity (22.4%, 34/152) and CHIKV-ZIKV co-circulating antibody seropositivity (17.8%, 27/152) were notably higher in the southern region than in the central and northern regions. This investigation revealed an unexpectedly high antibody seropositivity and concealed endemicity of CHIKV and ZIKV in three Nigerian regions. The seropositivity of detectable antibodies differed among the three geographical locations.

Correction to: Prevalence of dengue fever virus antibodies and associated risk factors among residents of El-Gadarif state, Sudan.

Eldigail MH, Adam GK, Babiker RA, Khalid F, Adam IA, Omer OH, Ahmed ME, Brair SL, Haroun EM, AbuAisha H, Karrar AE, Abdalla HS, Aradaib IE.

24-03-2023

BMC Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36964506/>

Replication in the presence of dengue convalescent serum impacts Zika virus neutralization sensitivity and fitness.

Marano JM, Weger-Lucarelli J.

Mar-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36968111/>

Introduction: Flaviviruses like dengue virus (DENV) and Zika virus (ZIKV) are mosquito-borne viruses that cause febrile, hemorrhagic, and neurological diseases in humans, resulting in 400 million infections annually. Due to their co-circulation in many parts of the world, flaviviruses must replicate in the presence of pre-existing adaptive immune responses targeted at serologically closely related pathogens, which can provide protection or enhance disease. However, the impact of pre-existing cross-reactive immunity as a driver of flavivirus evolution, and subsequently the implications on the emergence of immune escape variants, is poorly understood. Therefore, we investigated how replication in the presence of convalescent dengue serum drives ZIKV evolution.

Methods: We used an *in vitro* directed evolution system, passaging ZIKV in the presence of serum from humans previously infected with DENV (anti-DENV) or serum from DENV-naïve patients (control serum). Following five passages in the presence of serum, we performed next-

generation sequencing to identify mutations that arose during passaging. We studied two non-synonymous mutations found in the anti-DENV passaged population (E-V355I and NS1-T139A) by generating individual ZIKV mutants and assessing fitness in mammalian cells and live mosquitoes, as well as their sensitivity to antibody neutralization. **Results and discussion:** Both viruses had increased fitness in Vero cells with and without the addition of anti-DENV serum and in human lung epithelial and monocyte cells. In *Aedes aegypti* mosquitoes-using blood meals with and without anti-DENV serum-the mutant viruses had significantly reduced fitness compared to wild-type ZIKV. These results align with the trade-off hypothesis of constrained mosquito-borne virus evolution. Notably, only the NS1-T139A mutation escaped neutralization, while E-V355I demonstrated enhanced neutralization sensitivity to neutralization by anti-DENV serum, indicating that neutralization escape is not necessary for viruses passaged under cross-reactive immune pressures. Future studies are needed to assess cross-reactive immune selection in humans and relevant animal models or with different flaviviruses.

Identification of suitable house-keeping genes during chikungunya virus infection.

Agrawal N, Khanna M, Dhawan G.

Mar-Apr 2023

Indian J Med Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36967216/>

Purpose: Quantitative PCR (qPCR) is a reliable and robust technique for gene expression analysis, but its efficacy is dependent on the normalization of qPCR data with the stably expressed reference gene. Selection of a suitable reference gene is mandatory for accurate gene expression analysis, till data the most appropriate reference gene during chikungunya virus infection has not been elucidated. **Method:** In this study the expression of reference genes (GAPDH, GUSB, HPRT, Beta-actin, 18S rRNA) was analysed during chikungunya virus infection by quantitative PCR. The stability of the house-keeping genes was evaluated with three bioinformatics softwares: BestKeeper, NormFinder and GeNorm. **Result:** The significant variation in the expression of house-keeping genes (GusB, Beta-actin, HPRT) was observed during chikungunya virus infection; whereas GAPDH and 18S rRNA was most stable. The stability of reference genes analysed by the bioinformatics software further corroborate the results of qPCR. **Conclusion:** This is first study that identifies and validates the most suitable reference gene for normalization of qPCR data during chikungunya based gene expression analysis. This could serve as a reference study for the researchers working on different aspects of chikungunya virus infections.

The 8-bromobaicalein inhibited the replication of dengue, and Zika viruses and targeted the dengue polymerase.

Boonyasuppayakorn S, Saelee T, Huynh TNT, Hairani R, Hengphasatporn K, Loeanurit N, Cao V, Vibulakhaophan V, Siripitakpong P, Kaur P, Chu JJH, Tunghirun C,

Choksupmanee O, Chimnaronk S, Shigeta Y, Rungrotmongkol T, Chavasiri W.

25-03-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/36966240/>

Development of NS2B-NS3 protease inhibitor that impairs Zika virus replication.

Lin WW, Huang YJ, Wang YT, Lin YS, Mazibuko N, Chen CS, Cheng TL, Chang CS, Leu YL, Chen CY, Chuang CH.

23-03-2023

Virus Res.

<https://pubmed.ncbi.nlm.nih.gov/36965673/>

Infectivity of three Mayaro Virus geographic isolates in human cell lines.

Patel AR, Dulcey M, Abid N, Cash MN, Dailey J, Salemi M, Mavian C, Vittor AY.

23-03-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36965613/>

Biosynthesis of zinc oxide nanoparticles using *Indigofera tinctoria* and their efficacy against dengue vector, *Aedes aegypti* (Diptera: Culicidae).

Chithiga A, Manimegalai K.

28-03-2032

Exp Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36997017/>

Dengue fever is a viral mosquito borne disease transmitted by day biting mosquito, *Aedes aegypti*. No medicine has been proven to be effective for the complete cure of dengue and mosquito control remains to be the only effective option. Increased cases of dengue contraction are being enormously reported worldwide every year. Thus, the urge for an effective measure remains a factor of major concern. In the present study, biosynthesized spherical-like structured zinc oxide (ZnO) nanoparticles using *Indigofera tinctoria* leaf extracts are employed as a mosquito controlling agent. The biosynthesized nanoparticles are characterized by UV-Vis, FTIR, FESEM, EDAX, XRD, Zeta Potential, and DLS analysis. The efficacy of the green synthesized ZnO nanoparticles were tested against different larval and pupal stages of *A. aegypti*. Further, it is established that a significant LC₅₀ values of 4.030 ppm in first instar and 7.213 ppm in pupae of *A. aegypti* is due to the impact of synthesized ZnO. Histological studies confirmed that effective and destructive changes were observed in larval body tissues particularly in the fat cells and the midgut. Therefore, this study highlights the application of biosynthesized ZnO nanoparticles as a potential candidate for safe and eco-friendly agent against the dengue vector, *A. aegypti*.

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

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

17-03-2032

Virology.

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

Early diagnosis of dengue: Diagnostic utility of the SD BIOLINE Deng-ue Duo rapid test in Reunion Island.

Maillard O, Belot J, Adenis T, Rollot O, Adenis A, Guihard B, Gérardin P, Bertolotti A.

30-03-2032

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36996260/>

Background: In Reunion Island, dengue outbreaks have been occurring since 2018. The healthcare facilities are facing the problem of managing a massive influx of patients and a growing care burden. The aim of this study was to evaluate the performance of the SD Bioline Dengue Duo rapid diagnostic test in adults consulting at an emergency department during the 2019 epidemic.

Methodology/principal findings: This retrospective study of diagnostic accuracy included patients over 18 years old, suspected of dengue, who were admitted to emergency units of the University Hospital of Reunion between the 1st of January and 30th of June, 2019, and were tested for dengue fever with the SD Bioline Dengue Duo rapid diagnostic test and reverse transcriptase polymerase chain reaction. Over the study period, 2099 patients were screened retrospectively. Of them, 671 patients matched the inclusion criteria. The overall rapid diagnostic test performance was 42% for sensitivity and 15% for specificity. The non-structural 1 antigen component had a good specificity of 82% but a low sensitivity of 12%. The immunoglobulin M component had a sensitivity of 28% and a specificity of 33%. Sensitivities were slightly improved beyond the 5th day of illness compared to the early stage for all components, but only the non-structural 1 antigen component had a better specificity of 91%. Furthermore, predictive values were low and post-test probabilities never improved pre-test probabilities in our setting. **Conclusions/significance:** These results suggest that the SD Bioline Dengue Duo RDT did not achieve sufficient performance levels to rule in, or discard, an early point of care dengue diagnosis in the emergency department during the 2019 epidemic in Reunion.

The anti-immune dengue subgenomic flaviviral RNA is present in vesicles in mosquito saliva and is associated with increased infectivity.

Yeh SC, Strilets T, Tan WL, Castillo D, Medkour H, Rey-Cadilhac F, Serrato-Pomar IM, Rachenne F, Chowdhury A, Chuo V, Azar SR, Singh MK, Hamel R, Missé D, Kini RM, Kenney LJ, Vasilakis N, Marti-Renom MA, Nir G, Pompon J, Garcia-Blanco MA.

30-03-2032

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36996041/>

Understanding antibody-dependent enhancement in dengue: Are afucosylated IgG1s a concern?

Teo A, Tan HD, Loy T, Chia PY, Chua CLL.

30-03-2032

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36996026/>

A Unique Case of Unilateral Oculomotor Nerve Palsy Secondary to Dengue Fever.

Loh SA, Wan Abdul Rahman WMH, Sonny Teo KS, Abu N. 21-02-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36994298/>

A wide range of ocular complications may arise from the mosquito-borne illness, dengue fever. We report a case of isolated unilateral oculomotor nerve palsy due to complications of dengue fever. A 50-year-old male with serologically confirmed dengue fever presented with a sudden onset of double vision with left eyelid drooping and left eye outward deviation on his day 8 of illness. Ocular examination revealed binocular diplopia with complete left eye ptosis and restriction of all left eye movements except for abduction. His left eye pupil was 8 mm dilated with a negative relative afferent pupillary defect (RAPD). A clinical diagnosis of left eye oculomotor nerve palsy with pupil involvement was established. Urgent contrasted brain imaging tests were performed and revealed to be normal. He was managed conservatively and had complete resolution of symptoms with good vision recovery within 3.5 months. Cranial mononeuropathy may be one of the various complications following dengue fever, as demonstrated in this case report. As it is an uncommon presentation, there is a need to exclude other acute causes of cranial nerve palsy. Visual prognosis is still favorable with judicious monitoring and without any treatment of steroids or immunoglobulin.

Gain without pain: Adaptation and increased virulence of Zika virus in vertebrate host without fitness cost in mosquito vector.

Jaeger AS, Marano J, Riemersma K, Castañeda D, Pritchard E, Pritchard J, Bohm EK, Baczenas JJ, O'Connor SL, Weger-Lucarelli J, Friedrich TC, Aliota MT.

20-03-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993525/>

Zika virus (ZIKV) is now in a post-pandemic period, for which the potential for re-emergence and future spread is unknown. Adding to this uncertainty is the unique capacity of ZIKV to directly transmit between humans via sexual transmission. Recently, we demonstrated that direct transmission of ZIKV between vertebrate hosts leads to rapid adaptation resulting in enhanced virulence in mice and the emergence of three amino acid substitutions (NS2A-A117V, NS2A-A117T, and NS4A-E19G) shared among all vertebrate-passaged lineages. Here, we further characterized these host-adapted viruses and found that vertebrate-passaged viruses also have enhanced

transmission potential in mosquitoes. To understand the contribution of genetic changes to the enhanced virulence and transmission phenotype, we engineered these amino acid substitutions, singly and in combination, into a ZIKV infectious clone. We found that NS4A-E19G contributed to the enhanced virulence and mortality phenotype in mice. Further analyses revealed that NS4A-E19G results in increased neurotropism and distinct innate immune signaling patterns in the brain. None of the substitutions contributed to changes in transmission potential in mosquitoes. Together, these findings suggest that direct transmission chains could enable the emergence of more virulent ZIKV strains without compromising mosquito transmission capacity, although the underlying genetics of these adaptations are complex.

Editorial: Novel strategies for controlling mosquito-borne diseases.

Deng SQ, Cai Y, Wang DQ.

13-03-2023

Front Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36992881/>

Role of the Microbiome in *Aedes* spp. Vector Competence: What Do We Know?

Ferreira QR, Lemos FFB, Moura MN, Nascimento JOS, Novaes AF, Barcelos IS, Fernandes LA, Amaral LSB, Barreto FK, Melo FF.

17-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992487/>

Aedes aegypti and *Aedes albopictus* are the vectors of important arboviruses: dengue fever, chikungunya, Zika, and yellow fever. Female mosquitoes acquire arboviruses by feeding on the infected host blood, thus being able to transmit it to their offspring. The intrinsic ability of a vector to infect itself and transmit a pathogen is known as vector competence. Several factors influence the susceptibility of these females to be infected by these arboviruses, such as the activation of the innate immune system through the Toll, immunodeficiency (Imd), JAK-STAT pathways, and the interference of specific antiviral response pathways of RNAi. It is also believed that the presence of non-pathogenic microorganisms in the microbiota of these arthropods could influence this immune response, as it provides a baseline activation of the innate immune system, which may generate resistance against arboviruses. In addition, this microbiome has direct action against arboviruses, mainly due to the ability of *Wolbachia* spp. to block viral genome replication, added to the competition for resources within the mosquito organism. Despite major advances in the area, studies are still needed to evaluate the microbiota profiles of *Aedes* spp. and their vector competence, as well as further exploration of the individual roles of microbiome components in activating the innate immune system.

Host Cell Targets for Unconventional Antivirals against RNA Viruses.

Roa-Linares VC, Escudero-Flórez M, Vicente-Manzanares M, Gallego-Gómez JC.

17-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992484/>

Vector Competence for Zika Virus Changes Depending on the *Aedes aegypti*'s Region of Origin in Manaus: A Study of an Endemic Brazilian Amazonian City.

da Costa Paz A, Chaves BA, Godoy RSM, Coelho DF, Vieira Júnior AB, Alencar RM, Alcântara JA, Félix LDS, Oliveira CCA, Monteiro WM, Lacerda MVG, Secundino NFC, Pimenta PFP.

17-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992479/>

Investigation of Dengue Infection in Asymptomatic Individuals during a Recent Outbreak in La Réunion.

De Santis O, Pothin E, Bouscaren N, Irish SR, Jaffar-Bandjee MC, Menudier L, Ramis J, Schultz C, Lamaurt F, Wisniak A, Bertolotti A, Hafsia S, Dussart P, Baril L, Mavingui P, Flahault A.

14-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992451/>

The number of dengue cases has increased dramatically over the past 20 years and is an important concern, particularly as the trends toward urbanization continue. While the majority of dengue cases are thought to be asymptomatic, it is unknown to what extent these contribute to transmission. A better understanding of their importance would help to guide control efforts. In 2019, a dengue outbreak in La Reunion resulted in more than 18,000 confirmed cases. Between October 2019 and August 2020, 19 clusters were investigated in the south, west, and east of the island, enabling the recruitment of 605 participants from 368 households within a 200 m radius of the home of the index cases (ICs). No active asymptomatic infections confirmed by RT-PCR were detected. Only 15% were possible asymptomatic dengue infections detected by the presence of anti-dengue IgM antibodies. Only 5.3% of the participants had a recent dengue infection confirmed by RT-PCR. Although the resurgence of dengue in La Réunion is very recent (2016), the rate of anti-dengue IgG positivity, a marker of past infections, was already high at 43% in this study. Dengue transmission was focal in time and space, as most cases were detected within a 100-m radius of the ICs, and within a time interval of less than 7 days between infections detected in a same cluster. No particular demographic or socio-cultural characteristics were associated with dengue infections. On the other hand, environmental risk factors such as type of housing or presence of rubbish in the streets were associated with dengue infections.

Zika Virus Infection Damages the Testes in Pubertal Common Squirrel Monkeys (*Saimiri collinsi*).

Benchimol GDC, Santos JB, Lopes ASDC, Oliveira KG, Okada EST, de Alcantara BN, Pereira WLA, Leão DL, Martins ACC, Carneiro LA, Imbeloni AA, Makiama ST, de Castro LPPA, Coutinho LN, Casseb LMN, Vasconcelos PFDC, Domingues SFS, Medeiros DBA, Scalercio SRRA.

23-02-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992324/>

During the Zika virus (ZIKV) outbreak and after evidence of its sexual transmission was obtained, concerns arose about the impact of the adverse effects of ZIKV infection on human fertility. In this study, we evaluated the clinical-laboratory aspects and testicular histopathological patterns of pubertal squirrel monkeys (*Saimiri collinsi*) infected with ZIKV, analyzing the effects at different stages of infection. The susceptibility of *S. collinsi* to ZIKV infection was confirmed by laboratory tests, which detected viremia (mean 1.63×10^6 RNA copies/ μ L) and IgM antibody induction. Reduced fecal testosterone levels, severe testicular atrophy and prolonged orchitis were observed throughout the experiment by ultrasound. At 21 dpi, testicular damage associated with ZIKV was confirmed by histopathological and immunohistochemical (IHC) analyses. Tubular retraction, the degeneration and necrosis of somatic and germ cells in the seminiferous tubules, the proliferation of interstitial cells and an inflammatory infiltrate were observed. ZIKV antigen was identified in the same cells where tissue injuries were observed. In conclusion, squirrel monkeys were found to be susceptible to the Asian variant of ZIKV, and this model enabled the identification of multifocal lesions in the seminiferous tubules of the infected group evaluated. These findings may suggest an impact of ZIKV infection on male fertility.

Congenital Zika Syndrome and Disabilities of Feeding and Breastfeeding in Early Childhood: A Systematic Review.

Antoniou E, Andronikidi PE, Eskitzis P, Iliadou M, Palaska E, Tziritidou-Chatzopoulou M, Rigas N, Orovou E.

22-02-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992310/>

Determinants of Chikungunya and O'nyong-Nyong Virus Specificity for Infection of Aedes and Anopheles Mosquito Vectors.

Cottis S, Blisnick AA, Failloux AB, Vernick KD.

21-02-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992298/>

Zika Vaccine Microparticles (MPs)-Loaded Dissolving Microneedles (MNs) Elicit a Significant Immune Response in a Pre-Clinical Murine Model.

Kale A, Joshi D, Menon I, Bagwe P, Patil S, Vijayanand S, Braz Gomes K, Uddin MN, D'Souza MJ.

03-03-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36992167/>

Although the global Zika epidemic in 2015-16 fueled vaccine development efforts, there is no approved Zika vaccine or treatment available to date. Current vaccine platforms in clinical trials are administered via either subcutaneous or intramuscular injections, which are painful and decrease compliance. Therefore, in the present study, we explored Zika vaccine microparticles (MPs)-loaded dissolving microneedles (MNs) with adjuvant MPs encapsulating Alhydrogel® and MPL-A* administered via the transdermal route as a pain-free vaccine strategy. We characterized the MNs for needle length, pore formation, and dissolvability when applied to murine skin. Further, we evaluated the in vivo efficacy of vaccine MPs-loaded MNs with or without adjuvants by measuring the immune response after transdermal immunization. The vaccine MPs-loaded dissolving MNs with adjuvants induced significant IgG, IgG1, and IgG2a titers in immunized mice compared to the untreated control group. After the dosing regimen, the animals were challenged with Zika virus, monitored for seven days, and sacrificed to collect spleen and lymph nodes. The lymphocytes and splenocytes from the immunized mice showed significant expressions of helper (CD4) and cytotoxic (CD8a) cell surface markers compared to the control group. Thus, this study puts forth a 'proof-of-concept' for a pain-free transdermal vaccine strategy against Zika.

Knowledge, Attitudes and Practices toward Dengue Fever, Vector Control, and Vaccine Acceptance Among the General Population in Countries from Latin America and Asia Pacific: A Cross-Sectional Study (GEMKAP).

Shafie AA, Moreira ED Jr, Di Pasquale A, Demuth D, Yin JYS.

02-03-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36992159/>

Dengue represents a major public health concern. With effective vaccines in development, it is important to identify motivational factors to maximize dengue vaccine uptake. A cross-sectional, quantitative, electronic survey was administered to a nationally representative adult population ($n = 3800$) in Argentina, Brazil, Colombia, Mexico, Indonesia, Malaysia, and Singapore. Willingness to vaccinate against dengue, and Knowledge, Attitudes, and Practices (KAP) toward dengue, vector control, prevention, and vaccination were determined. The Capability, Opportunity, Motivation for Behavior change (COM-B) framework was used to identify factors correlated with dengue vaccine(s) uptake. KAP scores (standardized, 0-100% scale) resulted in a low global score for Knowledge (48%) and Practice (44%), and a moderate score for Attitude (66%); scores were comparable across countries. Of all respondents, 53% had a high willingness (Score: 8-10/10) to vaccinate against dengue, which was higher (59%) in Latin America (Argentina, Brazil, Colombia, Mexico) than in Asia Pacific (40%) (Indonesia, Malaysia, Singapore). Key factors significantly ($p < 0.05$) associated with increased willingness to vaccinate included

accessibility to the public (subsidies and incentives) and trust in the healthcare system and government. A common approach to dengue prevention across endemic countries—with some country-specific customization, including education, vaccination, and vector control (multi-pronged)—may reduce dengue burden and improve outcomes.

Evaluation of repRNA vaccine for induction and in utero transfer of maternal antibodies in a pregnant rabbit model.

Khandhar AP, Landon CD, Archer J, Krieger K, Warner NL, Randall S, Berube BJ, Erasmus JH, Sather DN, Staats HF.
16-03-2023

Mol Ther.

<https://pubmed.ncbi.nlm.nih.gov/36965482/>

Functionalized sulfonyl anthranilic acid derivatives inhibit replication of all the four dengue serotypes.

Felicetti T, Gwee CP, Burali MS, Chan KWK, Alonso S, Pismataro MC, Sabatini S, Barreca ML, Cecchetti V, Vasudevan SG, Manfroni G.

16-03-2023

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/36965228/>

Dengue virus (DENV), a mosquito-borne flavivirus, continues to be a major public health threat in many countries and no approved antiviral therapeutics are available yet. In this work, we designed and synthesized a series of sulfonyl anthranilic acid (SAA) derivatives using a ligand-based scaffold morphing approach of the 2,1-benzothiazine 2,2-dioxide core, previously used by us to develop DENV polymerase inhibitors resulting devoid of any cell-based antiviral activity. Several derivatives based on the new SAA chemotype exhibited potent inhibition against DENV infection in the cell-based assay but did not inhibit DENV NS5 polymerase activity in the in vitro de novo initiation and elongation assays. Notably, best compounds 26 and 39 showed EC₅₀ values in the range of 0.54-1.36 µM against cells infected with the four dengue serotypes (DENV-1-4). Time-of-drug-addition assay revealed that analogue 26 is a post-entry replication inhibitor that appears to be specific for cells of primate origin, implicating a host target with a high barrier to resistance. In conclusion, SAA derivatives offer a valuable starting point for developing effective Dengue antiviral therapeutics.

Climate change and Aedes albopictus risks in China: current impact and future projection.

Liu H, Huang X, Guo X, Cheng P, Wang H, Liu L, Zang C, Zhang C, Wang X, Zhou G, Gong M.

24-03-2023

Infect Dis Poverty.

<https://pubmed.ncbi.nlm.nih.gov/36964611/> ;

Associations between severe and notifiable respiratory infections during the first trimester of pregnancy and congenital anomalies at birth: a register-based cohort study.

Chughtai AA, He WQ, Liu B.

24-03-2023

BMC Pregnancy Childbirth.

<https://pubmed.ncbi.nlm.nih.gov/36964492/>

Background: Evidence regarding the association between acute respiratory infections during pregnancy and congenital anomalies in babies, is limited and conflicting. The aim of this study was to examine the association between acute respiratory infections during the first trimester of pregnancy and congenital anomalies in babies using record linkage. **Methods:** We linked a perinatal register to hospitalisation and disease notifications in the Australian state of New South Wales (NSW) between 2001 to 2016. We quantified the risk of congenital anomalies, identified from the babies' linked hospital record in relation to notifiable respiratory and other infections during pregnancy using generalized Estimating Equations (GEE) adjusted for maternal sociodemographic and other characteristics. **Results:** Of 1,453,037 birth records identified from the perinatal register between 2001 and 2016, 11,710 (0.81%) mothers were hospitalised for acute respiratory infection, 2850 (0.20%) had influenza and 1011 (0.07%) had high risk infections (a record of cytomegalovirus, rubella, herpes simplex, herpes zoster, toxoplasmosis, syphilis, chickenpox (varicella) and zika) during the pregnancy. During the first trimester, acute respiratory infection, influenza and high-risk infections were reported by 1547 (0.11%), 399 (0.03%) and 129 (0.01%) mothers. There were 15,644 (1.08%) babies reported with major congenital anomalies, 2242 (0.15%) with cleft lip/ plate, 7770 (0.53%) with all major cardiovascular anomalies and 1746 (0.12%) with selected major cardiovascular anomalies. The rate of selected major cardiovascular anomalies was significantly higher if the mother had an acute respiratory infection during the first trimester of pregnancy (AOR 3.64, 95% CI 1.73 to 7.66). The rates of all major congenital anomalies and all major cardiovascular anomalies were also higher if the mother had an acute respiratory infection during the first trimester of pregnancy, however the difference was not statistically significant. Influenza during the first trimester was not associated with major congenital anomalies, selected major cardiovascular anomalies or all major cardiovascular anomalies in this study. **Conclusion:** This large population-based study found severe acute respiratory infection in first trimester of pregnancy was associated with a higher risk of selected major cardiovascular anomalies in babies. These findings support measures to prevent acute respiratory infections in pregnant women including through vaccination.

Geographic clustering of travel-acquired infections in Ontario, Canada, 2008-2020.

Harish V, Buajitti E, Burrows H, Posen J, Bogoch II, Corbeil A, Gubbay JB, Rosella LC, Morris SK.

17-03-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36963058/>

As the frequency of international travel increases, more individuals are at risk of travel-acquired infections (TAIs). In this ecological study of over 170,000 unique tests from Public Health Ontario's laboratory, we reviewed all laboratory-reported cases of malaria, dengue, chikungunya, and enteric fever in Ontario, Canada between 2008-2020 to identify high-resolution geographical clusters for potential targeted pre-travel prevention. Smoothed standardized incidence ratios (SIRs) and 95% posterior credible intervals (CIs) were estimated using a spatial Bayesian hierarchical model. High- and low-incidence areas were described using data from the 2016 Census based on the home forward sortation area of patients testing positive. A second model was used to estimate the association between drivetime to the nearest travel clinic and incidence of TAI within high-incidence areas. There were 6,114 microbiologically confirmed TAIs across Ontario over the study period. There was spatial clustering of TAIs (Moran's $I = 0.59$, $p < 0.0001$). Compared to low-incidence areas, high-incidence areas had higher proportions of immigrants ($p < 0.0001$), were lower income ($p = 0.0027$), had higher levels of university education ($p < 0.0001$), and less knowledge of English/French languages ($p < 0.0001$). In the high-incidence Greater Toronto Area (GTA), each minute increase in drive time to the closest travel clinic was associated with a 3% reduction in TAI incidence (95% CI 1-6%). While urban neighbourhoods in the GTA had the highest burden of TAIs, geographic proximity to a travel clinic in the GTA was not associated with an area-level incidence reduction in TAI. This suggests other barriers to seeking and adhering to pre-travel advice.

The World Health Organization's Disease Outbreak News: A retrospective database.

Carlson CJ, Boyce MR, Dunne M, Graeden E, Lin J, Abdellatif YO, Palys MA, Pavez M, Phelan AL, Katz R.

25-01-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962988/>

Dengue amid COVID-19 pandemic.

Tangsathapornpong A, Thisyakorn U.

06-02-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962879/>

The increasing in dengue cases nowadays is a global threat concern. Fifty per cent of the world's population is vulnerable to dengue infection with Asia contributing over two-thirds of the global burden. The double trouble of Coronavirus disease 2019 (COVID-19) arising from novel severe respiratory syndrome coronavirus (SARS-CoV-2) and dengue virus is a major challenge, particularly in developing countries due to overburdened public health systems and economic constraints including the ability to diagnose. The objective of this study was to analyze the prevalence of dengue in Thailand during the outbreak of

COVID-19. We studied data on dengue cases reported at epidemiological information centers, the Bureau of Epidemiology, and the Ministry of Public Health, Thailand during 2019 to 2021. Patients can be observed across all age groups, particularly adolescents and adults. Dengue was seen year-round, with highest incidence in the rainy seasons between June and September. Total number of cases was markedly declined by nearly 93 percentage from 2019 to 2021. Taken together, Thailand is still at risk of spreading of dengue in the midst of COVID-19 pandemic. Continuous status updates on dengue patients in Thailand should be incorporated into global health advisory on preventive measures before travelling.

The global burden of Chikungunya fever among children: A systematic literature review and meta-analysis.

Nyamwaya DK, Thumbi SM, Bejon P, Warimwe GM, Mokaya J.

21-12-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962807/>

Antibody Immunity to Zika Virus among Young Children in a Flavivirus-Endemic Area in Nicaragua.

Zepeda O, Espinoza DO, Martinez E, Cross KA, Becker-Dreps S, de Silva AM, Bowman NM, Premkumar L, Stringer EM, Bucardo F, Collins MH.

21-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992504/>

Molecular Mechanisms of Antiviral Agents against Dengue Virus.

Lee MF, Wu YS, Poh CL.

08-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992414/>

Dengue is a major global health threat causing 390 million dengue infections and 25,000 deaths annually. The lack of efficacy of the licensed Dengvaxia vaccine and the absence of a clinically approved antiviral against dengue virus (DENV) drive the urgent demand for the development of novel anti-DENV therapeutics. Various antiviral agents have been developed and investigated for their anti-DENV activities. This review discusses the mechanisms of action employed by various antiviral agents against DENV. The development of host-directed antivirals targeting host receptors and direct-acting antivirals targeting DENV structural and non-structural proteins are reviewed. In addition, the development of antivirals that target different stages during post-infection such as viral replication, viral maturation, and viral assembly are reviewed. Antiviral agents designed based on these molecular mechanisms of action could lead to the discovery and development of novel anti-DENV therapeutics for the treatment of dengue infections. Evaluations of combinations of antiviral drugs with different mechanisms of action could also lead to the

development of synergistic drug combinations for the treatment of dengue at any stage of the infection.

Tizoxanide Antiviral Activity on Dengue Virus Replication.

Yamamoto KA, Blackburn K, Goshe MB, Brown DT, Migowski E, Campanhon IB, Moreira MF, Ferreira DF, Soares MR.

07-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992406/>

Dengue virus is an important circulating arbovirus in Brazil responsible for high morbidity and mortality worldwide, representing a huge economic and social burden, in addition to affecting public health. In this study, the biological activity, toxicity, and antiviral activity against dengue virus type 2 (DENV-2) of tizoxanide (TIZ) was evaluated in Vero cell culture. TIZ has a broad spectrum of action in inhibiting different pathogens, including bacteria, protozoa, and viruses. Cells were infected for 1 h with DENV-2 and then treated for 24 h with different concentrations of the drug. The quantification of viral production indicated the antiviral activity of TIZ. The protein profiles in infected Vero cells treated and not treated with TIZ were analyzed using the label-free quantitative proteomic approach. TIZ was able to inhibit virus replication mainly intracellularly after DENV-2 penetration and before the complete replication of the viral genome. Additionally, the study of the protein profile of infected not-treated and infected-treated Vero cells showed that TIZ interferes with cellular processes such as intracellular trafficking and vesicle-mediated transport and post-translational modifications when added after infection. Our results also point to the activation of immune response genes that would eventually lead to a decrease of DENV-2 production. TIZ is a promising therapeutic molecule for the treatment of DENV-2 infections.

Growth Velocity and Nutritional Status in Children Exposed to Zika Virus during Pregnancy from Amazonas Cohort, Brazil.

Peixoto LFAA, Abtibol-Bernardino MR, Guerra CVC, de Oliveira GA, Chaves BCS, de Souza Rodrigues C, de Andrade ABCA, de Fátima Redivo E, Fernandes SSA, Otani RH, da Silva Neto AV, da Silva Balieiro AA, Cabral CRB, Baia-da-Silva D, Castilho MDC, Bôto-Menezes CH, Alecrim MDGC, Leal MDC, Benzecry SG, Martinez-Espinosa FE.

01-03-2023

Viruses.

Identification of Zika Virus NS1-Derived Peptides with Potential Applications in Serological Tests.

Prudencio CR, Gomes da Costa V, Rocha LB, Costa HHM, Orts DJB, da Silva Santos FR, Rahal P, Lino NAB, da Conceição PJP, Bittar C, Machado RRG, Durigon EL, Araujo JP Jr, Polatto JM, da Silva MA, de Oliveira JA, Mitsunari T, Pereira LR, Andreata-Santos R, de Souza Ferreira LC, Luz D, Piazza RMF.

28-02-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992364/>

Zika virus (ZIKV), a mosquito-borne pathogen, is an emerging arbovirus associated with sporadic symptomatic cases of great medical concern, particularly among pregnant women and newborns affected with neurological disorders. Serological diagnosis of ZIKV infection is still an unmet challenge due to the co-circulation of the dengue virus, which shares extensive sequence conservation of structural proteins leading to the generation of cross-reactive antibodies. In this study, we aimed to obtain tools for the development of improved serological tests for the detection of ZIKV infection. Polyclonal sera (pAb) and a monoclonal antibody (mAb 2F2) against a recombinant form of the ZIKV nonstructural protein 1 (NS1) allowed the identification of linear peptide epitopes of the NS1 protein. Based on these findings, six chemically synthesized peptides were tested both in dot blot and ELISA assays using convalescent sera collected from ZIKV-infected patients. Two of these peptides specifically detected the presence of ZIKV antibodies and proved to be candidates for the detection of ZIKV-infected subjects. The availability of these tools opens perspectives for the development of NS1-based serological tests with enhanced sensitivity regarding other flaviviruses.

Chikungunya Virus: Priority Pathogen or Passing Trend?

Montalvo Zurbia-Flores G, Reyes-Sandoval A, Kim YC.

01-03-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36992153/>

Chikungunya virus (CHIKV) is considered a priority pathogen and a major threat to global health. While CHIKV infections may be asymptomatic, symptomatic patients can develop chikungunya fever (CHIKF) characterized by severe arthralgia which often transitions into incapacitating arthritis that could last for years and lead to significant loss in health-related quality of life. Yet, Chikungunya fever (CHIKF) remains a neglected tropical disease due to its complex epidemiology and the misrepresentation of its incidence and disease burden worldwide. Transmitted to humans by infected *Aedes* mosquitoes, CHIKV has dramatically expanded its geographic distribution to over 100 countries, causing large-scale outbreaks around the world and putting more than half of the population of the world at risk of infection. More than 50 years have passed since the first CHIKV vaccine was reported to be in development. Despite this, there is no licensed vaccine or antiviral treatments against CHIKV to date. In this review, we highlight the clinical relevance of developing chikungunya vaccines by discussing the poor understanding of long-term disease burden in CHIKV endemic countries, the complexity of CHIKV epidemiological surveillance, and emphasising the impact of the global emergence of CHIKV infections. Additionally, our review focuses on the recent progress of chikungunya vaccines in development, providing insight into the most advanced vaccine candidates in the pipeline and the potential implications of their roll-out.

Changing Ecotypes of Dengue Virus 2 Serotype in Nigeria and the Emergence of Cosmopolitan and Asian I Lineages, 1966-2019.

Onoja BA, Maiga M, Adesola RO, Adamu AM, Adegboye OA.

25-02-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36992135/>

Spatiotemporal overlapping of dengue, chikungunya, and malaria infections in children in Kenya.

Khan A, Bisanzio D, Mutuku F, Ndenga B, Grossi-Soyster EN, Jembe Z, Maina PW, Chebii PK, Ronga CO, Okuta V, LaBeaud AD.

29-03-2023

BMC Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36991340/>

Malaria, chikungunya virus (CHIKV), and dengue virus (DENV) are endemic causes of fever among children in Kenya. The risks of infection are multifactorial and may be influenced by built and social environments. The high resolution overlapping of these diseases and factors affecting their spatial heterogeneity has not been investigated in Kenya. From 2014-2018, we prospectively followed a cohort of children from four communities in both coastal and western Kenya. Overall, 9.8% were CHIKV seropositive, 5.5% were DENV seropositive, and 39.1% were malaria positive (3521 children tested). The spatial analysis identified hot-spots for all three diseases in each site and in multiple years. The results of the model showed that the risk of exposure was linked to demographics with common factors for the three diseases including the presence of litter, crowded households, and higher wealth in these communities. These insights are of high importance to improve surveillance and targeted control of mosquito-borne diseases in Kenya.

Endemic or regionally limited bacterial and viral infections in haematopoietic stem-cell transplantation recipients: a Worldwide Network for Blood and Marrow Transplantation (WBMT) Review.

Muhsen IN, Galeano S, Niederwieser D, Koh MBC, Ljungman P, Machado CM, Kharfan-Dabaja MA, de la Camara R, Koderia Y, Szer J, Rasheed W, Cesaro S, Hashmi SK, Seber A, Atsuta Y, Saleh MFM, Srivastava A, Styczynski J, Alrajhi A, Almaghrabi R, Abid MB, Chemaly RF, Gergis U, Brissot E, El Fakih R, Riches M, Mikulska M, Worel N, Weisdorf D, Greinix H, Cordonnier C, Aljurf M.

Apr-2023

Lancet Haematol.

<https://pubmed.ncbi.nlm.nih.gov/36990623/>

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

Zheng X, Wang R, Yin C.

24-03-2023

Virology.

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

Dengue virus (DENV), Japanese encephalitis virus (JEV) and Zika virus (ZIKV) are the three most important flaviviruses, which can cause health problems worldwide. All these flaviviruses can cause liver damage, however, the mechanism of liver injury is still unclear. Metabolomics can give insight into the full complexity of a disease. In our study, we used an LC-MS method to analysis the metabolites in liver samples of the three flaviviruses-infected mice and the non-infected mice. Compared with the control mice, the liver of the DENV-infected, JEV-infected, and ZIKV-infected mice had 32, 34, and 55 differential metabolites. We also found that there were obvious differences in some metabolic pathways among the four groups. Metabonomic analysis of liver is very important for understanding the pathogenesis of flaviviruses.

Differences in gene expression in field populations of Wolbachia-infected Aedes aegypti mosquitoes with varying release histories in northern Australia.

Wimalasiri-Yapa BMCR, Huang B, Ross PA, Hoffmann AA, Ritchie SA, Frentiu FD, Warrilow D, van den Hurk AF.

29-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36989319/>

Astrocytes derived from neural progenitor cells are susceptible to Zika virus infection.

Rubio-Hernández EI, Comas-García M, Coronado-Ipiña MA, Colunga-Saucedo M, González Sánchez HM, Castillo CG.

29-03-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/36989308/>

Zika virus (ZIKV) was first isolated in 1947. From its isolation until 2007, symptoms of ZIKV-caused disease were limited (e.g., fever, hives, and headache); however, during the epidemic in Brazil in 2014, ZIKV infection caused Guillain-Barré syndrome in adults and microcephaly in fetuses and infants of women infected during pregnancy. The neurovirulence of ZIKV has been studied using neural progenitor cells (NPCs), brain organoids, neurons, and astrocytes. NPCs and astrocytes appear to be the most susceptible cells of the Central Nervous System to ZIKV infection. In this work, we aimed to develop a culture of astrocytes derived from a human NPC cell line. We analyze how ZIKV affects human astrocytes and demonstrate that 1) ZIKV infection reduces cell viability, increases the production of Reactive Oxygen Species (ROS), and results in high viral titers; 2) there are changes in the expression of genes that facilitate the entry of the virus into the cells; 3) there are changes in the expression of genes involved in the homeostasis of the glutamatergic system; and 4) there are ultrastructural changes in mitochondria and lipid droplets associated with production of virions. Our findings reveal new evidence of how ZIKV compromises

astrocytic functionality, which may help understand the pathophysiology of ZIKV-associated congenital disease.

Clinical evaluation of BioFire® multiplex-PCR panel for acute undifferentiated febrile illnesses in travellers: a prospective multicenter study.

Camprubí-Ferrer D, Cobuccio L, Van Den Broucke S, Balerdi-Sarasola L, Genton B, Bottieau E, Navero-Castillejos J, Martinez MJ, Jay C, Grange A, Borland S, Vaughn M, Rodríguez-Valero N, Almuedo-Riera A, D'Acremont V, Subirà C, Alba T, Cruz A, Van Esbroeck M, Smith C, Hillman A, Hanberg B, Trausch R, Spanpanato N, Muñoz J.

29-03-2023

J Travel Med.

<https://pubmed.ncbi.nlm.nih.gov/36988415/>

Background: Identifying the causes of Acute Undifferentiated Febrile Illness(AUFI) is key to improve the management of returning travellers with fever. We evaluated a BioFire®FilmArray® prototype panel of multiplex nucleic acid amplification tests(NAAT) targeting different relevant pathogens in travellers returning with fever. **Methods:** Prospective, multicenter study to evaluate a prototype panel in whole blood samples of adult international travellers presenting with AUFI in three European travel Clinics/Hospitals (November2017-November2019). We evaluated 15 target analytes: Plasmodium spp., P.falciparum, P.knowlesi, P.malariae, P.ovale, P.vivax, chikungunya virus, dengue virus, Zika virus, Anaplasma phagocytophilum, Borrelia spp., Leptospira spp., Orientia tsutsugamushi, Rickettsia spp., Salmonella spp. Results were compared with composite reference standards(CRS) for each target infection, including direct methods (smear microscopy, rapid diagnostic test(RDT), reference NAAT, blood cultures) and indirect methods(paired serology). **Findings:** Among 455 travellers with AUFI, 229 target infections were diagnosed; the prototype panel detected 143 (overall sensitivity and specificity of 62.5% and 99.8%, respectively). The panel identified all Plasmodium infections(n = 82). Sensitivity for dengue(n = 71) was 92.9%; 80.8% and 68.5% compared to RDT, NAAT and CRS. Compared to direct methods and CRS, respectively, the prototype panel detected 4/4 and 4/6 chikungunya, 2/2 and 4/29 Leptospira spp., 1/1 and 1/6 O.tsutsugamushi, 2/2 and 2/55 Rickettsia spp., but 0/2 and 0/10 Zika, 0/1 and 0/11 A.phagocytophilum, 0/3 Borrelia spp. diagnosed by serology and 1/7 Salmonella spp. diagnosed by blood cultures. 77/86 (89.5%) infections not detected by the panel were diagnosed by serology. **Interpretation:** The prototype panel allowed rapid and reliable diagnosis for malaria, dengue and chikungunya. Further improvements are needed to improve its sensitivity for Zika and important travel-related bacterial infections.

The Importance of Epigallocatechin as a Scaffold for Drug Development against Flaviviruses.

Coronado MA, Gering I, Sevenich M, Olivier DS, Mastalipour M, Amaral MS, Willbold D, Eberle RJ.

01-03-2023

Pharmaceutics.

<https://pubmed.ncbi.nlm.nih.gov/36986663/>

Arboviruses such as Dengue, yellow fever, West Nile, and Zika are flaviviruses vector-borne RNA viruses transmitted biologically among vertebrate hosts by blood-taking vectors. Many flaviviruses are associated with neurological, viscerotropic, and hemorrhagic diseases, posing significant health and socioeconomic concerns as they adapt to new environments. Licensed drugs against them are currently unavailable, so searching for effective antiviral molecules is still necessary. Epigallocatechin molecules, a green tea polyphenol, have shown great virucidal potential against flaviviruses, including DENV, WNV, and ZIKV. The interaction of EGCG with the viral envelope protein and viral protease, mainly identified by computational studies, describes the interaction of these molecules with viral proteins; however, how the viral NS2B/NS3 protease interacts with epigallocatechin molecules is not yet fully deciphered. Consequently, we tested the antiviral potential of two epigallocatechin molecules (EGC and EGCG) and their derivative (AcEGCG) against DENV, YFV, WNV, and ZIKV NS2B/NS3 protease. Thus, we assayed the effect of the molecules and found that a mixture of the molecules EGC (competitive) and EGCG (noncompetitive) inhibited the virus protease of YFV, WNV, and ZIKV more effectively with IC₅₀ values of 1.17 ± 0.2 µM, 0.58 ± 0.07 µM, and 0.57 ± 0.05 µM, respectively. As these molecules fundamentally differ in their inhibitory mode and chemical structure, our finding may open a new line for developing more effective allosteric/active site inhibitors to combat flaviviruses infection.

Anti-Zika Virus Activity and Isolation of Flavonoids from Ethanol Extracts of Curatella americana L. Leaves.

Lima LD, Reis ACC, Sousa JAC, Valente GM, de Mello Silva B, Magalhães CLB, Kohlhoff M, Teixeira LFM, Brandão GC.

10-03-2023

Molecules.

<https://pubmed.ncbi.nlm.nih.gov/36985517/>

Terpenic Constituents of Essential Oils with Larvicidal Activity against Aedes Aegypti: A QSAR and Docking Molecular Study.

Cruz-Castillo AU, Rodríguez-Valdez LM, Correa-Basurto J, Noguera-Torres B, Andrade-Ochoa S, Nevárez-Moorillón GV.

07-03-2023

Molecules.

<https://pubmed.ncbi.nlm.nih.gov/36985426/>

Aedes aegypti is a vector for the arbovirus responsible for yellow fever, Zika and Chikungunya virus. Essential oils and their constituents are known for their larvicidal properties and are strong candidates for mosquito control. This work aimed to develop a quantitative structure-activity study

and molecular screening for the search and design of new larvicidal agents. Twenty-five monoterpenes with previously evaluated larvicidal activity were built and optimized using computational tools. QSAR models were constructed through genetic algorithms from the larvicidal activity and the calculation of theoretical descriptors for each molecule. Docking studies on acetylcholinesterase (AChE) and sterol carrier protein (SCP-2) were also carried out. Results demonstrate that the epoxide groups in the structure of terpenes hinder larvicidal activity, while lipophilicity plays an important role in enhancing biological activity. Larvicidal activity correlates with the interaction of the sterol-carrier protein. Of the 25 compounds evaluated, carvacrol showed the highest larvicidal activity with an LC₅₀ of 8.8 µg/mL. The information included in this work contributes to describing the molecular, topological, and quantum mechanical properties related to the larvicidal activity of monoterpenes and their derivatives.

Association of Dengue Virus Serotypes 1&2 with Severe Dengue Having Deletions in Their 3'Untranslated Regions (3'UTRs).

Maisnam D, Billoria A, Prasad VSV, Venkataramana M.

06-03-2023

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/36985238/>

First cases of SARS-CoV-2 infection and secondary transmission in Kisumu, Kenya.

Tippett Barr BA, Herman-Roloff A, Mburu M, Murnane PM, Sang N, Bukusi E, Oele E, Odhiambo A, Lewis-Kulzer J, Onyango CO, Hunsperger E, Odhiambo F, Joseph RH, Munyua P, Othieno K, Mulwa E, Akelo V, Muok E, Bulterys M, Nzioka C, Cohen CR.

08-09-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962806/>

We investigated the first 152 laboratory-confirmed SARS-CoV-2 cases (125 primary and 27 secondary) and their 248 close contacts in Kisumu County, Kenya. Conducted June 10-October 8, 2020, this study included interviews and sample collection at enrolment and 14-21 days later. Median age was 35 years (IQR 28-44); 69.0% reported COVID-19 related symptoms, most commonly cough (60.0%), headache (55.2%), fever (53.3%) and loss of taste or smell (43.8%). One in five were hospitalized, 34.4% >25 years of age had at least one comorbidity, and all deaths had comorbidities. Adults ≥25 years with a comorbidity were 3.15 (95% CI 1.37-7.26) times more likely to have been hospitalized or died than participants without a comorbidity. Infectious comorbidities included HIV, tuberculosis, and malaria, but no current cases of influenza, respiratory syncytial virus, dengue fever, leptospirosis or chikungunya were identified. Thirteen (10.4%) of the 125 primary infections transmitted COVID-19 to 27 close contacts, 158 (63.7%) of whom resided or worked within the same household. Thirty-one percent (4 of 13) of those who transmitted COVID-19 to secondary cases were health care workers; no known secondary

transmissions occurred between health care workers. This rapid assessment early in the course of the COVID-19 pandemic identified some context-specific characteristics which conflicted with the national line-listing of cases, and which have been substantiated in the year since. These included over two-thirds of cases reporting the development of symptoms during the two weeks after diagnosis, compared to the 7% of cases reported nationally; over half of cases reporting headaches, and nearly half of all cases reporting loss of taste and smell, none of which were reported at the time by the World Health Organization to be common symptoms. This study highlights the importance of rapid in-depth assessments of outbreaks in understanding the local epidemiology and response measures required.

Facebook and mosquito-borne disease outbreaks: An analysis of public responses to federal health agencies' posts about dengue and Zika in 2016.

Carvajal P, Balanay JAG, Shearman S, Richards SL.

12-09-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962780/>

Responses of Facebook users to four United States federal health agencies' social media posts about dengue and Zika (mosquito-borne diseases), surveillance, and control during the Zika outbreak in 2016 were tracked. Official Facebook pages of health agencies were analyzed, and a qualitative analysis program was used to perform a thematic analysis of the data on public responses to health agency posts. Public sentiment analysis showed that Facebook users had a negative sentiment towards health information observed in this study. Themes were identified in the studied posts, giving insight into the nature of public discussions and responses to federal health agencies. Themes were assessed based on the way the agencies' mosquito-borne disease information was received by the public through the social media platform, Facebook. Results indicate that public perception/understanding of mosquito-borne disease outbreaks can be assessed by analyzing public interactions with health agencies on Facebook. The importance of maximizing effectiveness by addressing issues in sharing health education information, risk communication, and monitoring of public responses by health agencies through social media platforms is discussed.

Epidemiological and virological factors determining dengue transmission in Sri Lanka during the COVID-19 pandemic.

Ariyaratne D, Gomes L, Jayadas TTP, Kuruppu H, Kodituwakku L, Jeewandara C, Pannila Hetti N, Dheerasinghe A, Samaraweera S, Ogg GS, Malavige GN.

03-08-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962516/>

With the onset of the COVID-19 pandemic in early 2020 there was a drastic reduction in the number of dengue cases in Sri Lanka, with an increase towards the end of 2021. We sought to study the contribution of virological

factors, human mobility, school closure and mosquito factors in affecting these changes in dengue transmission in Sri Lanka during this time. To understand the reasons for the differences in the dengue case numbers in 2020 to 2021 compared to previous years, we determined the association between the case numbers in Colombo (which has continuously reported the highest number of cases) with school closures, stringency index, changes in dengue virus (DENV) serotypes and vector densities. There was a 79.4% drop in dengue cases from 2019 to 2020 in Colombo. A significant negative correlation was seen with the number of cases and school closures (Spearman's $r = -0.4732$, $p < 0.0001$) and a negative correlation, which was not significant, between the stringency index and case numbers (Spearman's $r = -0.3755$, $p = 0.0587$). There was no change in the circulating DENV serotypes with DENV2 remaining the most prevalent serotype by early 2022 (65%), similar to the frequencies observed by end of 2019. The *Aedes aegypti* premise and container indices showed positive but insignificant correlations with dengue case numbers (Spearman $r = 0.8827$, $p = 0.93$). Lockdown measures, especially school closures seemed to have had a significant impact on the number of dengue cases, while the vector indices had a limited effect.

Demographic characteristics, clinical symptoms, biochemical markers and probability of occurrence of severe dengue: A multicenter hospital-based study in Bangladesh.

Yang J, Mosabbir AA, Raheem E, Hu W, Hossain MS.

15-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36921001/>

Ethyl palmitate, an anti-chikungunya virus principle from *Sauropus androgynus*, a medicinal plant used to alleviate fever in ethnomedicine.

Sagna A, Nair RVR, Hulyalkar N, Rajasekharan S, Nair VTG, Sivakumar KC, Suja SR, Baby S, Sreekumar E.

12-06-2023

J Ethnopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/36914036/>

Infection with chikungunya virus confers heterotypic cross-neutralizing antibodies and memory B-cells against other arthritogenic alphaviruses predominantly through the B domain of the E2 glycoprotein.

Powers JM, Lyski ZL, Weber WC, Denton M, Streblow MM, Mayo AT, Haese NN, Nix CD, Rodríguez-Santiago R, Alvarado LI, Rivera-Amill V, Messer WB, Streblow DN.

13-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36913428/>

Infections with Chikungunya virus, a mosquito-borne alphavirus, cause an acute febrile syndrome often followed by chronic arthritis that persists for months to

years post-infection. Neutralizing antibodies are the primary immune correlate of protection elicited by infection, and the major goal of vaccinations in development. Using convalescent blood samples collected from both endemic and non-endemic human subjects at multiple timepoints following suspected or confirmed chikungunya infection, we identified antibodies with broad neutralizing properties against other alphaviruses within the Semliki Forest complex. Cross-neutralization generally did not extend to the Venezuelan Equine Encephalitis virus (VEEV) complex, although some subjects had low levels of VEEV-neutralizing antibodies. This suggests that broadly neutralizing antibodies elicited following natural infection are largely complex restricted. In addition to serology, we also performed memory B-cell analysis, finding chikungunya-specific memory B-cells in all subjects in this study as remotely as 24 years post-infection. We functionally assessed the ability of memory B-cell derived antibodies to bind to chikungunya virus, and related Mayaro virus, as well as the highly conserved B domain of the E2 glycoprotein thought to contribute to cross-reactivity between related Old-World alphaviruses. To specifically assess the role of the E2 B domain in cross-neutralization, we depleted Mayaro and Chikungunya virus E2 B domain specific antibodies from convalescent sera, finding E2B depletion significantly decreases Mayaro virus specific cross-neutralizing antibody titers with no significant effect on chikungunya virus neutralization, indicating that the E2 B domain is a key target of cross-neutralizing and potentially cross-protective neutralizing antibodies.

Cost-effectiveness of sub-national geographically targeted vaccination programs: A systematic review.

Getchell M, Mantaring EJ, Yee K, Pronyk P.

31-03-2023

Vaccine.

<https://pubmed.ncbi.nlm.nih.gov/36781333/>

Immunization is an essential component of national health plans. However, the growing number of new vaccine introductions, vaccination campaigns and increasing administrative costs create logistic and financial challenges, especially in resource-limited settings. Sub-national geographic targeting of vaccination programs is a potential strategy for governments to reduce the impact of infectious disease outbreaks while optimizing resource allocation and reducing costs, promoting sustainability of critically important national immunization plans. We conducted a systematic review of peer-reviewed literature to identify studies that investigated the cost-effectiveness of geographically targeted sub-national vaccination programs, either through routine immunization or supplementary immunization activities. A total of 16 studies were included in our review, covering nine diseases of interest: cholera, dengue, enterotoxigenic *Escherichia coli* (ETEC), hepatitis A, Japanese encephalitis, measles, rotavirus, Shigella and typhoid fever. All studies modelled cost-effectiveness of geographically targeted vaccination. Despite the variation in study design, disease focus and country context, studies generally found that in countries where a heterogenous burden of disease exists,

sub-national geographic targeting of vaccination programs in areas of high disease burden was more cost-effective than a non-targeted strategy. Sensitivity analysis revealed that cost-effectiveness was most sensitive to variations in vaccine price, vaccine efficacy, mortality rate, administrative and operational costs, discount rate, and treatment costs. This systematic review identified several key characteristics related to geographic targeting of vaccination, including the vaccination strategy used, variations in modelling parameters and their impact on cost-effectiveness. Additional research and guidance is needed to support the appropriateness and feasibility of geographically targeted vaccination and to determine what country context would make this a viable complement to routine immunization programs.

The Dengue virus protease NS2B3 cleaves cyclic GMP-AMP synthase to suppress cGAS activation.

Bhattacharya M, Bhowmik D, Tian Y, He H, Zhu F, Yin Q.
Mar-2023

J Biol Chem.

<https://pubmed.ncbi.nlm.nih.gov/36754281/>

Positive-strand RNA viruses-a Keystone Symposia report.

Cable J, Denison MR, Kielian M, Jackson WT, Bartenschlager R, Ahola T, Mukhopadhyay S, Fremont DH, Kuhn RJ, Shannon A, Frazier MN, Yuen KY, Coyne CB, Wolthers KC, Ming GL, Guenther CS, Moshiri J, Best SM, Schoggins JW, Jurado KA, Ebel GD, Schäfer A, Ng LFP, Kikkert M, Sette A, Harris E, Wing PAC, Eggenberger J, Krishnamurthy SR, Mah MG, Meganck RM, Chung D, Maurer-Stroh S, Andino R, Korber B, Perlman S, Shi PY, Bárcena M, Aicher SM, Vu MN, Kenney DJ, Lindenbach BD, Nishida Y, Rénia L, Williams EP.

Mar-2023

Ann N Y Acad Sci.

<https://pubmed.ncbi.nlm.nih.gov/36697369/>

Spontaneous coronary hematoma concomitant with myocarditis: the first report of double cardiac complication of dengue.

Corré J, Vally S, Boiron P, Bouillaud Y, Travers JY.

Apr-2023

ESC Heart Fail.

<https://pubmed.ncbi.nlm.nih.gov/36547007/>

We reported the case of a 33-year-old male who presented a dengue infection complicated by spontaneous coronary artery intramural hematoma associated with acute myocarditis. The initial presentation was a typical acute coronary syndrome with ST-segment elevation. Coronary angiography and endocoronary optical coherence tomography confirmed the diagnosis of left anterior descending artery intramural hematoma. Cardiac magnetic resonance imaging revealed not only typical ischaemic injury but also lesions of acute myocarditis confirmed by native T1- and T2-mapping, sub-epicardial late gadolinium enhancement and pericardial effusion. This case highlights the multiple cardiac damages

caused by dengue virus, their possible association (coincidental or linked?), and the impact of multimodal imaging on diagnosis and management.

Therapeutic plasma exchange and continuous renal replacement therapy in pediatric dengue-associated acute liver failure: A case series from Vietnam.

Thanh NT, Dat NT, Thinh TN, Phuong NTM, Thanh MTH, Bao NT, Son PT, Viet DC, Tung TH, Thien V, Luan VT.

Apr-2023

Transfus Apher Sci.

<https://pubmed.ncbi.nlm.nih.gov/36522271/>

Prenatal and Postnatal Zika Intrauterine Infection: Diagnostic Imaging Techniques and Placental Pathology.

Castro PT, Werner H, Araujo Júnior E, Bonasoni MP, Tonni G.

Apr-2023

Fetal Pediatr Pathol.

<https://pubmed.ncbi.nlm.nih.gov/36125260/>

Introduction: Zika virus (ZIKV) is an arbovirus (arthropod-borne virus) in the genus *Flavivirus* and *Flaviviridae* family. In November 2015, several cases of microcephaly in Northeastern of Brazil suggested ZIKV involvement. **Case Report:** A 33-year-old primigravida developed fever and cutaneous rash at 7th week of gestation (WGA). The ultrasound and MRI examination showed head circumference < 5th centile and enlargement of lateral ventricles. The infant was delivered at 39th WGA with microcephaly. Microscopy of the placenta showed chronic villitis and intervillitis, nodular stromal fibrosis in the stem villi, and vascular thickening. Postnatal CT showed collapsed cranium due to growth impairment of the supratthalamic brain, multiple cerebral calcifications, parenchymal atrophy, and ventricular dilatation. Now, at 6 years old, the child suffers from severe neurologic symptoms, including seizures. **Conclusion:** This case gathers images of prenatal and postnatal period, and placental histopathology. The long-term follow-up highlights the dramatic neurological sequelae induced by ZIKV.

Exploring the unseen effect of COVID 19 pandemic on blood transfusion services in a tertiary care centre.

Kaur P, Bedi RK, Mittal K, Sood T.

Apr-2023

Transfus Apher Sci.

<https://pubmed.ncbi.nlm.nih.gov/36088214/>

Background: The coronavirus pandemic confronted blood transfusion services with major challenges. The present study was conducted to explore the effect of the COVID-19 pandemic on blood transfusion services including seroprevalence of transfusion-transmitted infections. **Material and methods:** A retrospective cross-sectional study was conducted and data on blood donation, utilization, camps, plateletpheresis and seroprevalence of transfusion-transmitted infections (TTI) was retrieved

from software from March to September 2020 and 2021 and compared with corresponding time periods of three preceding non-pandemic years. **Results:** There was a decline of 53.79% and 34.4% in blood donations in 2020 and 2021 respectively with a significant reduction in voluntary donations from 91.8% in the pre-pandemic period to 72.2% in 2020 and 77.7% in 2021. Replacement donors increased by 60.81% and 72.89% in 2020 and 2021 respectively. There was a decline of 48.4% in the number of plateletpheresis procedures in 2020 which increased in 2021 during the dengue outbreak. The decline in total blood donations and issue of packed red blood cells was statistically significant but supply and demand were balanced with no deficit. TTI seroprevalence increased from 1.01% to 1.49%($p<0.001$) and 1.51%($p<0.001$) in 2020 and 2021 respectively. Replacement donors showed a significantly higher TTI prevalence as compared to voluntary donors($p<0.001$). A significant increase in prevalence was observed for Syphilis (0.4%) in 2020 and HBsAg (0.54%), HCV(0.63%) and syphilis (0.25%) in 2021. **Conclusion:** The potential consequences of the COVID-19 pandemic on blood safety cannot be undermined. Developing a strong database of regular voluntary donors can be instrumental in dealing with future waves and surges in infections.

Serum soluble interleukin-2 receptor (sIL-2R) is an accurate biomarker for dengue-associated hemophagocytic lymphohistiocytosis syndrome diagnosed by Hscore.

Mahabala C, Koushik VK, Manjrekar PA, Balanthimogru P.

Apr-2023

Infection.

<https://pubmed.ncbi.nlm.nih.gov/35999341/>

Designing of nanobodies against Dengue virus Capsid: a computational affinity maturation approach.

Chaudhuri D, Majumder S, Datta J, Giri K.

Apr-2023

J Biomol Struct Dyn.

<https://pubmed.ncbi.nlm.nih.gov/35067204/>

Dengue virus, an arbovirus, is one of the most prevalent diseases in the tropical environment and leads to huge number of casualties every year. No therapeutics are available till date against the viral disease and the only medications provide symptomatic relief. In this study, we have focused on utilizing conventional nanobodies and repurposing them for Dengue. Computationally affinity matured, best binding nanobodies tagged with constant antibody regions, could be proposed as therapeutics. These could also be applied for drug delivery purposes due to their high specificity against the viral Capsid. Another application of these nanobodies has been thought to utilize them for diagnostic purposes, to use the nanobodies for viral detection from patient samples at the earliest stage using ELISA. This study may open a new avenue for immunologic study in foreseeable future with the usage of the same molecules for multiple purposes.

Highlights Natural nanobodies against viruses were modified for use against Dengue virus Capsid conserved regions. Computational affinity maturation was performed making use of change in binding affinities upon mutating various residues in the complementary determining regions. Docking studies performed to inspect the docking groove, interface analysis and energy calculations. MM/GBSA calculations done to calculate binding free energy of the complex to determine stability of the complex. Communicated by Ramaswamy H. Sarma.

Development of a machine learning model for early prediction of plasma leakage in suspected dengue patients.

Zargari Marandi R, Leung P, Sigera C, Murray DD, Weeratunga P, Fernando D, Rodrigo C, Rajapakse S, MacPherson CR.

13-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36913411/>

Evaluation of analgesic and prophylactic activity of curcumin against chikungunya-infected acute/chronic arthralgic mice.

Sengupta S, Tripathi A.

Mar-2023

J Med Virol.

<https://pubmed.ncbi.nlm.nih.gov/36905112/>

Chikungunya virus (CHIKV) infection, a global public health problem, might lead to acute/chronic polyarthritis causing long-term morbidity among infected patients. But, except nonsteroidal anti-inflammatory drugs (NSAIDs) with gastrointestinal, cardiovascular, and immune-related side-effects, no Food and Drug Administration (FDA)-approved analgesic drug is available till date for the treatment of CHIKV-induced arthritis. Curcumin, a plant product with minimal toxicity has been FDA-approved as a Generally Recognized As Safe drug. This study aimed to determine the analgesic and prophylactic effect of curcumin, if any, among CHIKV-induced arthralgic mice. Arthritic pain was evaluated by von Frey assay, locomotory behavior by open-field test, and feet swelling by calipers. Cartilage integrity and proteoglycan loss were evaluated by Safranin O staining followed by Osteoarthritis Research Society International (OARSI), Standardized Microscopic Arthritis Scoring of Histological sections (SMASH) score, and type II collagen loss by immunohistochemistry. Mice were administered high (HD), mid (MD), and low (LD) curcumin doses, before (PT: pretreatment), during (CT: cotreatment) and after (Post-T: posttreatment) CHIKV-infection. Curcumin treatment using PT_{HD} (2000 mg/kg), CT_{HD}, and Post-T_{MD} (1000 mg/kg) significantly alleviated CHIKV-induced arthritic pain by improving pain-threshold, locomotory behavior and reducing feet swelling of infected mice. Also, decreased proteoglycan loss and cartilage erosion with lower OARSI, SMASH scores were observed among these three subgroups compared to infected ones. Compared to infected ones, one- to twofold increased intensity of type II collagen in knee medial femoral condyle and medial tibial plateau regions of these

subgroups was observed by immunohistochemical staining. Thus, this study highlighted both the analgesic (CT, Post-T), and prophylactic (PT) activity of curcumin in alleviating CHIKV-induced acute/chronic arthritis within mouse model.

Constitutive expression and distinct properties of IFN-epsilon protect the female reproductive tract from Zika virus infection.

Coldbeck-Shackley RC, Romeo O, Rosli S, Gearing LJ, Gould JA, Lim SS, Van der Hoek KH, Eyre NS, Shue B, Robertson SA, Best SM, Tate MD, Hertzog PJ, Beard MR. 10-03-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36897927/>

Identification of an effective fraction from Ampelopsis Radix with anti-dengue virus activities in vitro and in vivo.

Tian C, Huang H, Zheng Y, He X, Yan L, Shi L, Yang T, Chen X, Yang J, Lu Z, Cao H, Zhao W, Qin Z, Yu J, Tang Q, Tong X, Liu J, Yu L. 12-06-2023

J Ethnopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/36870463/>

Ethnopharmacological relevance: Dengue virus (DENV) infection is a global public health issue without effective therapeutic interventions. Chinese medicine with heat-clearing and detoxifying properties has been frequently used in the treatment of viral infection. Ampelopsis Radix (AR) is a traditional Chinese medicine for clearing heat and detoxification that has been widely used in the prevention and treatment of infectious diseases. However, no studies on the effects of AR against viral infection have been reported, thus far. **Aim of the study:** To explore the anti-DENV activities of the fraction (AR-1) obtained from AR both in vitro and in vivo. **Materials and methods:** The chemical composition of AR-1 was identified by liquid chromatography-tandem MS (LC-MS/MS). The antiviral activities of AR-1 were studied in baby hamster kidney fibroblast BHK-21 cells, ICR suckling mice and induction of interferon α/β (IFN- α/β) and IFN- γ R^{-/-} (AG129) mice. **Results:** Based on LC-MS/MS analysis, 60 compounds (including flavonoids, phenols, anthraquinones, alkaloids and other types) were tentatively characterized from AR-1. AR-1 inhibited the cytopathic effect, the production of progeny virus and the synthesis of viral RNA and proteins by blocking DENV-2 binding to BHK-21 cells. Moreover, AR-1 significantly attenuated weight loss, decreased clinical scores and prolonged the survival of DENV-infected ICR suckling mice. Critically, the viral load in blood, brain and kidney tissues and the pathological changes in brain were remarkably alleviated after AR-1 treatment. Further study on AG129 mice showed that AR-1 obviously improved the clinical manifestations and survival rate, reduced viremia, attenuated gastric distension and relieved the pathological lesions caused by DENV. **Conclusions:** In summary, this is the first report that AR-1 exhibits anti-DENV effects both in vitro and in vivo, which suggests that

AR-1 may be developed as a therapeutic candidate against DENV infection.

Emergent variant modeling of the serological repertoire to norovirus in young children.

Lindesmith LC, Brewer-Jensen PD, Conrad H, O'Reilly KM, Mallory ML, Kelly D, Williams R, Edmunds WJ, Allen DJ, Breuer J, Baric RS. 21-03-2023

Cell Rep Med.

<https://pubmed.ncbi.nlm.nih.gov/36854303/>

Human norovirus is the leading cause of acute gastroenteritis. Young children and the elderly bear the greatest burden of disease, representing more than 200,000 deaths annually. Infection prevalence peaks at younger than 2 years and is driven by novel GII.4 variants that emerge and spread globally. Using a surrogate neutralization assay, we characterize the evolution of the serological neutralizing antibody (nAb) landscape in young children as they transition between sequential GII.4 pandemic variants. Following upsurge of the replacement variant, antigenic cartography illustrates remodeling of the nAb landscape to the new variant accompanied by improved nAb titer. However, nAb relative avidity remains focused on the preceding variant. These data support immune imprinting as a mechanism of immune evasion and GII.4 virus persistence across a population. Understanding the complexities of immunity to rapidly evolving and co-circulating viral variants, like those of norovirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), and dengue viruses, will fundamentally inform vaccine design for emerging pathogens.

Association of exosomal miR-96-5p and miR-146a-5p with the disease severity in dengue virus infection.

Pradhan A, Aneja A, Ghosh S, Devvanshi H, C D, Sahu R, Ross C, Kshetrapal P, Maitra A, Das S. Mar-2023

J Med Virol.

<https://pubmed.ncbi.nlm.nih.gov/36840403/>

In Vitro Dengue Virus Inhibition by Aqueous Extracts of Aegle marmelos, Munronia pinnata and Psidium guajava.

Jayasekara KG, Soysa P, Suresh TS, Goonasekara CL, Gunasekera KM. Mar-2023

Altern Lab Anim.

<https://pubmed.ncbi.nlm.nih.gov/36793154/>

Dengue is an arboviral (insect-transmitted) infection of global concern. Currently, there are still no specific dengue antiviral agents to treat the disease. Plant extracts have been used in traditional medicine for treating various viral infections - thus, in the present study, aqueous extracts of dried flowers of *Aegle marmelos* (AM), whole plant of *Munronia pinnata* (MP) and leaves of *Psidium guajava* (PG) were investigated for their potential capacity to inhibit

dengue virus infection of Vero cells. The maximum non-toxic dose (MNTD) and the 50% cytotoxic concentration (CC₅₀) were determined by using the MTT assay. A plaque reduction antiviral assay was carried out with dengue virus types 1 (DV1), 2 (DV2), 3 (DV3) and 4 (DV4), in order to calculate the half-maximum inhibitory concentration (IC₅₀). AM extract inhibited all four virus serotypes tested; MP extract inhibited DV1, DV2 and DV4, but not DV3; PG extract inhibited DV1, DV2 and DV4, but not DV3. Thus, the results suggest that AM is a promising candidate for the pan-serotype inhibition of dengue viral activity.

Negative regulation of type I interferon signaling by integrin-linked kinase permits dengue virus replication.

Kao YS, Wang LC, Chang PC, Lin HM, Lin YS, Yu CY, Chen CC, Lin CF, Yeh TM, Wan SW, Wang JR, Ho TS, Chu CC, Zhang BC, Chang CP.

17-03-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36930690/>

Dengue virus (DENV) infection can induce life-threatening dengue hemorrhagic fever/dengue shock syndrome in infected patients. DENV is a threat to global health due to its growing numbers and incidence of infection in the last 50 years. During infection, DENV expresses ten structural and nonstructural proteins modulating cell responses to benefit viral replication. However, the lack of knowledge regarding the cellular proteins and their functions in enhancing DENV pathogenesis impedes the development of antiviral drugs and therapies against fatal DENV infection. Here, we identified that integrin-linked kinase (ILK) is a novel enhancing factor for DENV infection by suppressing type I interferon (IFN) responses. Mechanistically, ILK binds DENV NS1 and NS3, activates Akt and Erk, and induces NF-κB-driven suppressor of cytokine signaling 3 (SOCS3) expression. Elevated SOCS3 in DENV-infected cells inhibits phosphorylation of STAT1/2 and expression of interferon-stimulated genes (ISGs). Inhibiting ILK, Akt, or Erk activation abrogates SOCS3 expression. In DENV-infected mice, the treatment of an ILK inhibitor significantly reduces viral loads in the brains, disease severity, and mortality rate. Collectively, our results show that ILK is a potential therapeutic target against DENV infection.

Sociodemographic and environmental factors associated with dengue, Zika, and chikungunya among adolescents from two Brazilian capitals.

Dalvi APR, Gibson G, Ramos AN Jr, Bloch KV, Sousa GDS, Silva TLND, Braga JU, Castro MC, Werneck GL.

16-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36928657/>

Blocking NS3-NS4B interaction inhibits dengue virus in non-human primates.

Goethals O, Kaptein SJF, Kesteleyn B, Bonfanti JF, Van Wesenbeeck L, Bardiot D, Verschoor EJ, Verstrepen BE, Fagrouch Z, Putnak JR, Kiemel D, Ackaert O, Straetemans

R, Lachau-Durand S, Geluykens P, Crabbe M, Thys K, Stoops B, Lenz O, Tambuyzer L, De Meyer S, Dallmeier K, McCracken MK, Gromowski GD, Rutvisuttinunt W, Jarman RG, Karasavvas N, Touret F, Querat G, de Lamballerie X, Chatel-Chaix L, Milligan GN, Beasley DWC, Bourne N, Barrett ADT, Marchand A, Jonckers THM, Raboisson P, Simmen K, Chaltin P, Bartenschlager R, Bogers WM, Neyts J, Van Loock M.

Mar-2023

Nature.

<https://pubmed.ncbi.nlm.nih.gov/36922586/>

Efficient generation and characterization of chimeric dengue viral-like particles.

Veena Rani N, Kapoor N, Krishnan A.

Apr-2023

Biochem Biophys Res Commun.

<https://pubmed.ncbi.nlm.nih.gov/36878035/>

Viral-like particles (VLPs) because of their non-infectious and high immunogenic properties have important applications in diagnostics, drug delivery, and vaccine production. They also serve as an attractive model system to study virus assembly and fusion processes. Unlike other flaviviruses, Dengue virus (DENV) is not very efficient in the production of VLPs on the expression of DENV structural proteins. On the other hand, the stem region and transmembrane region (TM) of G protein of Vesicular Stomatitis virus (VSV) alone are sufficient for budding. Here we generated chimeric VLPs replacing regions of stem and transmembrane domain (STEM) or only transmembrane domain (TM) of E protein of DENV-2 with corresponding regions of VSV G protein. Both chimeric proteins secreted VLPs at higher levels than the wild type (2-4 folds) without any significant change in the expression in the cell. Chimeric VLPs could be recognized by a conformational monoclonal antibody, 4G2. They were also found to interact with dengue-infected patient sera effectively thus implying that their antigenic determinants are preserved. In addition, they were able to bind to its putative receptor, heparin with similar affinity as the parent counterpart thus retaining its functional property. However, cell-cell fusion revealed that there is no significant increase in the fusion ability of chimeras as compared to the parent clone, whereas VSV G protein displayed high cell-cell fusion activity. Overall, this study suggests that chimeric dengue VLPs can be taken forward for their likely potential as vaccine production and serodiagnosis.

Current evidences of the efficacy of mosquito mass-trapping interventions to reduce Aedes aegypti and Aedes albopictus populations and Aedes-borne virus transmission.

Jaffal A, Fite J, Baldet T, Delaunay P, Jourdain F, Mora-Castillo R, Olive MM, Roiz D.

06-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36877728/>

Background: Over the past decades, several viral diseases transmitted by *Aedes* mosquitoes-dengue, chikungunya, Zika-have spread outside of tropical areas. To limit the transmission of these viruses and preserve human health, the use of mosquito traps has been developed as a complement or alternative to other vector control techniques. The objective of this work was to perform a systematic review of the existing scientific literature to assess the efficacy of interventions based on adult mosquito trap to control *Aedes* population densities and the diseases they transmit worldwide. **Methods and findings:** Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a systematic review was conducted using the PubMed and Scopus databases. Among the 19 selected papers, lethal ovitraps were used in 16 studies, host-seeking female traps in 3 studies. Furthermore, 16 studies focused on the control of *Ae. aegypti*. Our review showed great heterogeneity in the indicators used to assess trap efficacy: e.g., the number of host-seeking females, the number of gravid females, the proportion of positive containers, the viral infection rate in female mosquitoes or serological studies in residents. Regardless of the type of studied traps, the results of various studies support the efficacy of mass trapping in combination with classical integrated vector control in reducing *Aedes* density. More studies with standardized methodology, and indicators are urgently needed to provide more accurate estimates of their efficacy. **Conclusions:** This review highlights gaps in the demonstration of the efficacy of mass trapping of mosquitoes in reducing viral transmission and disease. Thus, further large-scale cluster randomized controlled trials conducted in endemic areas and including epidemiological outcomes are needed to establish scientific evidence for the reduction of viral transmission risk by mass trapping targeting gravid and/or host-seeking female mosquitoes.

[Structural Motifs and Spatial Structures of Helicase (NS3) and RNA-dependent RNA-polymerase (NS5) of a Flavi-like Kindia tick virus (unclassified Flaviviridae)].

Gladysheva AA, Gladysheva AV, Ternovoi VA, Loktev VB.
11-03-2023
Vopr Virusol.
<https://pubmed.ncbi.nlm.nih.gov/36961231/>

Science-Informed Health Policies for Oral and Systemic Health.

Slavkin HC, Dubois PA, Kleinman DV, Fuccillo R.
16-03-2023
J Healthc Leadersh.
<https://pubmed.ncbi.nlm.nih.gov/36960302/>

Oral, dental and craniofacial (ODC) health has a profound impact on general health and welfare throughout life, yet US dentists and physicians operate across misaligned silos. This protracted division limits access to optimal health, supports fee for services, and exacerbates health disparities. Early in the 20th century, the most frequent dental therapy was tooth extraction: removed infected

teeth were substituted by prosthetic appliances - commonly, dentures or nothing. Most adults assumed becoming edentulous was a normal corollary of aging. With the discovery of penicillin and other antibiotics, healthcare professionals and policy makers predicted infectious diseases would become irrelevant. However, given numerous health threats, including SARS-CoV-2, HIV, multidrug-resistant bacteria, Zika virus, Ebola virus, and now monkeypox, public and professional awareness of transmissible infectious diseases has never been more evident. Ironically, little attention has been paid to unmet transmissible, infectious, common oral diseases - dental caries and periodontal diseases. Therefore, these persist within "the silent and invisible epidemic". The preventable death of a young boy in 2007 from an infected untreated tooth that produced bacterial meningitis is a profound reminder that our nation has vast inequities in education, health, and welfare. The impact of oral infections on hospital-acquired pneumonia, post-operative infection in cardiac valve surgery, and even academic performances of disadvantaged children displayed through sociodemographic characteristics and access to care determinants also are profound! This paper asserts that current and emerging ODC health knowledge and science will inform health policies and advance equity in access to care, affordable costs, and optimal healthcare outcomes. We recommend that legal and regulatory systems and public health programs be required to ensure health equity. A fair healthcare system that addresses holistic healthcare must be transparent, accessible, integrated and provide a standard of oral healthcare based upon scientific evidence for all people across the lifespan.

Improving expression and assembly of difficult-to-express heterologous proteins in *Saccharomyces cerevisiae* by culturing at a sub-physiological temperature.

So KK, Le NMT, Nguyen NL, Kim DH.
23-03-2023
Microb Cell Fact.
<https://pubmed.ncbi.nlm.nih.gov/36959657/>

Immunization against Zika by entrapping live virus in a subcutaneous self-adjuvanting hydrogel.

Hao H, Wu S, Lin J, Zheng Z, Zhou Y, Zhang Y, Guo Q, Tian F, Zhao M, Chen Y, Xu X, Hou L, Wang X, Tang R.
23-03-2023
Nat Biomed Eng.
<https://pubmed.ncbi.nlm.nih.gov/36959404/>

Chikungunya Outbreak in Country with Multiple Vectorborne Diseases, Djibouti, 2019-2020.

Javelle E, de Laval F, Durand GA, Dia A, Ficko C, Bousquet A, Delaune D, Briolant S, Mérens A, Brossier C, Pommier H, Gala F, Courtiol A, Savreux Q, Sicard S, Sanchez JP, Robin F, Simon F, de Lamballerie X, Grard G, Leparco-Goffart I, de Santi VP.
Apr-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36958020/>

During 2019-2020, a chikungunya outbreak occurred in Djibouti City, Djibouti, while dengue virus and malaria parasites were cocirculating. We used blotting paper to detect arbovirus emergence and confirm that it is a robust method for detecting and monitoring arbovirus outbreaks remotely.

Transmission of Zika virus by dendritic cell subsets in skin and vaginal mucosa.

Eder J, Zijlstra-Willems E, Koen G, Kootstra NA, Wolthers KC, Geijtenbeek TB.

06-03-2023

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36949942/>

Zika virus is a member of the Flaviviridae family that has caused recent outbreaks associated with neurological malformations. Transmission of Zika virus occurs primarily *via* mosquito bite but also *via* sexual contact. Dendritic cells (DCs) and Langerhans cells (LCs) are important antigen presenting cells in skin and vaginal mucosa and paramount to induce antiviral immunity. To date, little is known about the first cells targeted by Zika virus in these tissues as well as subsequent dissemination of the virus to other target cells. We therefore investigated the role of DCs and LCs in Zika virus infection. Human monocyte derived DCs (moDCs) were isolated from blood and primary immature LCs were obtained from human skin and vaginal explants. Zika virus exposure to moDCs but not skin and vaginal LCs induced Type I Interferon responses. Zika virus efficiently infected moDCs but neither epidermal nor vaginal LCs became infected. Infection of a human full skin model showed that DC-SIGN expressing dermal DCs are preferentially infected over langerin+ LCs. Notably, not only moDCs but also skin and vaginal LCs efficiently transmitted Zika virus to target cells. Transmission by LCs was independent of direct infection of LCs. These data suggest that DCs and LCs are among the first target cells for Zika virus not only in the skin but also the genital tract. The role of vaginal LCs in dissemination of Zika virus from the vaginal mucosa further emphasizes the threat of sexual transmission and supports the investigation of prophylaxes that go beyond mosquito control.

Editorial: Biological drivers of vector-pathogen interactions - vol II.

Rego ROM, Lopez JE, Cabras-Cruz A.

06-03-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36949813/>

Epidemiological profile of arboviruses in two different scenarios: dengue circulation vs. dengue, chikungunya and Zika co-circulation.

Farias PCS, Pastor AF, Gonçalves JP, do Nascimento IDS, de Souza Ferraz ES, Lopes TRR, do Carmo RF, Côelho MRCD, Silva Júnior JVJ.

22-03-2023

BMC Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36949383/>

Background: The severity and distribution of dengue virus (DENV) infections have been attributed to a complex interaction among viral, host and environmental factors. Herein, we investigated the influence of chikungunya (CHIKV) and Zika (ZIKV) viruses on the epidemiological profile of dengue cases, using Recife, Pernambuco state, Brazil, as a study model. In addition, we described and compared the epidemiological profile related to each arbovirus (DENV vs. CHIKV vs. ZIKV). **Methods:** All cases of dengue, chikungunya and Zika reported to the Pernambuco Health Department in 2011-2013 (DENV circulation) and 2016-2018 (DENV, CHIKV and ZIKV co-circulation) were included in our study. The cases were classified by sex, age and race/color and their distribution was analyzed by the χ^2 test. Furthermore, the data were also analyzed for co-infections. Temperature, humidity and rainfall data were analyzed using one-way ANOVA and paired t-test. **Results:** During 2011-2013, 15,315 dengue cases were diagnosed, most of them female, brown and 20-29 age group. Between 2016 and 2018, 15,870 dengue cases were described, which presented the same profile described above. In the two triennia, the female/male dengue ratio fluctuated significantly, ranging from 1.07 to 1.52. Regarding chikungunya, 7076 cases were reported, most of them female and brown. The female/male ratio also fluctuated significantly, ranging from 1.62 to 2.1. Two main age groups were observed in chikungunya: ≤ 19 years (minority of diagnoses) and ≥ 20 years (majority of diagnoses). In the same triennium, 266 Zika cases were reported to the Pernambuco Health Department, mainly in females and in the 0-9 and 20-39 age groups. In general, 119 co-infections were identified: 117 DENV-CHIKV, 1 CHIKV-ZIKV and 1 DENV-CHIKV-ZIKV. Concerning climate data, only the humidity in 2011 was significantly different from the other years. **Conclusion:** The epidemiological profile of dengue cases did not change after the introduction of CHIKV and ZIKV. Females were the most diagnosed with dengue, chikungunya or Zika, however we found important differences in the age profile of these arboviruses, which should be considered by public health policies, as well as investigated in future studies of virus-host interaction.

Precursor to Dengue: Projecting Effects of Climate Change on Mosquito Density in Southeast Asia.

Osuolale O.

Mar-2023

Environ Health Perspect.

<https://pubmed.ncbi.nlm.nih.gov/36947409/>

First official record of Aedes (Stegomyia) albopictus (Diptera: Culicidae) in the Acre State, Northern Brazil.

Rocha RDC, Cardoso ADS, Souza JL, Pereira EDS, Amorim MF, Souza MSM, Medeiros CL, Monteiro MFM, Meneguetti DUO, Paula MB, Brilhante AF, Lima-Camara TN.

20-03-2023

Rev Inst Med Trop Sao Paulo.
<https://pubmed.ncbi.nlm.nih.gov/36946816/>

Aedes (*Stegomyia*) *albopictus* (Skuse, 1854) was reported in Brazil for the first time in 1986 and has shown marked expansion throughout the Brazilian territory. During a routine activity to control dengue fever conducted by the Division of Entomology of the Municipal Health Department in Rio Branco city, adults and immatures of Culicidae were collected in a peri-urban area. The identified Culicidae forms indicated that they belonged to the species *Ae. albopictus*. This is the first official record of the presence of *Ae. albopictus* in the Acre State, confirming its current presence in all Brazilian states.

Urban risk factors for human Rift Valley fever virus exposure in Kenya.

Gerken KN, Mutuku FM, Ndenga BA, Agola GA, Migliore E, Fabre EP, Malumbo S, Shaita KN, Rezende IM, LaBeaud AD.

14-07-2022

PLOS Glob Public Health.
<https://pubmed.ncbi.nlm.nih.gov/36962424/>

The Rift Valley fever virus (RVFV) is a zoonotic arbovirus that can also transmit directly to humans from livestock. Previous studies have shown consumption of sick animal products are risk factors for RVFV infection, but it is difficult to disentangle those risk factors from other livestock rearing activities. Urban areas have an increased demand for animal source foods, different vector distributions, and various arboviruses are understood to establish localized urban transmission cycles. Thus far, RVFV is an unevaluated public health risk in urban areas within endemic regions. We tested participants in our ongoing urban cohort study on dengue (DENV) and chikungunya (CHIKV) virus for RVFV exposure and found 1.6% (57/3,560) of individuals in two urban areas of Kenya had anti-RVFV IgG antibodies. 88% (50/57) of RVFV exposed participants also had antibodies to DENV, CHIKV, or both. Although livestock ownership was very low in urban study sites, RVFV exposure was overall significantly associated with seeing goats around the homestead (OR = 2.34 (CI 95%: 1.18-4.69, $p = 0.02$) and in Kisumu, RVFV exposure was associated with consumption of raw milk (OR = 6.28 (CI 95%: 0.94-25.21, $p = 0.02$). In addition, lack of piped water and use of small jugs (15-20 liters) for water was associated with a higher risk of RVFV exposure (OR = 5.36 (CI 95%: 1.23-16.44, $p = 0.01$) and this may contribute to interepidemic vector-borne maintenance of RVFV. We also investigated perception towards human vaccination for RVFV and identified high acceptance (91% (97/105) at our study sites. This study provides baseline evidence to guide future studies investigating the urban potential of RVFV and highlights the unexplored role of animal products in continued spread of RVFV.

March 2019 dengue fever outbreak at the Kenyan south coast involving dengue virus serotype 3, genotypes III and V.

Muthanje EM, Kimita G, Nyataya J, Njue W, Mulili C, Mugweru J, Mutai B, Kituyi SN, Waitumbi J.

24-03-2023

PLOS Glob Public Health.
<https://pubmed.ncbi.nlm.nih.gov/36962260/>

Influence of climate variables on dengue fever occurrence in the southern region of Thailand.

Abdulsalam FI, Antunez P, Yimthiang S, Jawjit W.

20-04-2022

PLOS Glob Public Health.
<https://pubmed.ncbi.nlm.nih.gov/36962156/>

Predict the incidence of Guillain Barré Syndrome and arbovirus infection in Mexico, 2014-2019.

Arriaga-Nieto L, Hernández-Bautista PF, Vallejos-Parás A, Grajales-Muñiz C, Rojas-Mendoza T, Cabrera-Gaytán DA, Grijalva-Otero I, Cacho-Díaz B, Jaimes-Betancourt L, Padilla-Velazquez R, Valle-Alvarado G, Perez-Andrade Y, Ovalle-Luna OD, Rivera-Mahey M.

25-03-2023

PLOS Glob Public Health.
<https://pubmed.ncbi.nlm.nih.gov/36962143/>

The Dengue (DENV), Zika (ZIKV), and Chikungunya (CHIKV) virus infections have been linked to Guillain-Barré syndrome (GBS). GBS has an estimated lethality of 4% to 8%, even with effective treatment. Mexico is considered a hyperendemic country for DENV due to the circulation of four serotypes, and the ZIKV and CHIKV viruses have also been circulating in the country. The objective of this study was to predict the number of GBS cases in relation to the cumulative incidence of ZIKV / DENV / CHIKV in Mexico from 2014 to 2019. A six-year time series ecological study was carried out from GBS cases registered in the Acute Flaccid Paralysis (AFP) Epidemiological Surveillance System (ESS), and DENV, ZIKV and CHIKV estimated cases from cases registered in the epidemiological vector-borne diseases surveillance system. The results shows that the incidence of GBS in Mexico is positively correlated with DENV and ZIKV. For every 1,000 estimated DENV cases, 1.45 GBS cases occurred on average, and for every 1,000 estimated ZIKV cases, 1.93 GBS cases occurred on average. A negative correlation between GBS and CHIKV estimated cases was found. The increase in the incidence of GBS cases in Mexico can be predicted by observing DENV and ZIKV cases through the epidemiological surveillance systems. These results can be useful in public health by providing the opportunity to improve capacities for the prevention of arbovirus diseases and for the timely procurement of supplies for the treatment of GBS.

Majority of pediatric dengue virus infections in Kenya do not meet 2009 WHO criteria for dengue diagnosis.

Khan A, Ndenga B, Mutuku F, Bosire CM, Okuta V, Ronga CO, Mutai NK, Musaki SK, Chebii PK, Maina PW, Jembe Z, Amugongo JS, Malumbo SL, Ng'ang'a CM, LaBeaud D.

20-04-2022

PLOS Glob Public Health.
<https://pubmed.ncbi.nlm.nih.gov/36962138/>

Prediction of dengue annual incidence using seasonal climate variability in Bangladesh between 2000 and 2018.

Hossain MP, Zhou W, Ren C, Marshall J, Yuan HY.

09-05-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962108/>

The incidence of dengue has increased rapidly in Bangladesh since 2010 with an outbreak in 2018 reaching a historically high number of cases, 10,148. A better understanding of the effects of climate variability before dengue season on the increasing incidence of dengue in Bangladesh can enable early warning of future outbreaks. We developed a generalized linear model to predict the number of annual dengue cases based on monthly minimum temperature, rainfall and sunshine prior to dengue season. Variable selection and leave-one-out cross-validation were performed to identify the best prediction model and to evaluate the model's performance. Our model successfully predicted the largest outbreak in 2018, with 10,077 cases (95% CI: [9,912-10,276]), in addition to smaller outbreaks in five different years (2003, 2006, 2010, 2012 and 2014) and successfully identified the increasing trend in cases between 2010 and 2018. We found that temperature was positively associated with the annual incidence during the late winter months (between January and March) but negatively associated during the early summer (between April and June). Our results might be suggest an optimal minimum temperature for mosquito growth of 21-23°C. This study has implications for understanding how climate variability has affected recent dengue expansion in neighbours of Bangladesh (such as northern India and Southeast Asia).

Magnitude and kinetics of the human immune cell response associated with severe dengue progression by single-cell proteomics.

Robinson ML, Glass DR, Duran V, Agudelo Rojas OL, Sanz AM, Consuegra M, Sahoo MK, Hartmann FJ, Bosse M, Gelvez RM, Bueno N, Pinsky BA, Montoya JG, Maecker H, Estupiñan Cardenas MI, Villar Centeno LA, Garrido EMR, Rosso F, Bendall SC, Einav S.

24-03-2023

Sci Adv.

<https://pubmed.ncbi.nlm.nih.gov/36961888/>

Approximately 5 million dengue virus-infected patients progress to a potentially life-threatening severe dengue (SD) infection annually. To identify the immune features and temporal dynamics underlying SD progression, we performed deep immune profiling by mass cytometry of PBMCs collected longitudinally from SD progressors (SDp) and uncomplicated dengue (D) patients. While D is characterized by early activation of innate immune responses, in SDp there is rapid expansion and activation of IgG-secreting plasma cells and memory and regulatory T cells. Concurrently, SDp, particularly children, demonstrate increased proinflammatory NK cells, inadequate expansion of CD16⁺ monocytes, and high expression of the FcγR CD64 on myeloid cells, yet a

signature of diminished antigen presentation. Syndrome-specific determinants include suppressed dendritic cell abundance in shock/hemorrhage versus enriched plasma cell expansion in organ impairment. This study reveals uncoordinated immune responses in SDp and provides insights into SD pathogenesis in humans with potential implications for prediction and treatment.

Erster Impfstoff gegen Dengue-Fieber zugelassen.

Facharztmagazine R.

Mar-2023

MMW Fortschr Med.

<https://pubmed.ncbi.nlm.nih.gov/36961720/>

Rage

RVG Peptide-Functionalized Favipiravir Nanoparticle Delivery System Facilitates Antiviral Therapy of Neurotropic Virus Infection in a Mouse Model.

Ren M, Zhou Y, Tu T, Jiang D, Pang M, Li Y, Luo Y, Yao X, Yang Z, Wang Y.

19-03-2023

Int J Mol Sci.

<https://pubmed.ncbi.nlm.nih.gov/36982925/>

Neurotropic viruses severely damage the central nervous system (CNS) and human health. Common neurotropic viruses include rabies virus (RABV), Zika virus, and poliovirus. When treating neurotropic virus infection, obstruction of the blood-brain barrier (BBB) reduces the efficiency of drug delivery to the CNS. An efficient intracerebral delivery system can significantly increase intracerebral delivery efficiency and facilitate antiviral therapy. In this study, a rabies virus glycopeptide (RVG) functionalized mesoporous silica nanoparticle (MSN) packaging favipiravir (T-705) was developed to generate T-705@MSN-RVG. It was further evaluated for drug delivery and antiviral treatment in a VSV-infected mouse model. The RVG, a polypeptide consisting of 29 amino acids, was conjugated on the nanoparticle to enhance CNS delivery. The T-705@MSN-RVG caused a significant decrease in virus titers and virus proliferation without inducing substantial cell damage in vitro. By releasing T-705, the nanoparticle promoted viral inhibition in the brain during infection. At 21 days post-infection (dpi), a significantly enhanced survival ratio (77%) was observed in the group inoculated with nanoparticle compared with the non-treated group (23%). The viral RNA levels were also decreased in the therapy group at 4 and 6 dpi compared with that of the control group. The T-705@MSN-RVG could be considered a promising system for CNS delivery for treating neurotropic virus infection.

Quantitative analysis of rabies virus-based synaptic connectivity tracing.

Tran-Van-Minh A, Ye Z, Rancz E.

30-03-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/36996085/>

Monosynaptically restricted rabies viruses have been used for more than a decade for synaptic connectivity tracing. However, the verisimilitude of quantitative conclusions drawn from these experiments is largely unknown. The primary reason is the simple metrics commonly used, which generally disregard the effect of starter cell numbers. Here we present an experimental dataset with a broad range of starter cell numbers and explore their relationship with the number of input cells across the brain using descriptive statistics and modelling. We show that starter cell numbers strongly affect input fraction and convergence index measures, making quantitative comparisons unreliable. Furthermore, we suggest a principled way to analyse rabies derived connectivity data by taking advantage of the starter vs input cell relationship that we describe and validate across independent datasets.

Profile of human anti-rabies care and post-exposure prophylaxis in the state of São Paulo.

Andrade BFMDC, Queiroz LH, Marinho M.

27-03-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/36995786/>

Epidemiological profile and management practices of animal bite cases in a tertiary care hospital of Haryana: A cross-sectional study.

Sachdeva A, Vinay, Kumar T, Yadav G, Tondwal J.

Dec-2022

J Family Med Prim Care.

<https://pubmed.ncbi.nlm.nih.gov/36994020/>

A regimen compression strategy for commercial vaccines leveraging an injectable hydrogel depot technology for sustained vaccine exposure.

Yan J, Ou BS, Saouaf OM, Meany EL, Eckman N, Appel EA.

25-03-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993717/>

Equitable global access to vaccines requires we overcome challenges associated with complex immunization schedules and their associated economic burdens that hinder delivery in under resourced environments. The rabies vaccine, for example, requires multiple immunizations for effective protection and each dose is cost prohibitive, and therefore inaccessibility disproportionately impacts low- and middle-income countries. In this work we developed an injectable hydrogel depot technology for sustained delivery of commercial inactivated rabies virus vaccines. In a mouse model, we showed that a single immunization of a hydrogel-based rabies vaccine elicited comparable antibody titers to a standard prime-boost bolus regimen of a commercial rabies vaccine, despite these hydrogel vaccines comprising only half of the total dose delivered in the bolus control. Moreover, these hydrogel-based vaccines elicited similar antigen-specific T-cell responses

and neutralizing antibody responses compared to the bolus vaccine. Notably, we demonstrated that while addition of a potent clinical TLR4 agonist adjuvant to the gels slightly improved binding antibody responses, inclusion of this adjuvant to the inactivated virion vaccine was detrimental to neutralizing responses. Taken together, these results suggest that these hydrogels can enable an effective regimen compression and dosesparing strategy for improving global access to vaccines.

Rabies virus-based barcoded neuroanatomy resolved by single-cell RNA and in situ sequencing.

Zhang A, Jin L, Yao S, Matsuyama M, van Velthoven C, Sullivan H, Sun N, Kellis M, Tasic B, Tasic B, Wickersham IR, Chen X.

18-03-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993334/>

Mapping the connectivity of diverse neuronal types provides the foundation for understanding the structure and function of neural circuits. High-throughput and low-cost neuroanatomical techniques based on RNA barcode sequencing have the potential to achieve circuit mapping at cellular resolution and a brain-wide scale, but existing Sindbis virus-based techniques can only map long-range projections using anterograde tracing approaches. Rabies virus can complement anterograde tracing approaches by enabling either retrograde labeling of projection neurons or monosynaptic tracing of direct inputs to genetically targeted postsynaptic neurons. However, barcoded rabies virus has so far been only used to map non-neuronal cellular interactions *in vivo* and synaptic connectivity of cultured neurons. Here we combine barcoded rabies virus with single-cell and *in situ* sequencing to perform retrograde labeling and transsynaptic labeling in the mouse brain. We sequenced 96 retrogradely labeled cells and 295 transsynaptically labeled cells using single-cell RNAseq, and 4,130 retrogradely labeled cells and 2,914 transsynaptically labeled cells *in situ*. We determined the transcriptomic identities of rabies virus-infected cells robustly using both single-cell RNA-seq and *in situ* sequencing. We then distinguished long-range projecting cortical cell types from multiple cortical areas and identified cell types with converging or diverging synaptic connectivity. Combining *in situ* sequencing with barcoded rabies virus thus complements existing sequencing-based neuroanatomical techniques and provides a potential path for mapping synaptic connectivity of neuronal types at scale.

Operational efficiency and out-of-pocket expenditure in attendees of anti-rabies vaccination: A time and motion study.

Patnaik A, Dash A, Pradhan S, Nanda S.

Nov-2022

J Family Med Prim Care.

<https://pubmed.ncbi.nlm.nih.gov/36993008/>

First Expert Elicitation of Knowledge on Possible Drivers of Observed Increasing

Human Cases of Tick-Borne Encephalitis in Europe.

Saegerman C, Humblet MF, Leandri M, Gonzalez G, Heyman P, Sprong H, L'Hostis M, Moutailler S, Bonnet SI, Haddad N, Boulanger N, Leib SL, Hoch T, Thiry E, Bournez L, Kerlik J, Velay A, Jore S, Jourdain E, Gilot-Fromont E, Brugger K, Geller J, Studahl M, Knap N, Avšič-Županc T, Růžek D, Zomer TP, Bødker R, Berger TFH, Martin-Latil S, De Regge N, Raffetin A, Lacour SA, Klein M, Lernout T, Quillery E, Hubálek Z, Ruiz-Fons F, Estrada-Peña A, Fravallo P, Kooh P, Ettore F, Gossner CM, Purse B.

20-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992499/>

Comparison of Pan-Lyssavirus RT-PCRs and Development of an Improved Protocol for Surveillance of Non-RABV Lyssaviruses.

Drzewnioková P, Marciano S, Leopardi S, Panzarin V, De Benedictis P.

04-03-2023

Viruses.

<https://pubmed.ncbi.nlm.nih.gov/36992389/>

Rabies is a zoonotic and fatal encephalitis caused by members of the *Lyssavirus* genus. Among them, the most relevant species is *Lyssavirus rabies*, which is estimated to cause 60,000 human and most mammal rabies deaths annually worldwide. Nevertheless, all lyssaviruses can invariably cause rabies, and therefore their impact on animal and public health should not be neglected. For accurate and reliable surveillance, diagnosis should rely on broad-spectrum tests able to detect all known lyssaviruses, including the most divergent ones. In the present study, we evaluated four different pan-lyssavirus protocols widely used at an international level, including two real-time RT-PCR assays (namely LN34 and JW12/N165-146), a hemi-nested RT-PCR and a one-step RT-PCR. Additionally, an improved version of the LN34 assay ((n) LN34) was developed to increase primer-template complementarity with respect to all lyssavirus species. All protocols were evaluated in silico, and their performance was compared in vitro employing 18 lyssavirus RNAs (encompassing 15 species). The (n) LN34 assay showed enhanced sensitivity in detecting most lyssavirus species, with limits of detection ranging from 10 to 100 RNA copies/μL depending on the strain, while retaining high sensitivity against *Lyssavirus rabies*. The development of this protocol represents a step forward towards improved surveillance of the entire *Lyssavirus* genus.

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

Kapur V.

16-03-2023

Vaccines (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36992260/>

Endemic or regionally limited bacterial and viral infections in haematopoietic stem-cell transplantation recipients: a Worldwide Network for Blood and Marrow Transplantation (WBMT) Review.

Muhsen IN, Galeano S, Niederwieser D, Koh MBC, Ljungman P, Machado CM, Kharfan-Dabaja MA, de la Camara R, Kodera Y, Szer J, Rasheed W, Cesaro S, Hashmi SK, Seber A, Atsuta Y, Saleh MFM, Srivastava A, Styczynski J, Alrajhi A, Almaghrabi R, Abid MB, Chemaly RF, Gergis U, Brissot E, El Fakih R, Riches M, Mikulska NA, Worel N, Weisdorf D, Greinix H, Cordonnier C, Aljurf M.

Apr-2023

Lancet Haematol.

<https://pubmed.ncbi.nlm.nih.gov/36990623/>

Structural insights into the multifunctionality of rabies virus P3 protein.

Sethi A, Rawlinson SM, Dubey A, Ang CS, Choi YH, Yan F, Okada K, Rozario AM, Brice AM, Ito N, Williamson NA, Hatters DM, Bell TDM, Arthanari H, Moseley GW, Gooley PR.

04-04-2023

Proc Natl Acad Sci U S A.

<https://pubmed.ncbi.nlm.nih.gov/36989298/>

Viruses form extensive interfaces with host proteins to modulate the biology of the infected cell, frequently via multifunctional viral proteins. These proteins are conventionally considered as assemblies of independent functional modules, where the presence or absence of modules determines the overall composite phenotype. However, this model cannot account for functions observed in specific viral proteins. For example, rabies virus (RABV) P3 protein is a truncated form of the pathogenicity factor P protein, but displays a unique phenotype with functions not seen in longer isoforms, indicating that changes beyond the simple complement of functional modules define the functions of P3. Here, we report structural and cellular analyses of P3 derived from the pathogenic RABV strain Nishigahara (Nish) and an attenuated derivative strain (Ni-CE). We identify a network of intraprotomer interactions involving the globular C-terminal domain and intrinsically disordered regions (IDRs) of the N-terminal region that characterize the fully functional Nish P3 to fluctuate between open and closed states, whereas the defective Ni-CE P3 is predominantly open. This conformational difference appears to be due to the single mutation N226H in Ni-CE P3. We find that Nish P3, but not Ni-CE or N226H P3, undergoes liquid-liquid phase separation and this property correlates with the capacity of P3 to interact with different cellular membrane-less organelles, including those associated with immune evasion and pathogenesis. Our analyses propose that discrete functions of a critical multifunctional viral protein depend on the conformational arrangements

of distant individual domains and IDRs, in addition to their independent functions.

Fatal Human Rabies Infection with Suspected Host-mediated Failure of Post-Exposure Prophylaxis Following a Recognized Zoonotic Exposure-Minnesota, 2021.

Holzbauer SM, Schrodtt CA, Prabhu RM, Asch-Kendrick RJ, Ireland M, Klumb C, Firestone MJ, Liu G, Harry K, Ritter JM, Levine MZ, Orciari LA, Wilkins K, Yager P, Gigante CM, Ellison JA, Zhao H, Niezgoda M, Li Y, Levis R, Scott D, Satheshkumar PS, Petersen BW, Rao AK, Bell WR, Bjerk SM, Forrest S, Gao W, Dasheiff R, Russell K, Pappas M, Kiefer J, Bickler W, Wiseman A, Jurantee J, Reichard RR, Smith KE, Lynfield R, Scheftel J, Wallace RM, Bonwitt J.

29-03-2023

Clin Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36988328/>

Design and Optimization of a Monkeypox virus Specific Serological Assay.

Taha TY, Townsend MB, Pohl J, Karem KL, Damon IK, Mbala Kingebeni P, Muyembe Tamfum JJ, Martin JW, Pittman PR, Huggins JW, Satheshkumar PS, Bagarozzi DA Jr, Reynolds MG, Hughes LJ.

01-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986317/>

Monkeypox virus (MPXV), a member of the *Orthopoxvirus* (OPXV) genus, is a zoonotic virus, endemic to central and western Africa that can cause smallpox-like symptoms in humans with fatal outcomes in up to 15% of patients. The incidence of MPXV infections in the Democratic Republic of the Congo, where the majority of cases have occurred historically, has been estimated to have increased as much as 20-fold since the end of smallpox vaccination in 1980. Considering the risk global travel carries for future disease outbreaks, accurate epidemiological surveillance of MPXV is warranted as demonstrated by the recent Mpox outbreak, where the majority of cases were occurring in non-endemic areas. Serological differentiation between childhood vaccination and recent infection with MPXV or other OPXVs is difficult due to the high level of conservation within OPXV proteins. Here, a peptide-based serological assay was developed to specifically detect exposure to MPXV. A comparative analysis of immunogenic proteins across human OPXVs identified a large subset of proteins that could potentially be specifically recognized in response to a MPXV infection. Peptides were chosen based upon MPXV sequence specificity and predicted immunogenicity. Peptides individually and combined were screened in an ELISA against serum from well-characterized Mpox outbreaks, vaccinee sera, and smallpox sera collected prior to eradication. One peptide combination was successful with ~86% sensitivity and ~90% specificity. The performance of the assay was assessed against the OPXV IgG ELISA in the context of a serosurvey by retrospectively screening a set of serum specimens from the region in Ghana believed to

have harbored the MPXV-infected rodents involved in the 2003 United States outbreak.

Rabies virus glycoprotein 29 (RVG29) promotes CAR-T immunotherapy for glioma.

Ji F, Xu L, Long K, Zhang F, Zhang M, Lu X, Xia M, Chen J, Du Y, Tang Y, Wu H, Shi Y, Ma R, Li J, Chen Z, Xu B, Zhang Q, Liang J, Jia S, Hu Z, Guo Z.

26-03-2023

Transl Res.

<https://pubmed.ncbi.nlm.nih.gov/36977441/>

Chimeric antigen receptor T cell (CAR-T) therapy has limited efficacy for treating glioma because of the infiltrative nature of the blood-brain barrier (BBB) and T cell exhaustion. Conjugation with rabies virus glycoprotein (RVG) 29 enhances the brain-related efficacy of various agents. Here we assess whether RVG enhances the ability of CAR-T cells to cross the BBB and improves their immunotherapy. We generated 70R CAR-T cells (anti-CD70 CAR-T modified with RVG29) and validated their tumor-killing efficacy in vitro and in vivo. We validated their effects on tumor regression in a human glioma mouse orthotopic xenograft model as well as in patient-derived orthotopic xenograft (PDOX) models. The signaling pathways activated in 70R CAR-T cells were revealed by RNA sequencing. The 70R CAR-T cells we generated showed effective antitumor function against CD70+ glioma cells both in vitro and in vivo. 70R CAR-T cells were better able to cross the BBB into the brain than CD70 CAR-T cells under the same treatment conditions. Moreover, 70R CAR-T cells significantly promote the regression of glioma xenografts and improve the physical characteristics of mice without causing overt adverse effects. RVG modification enables CAR-T cells to cross the BBB, and stimulation with glioma cells induces 70R CAR-T cells to expand in a resting state. The modification of RVG29 has a positive impact on CAR-T therapy for brain tumors and may have potential in CAR-T therapy for glioma.

A pilot study: Validation of dried blood spots (DBS) to assess SARS-CoV2 IgG antibody immunoassays in underserved minority population.

Yoo JY, De SL, Sarkar A, Adams JH, Groer M.

Apr-2023

Heliyon.

<https://pubmed.ncbi.nlm.nih.gov/36974321/>

Assessing the extent and public health impact of bat predation by domestic animals using data from a rabies passive surveillance program.

Wilson AG, Fehlner-Gardiner C, Wilson S, Pierce KN, McGregor GF, González C, Luszcz TMJ.

11-05-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962180/>

Domestic animals can serve as consequential conveyors of zoonotic pathogens across wildlife-human interfaces. Still,

there has been little study on how different domestic species and their behaviors influence the zoonotic risk to humans. In this study, we examined patterns of bat encounters with domestic animals that resulted in submission for testing at the rabies laboratories of the Canadian Food Inspection Agency (CFIA) during 2014-2020. Our goals were specifically to examine how the number of bats submitted and the number of rabies positive bats varied by the type of domestic animal exposure and whether domestic cats were indoor or free-roaming. The CFIA reported 6258 bat submissions for rabies testing, of which 41.5% and 8.7% had encounter histories with cats and dogs, respectively. A much smaller fraction of bat submissions (0.3%) had exposure to other domestic animals, and 49.5% had no domestic animal exposure. For the bat submissions related to cats, and where lifestyle was noted, 91.1% were associated with free-roaming cats and 8.9% with indoor cats. Model results indicated the probability of a rabies-positive bat was the highest with a history of dog association (20.2%), followed by bats with no animal exposure (16.7%), free-roaming cats (6.9%), cats with unspecified histories (6.0%) and the lowest probability associated with non-free-roaming (indoor) cats (3.8%). Although there was lower rabies prevalence in bats associated with cats compared to dogs, the 4.8 fold higher number of cat-bat interactions cumulatively leads to a greater overall rabies exposure risk to humans from any free-roaming outdoor cats. This study suggests that free-roaming owned cats may have an underappreciated role in cryptic rabies exposures in humans and as a significant predator of bats. Preventing free-roaming in cats is a cost-effective and underutilized public health recommendation for rabies prevention that also synergistically reduces the health burden of other feline-associated zoonotic diseases and promotes feline welfare and wildlife conservation.

[Lethal cases of lyssavirus encephalitis in humans after contact with bats in the Russian Far East in 2019-2021].

Poleshchuk EM, Tagakova DN, Sidorov GN, Orlova TS, Gordeiko NS, Kaiserov AZ.

11-03-2023

Vopr Virusol.

<https://pubmed.ncbi.nlm.nih.gov/36961235/>

Introduction: On the territory of Russia four species of lyssaviruses (genus *Lyssavirus*) were identified, three of them caused human deaths. **The aim of work:** to characterize fatal cases in humans after contacts with bats in the Far East in 2018-2021 and to perform typing of isolated pathogens. **Materials and methods:** Lyssavirus infection was confirmed in samples of sectional material from people who died in the Amur Region in 2019, in the Primorsky Krai in 2019 and 2021. Diagnostics was performed by fluorescent antibody test (FAT) and RT-PCR using diagnostic kits of domestic production. Viruses were isolated in a bioassay. The nucleoprotein sequences were analyzed after 1st passage. The analysis of phylogenetic relationships and the construction of a dendrogram were performed using the MEGA7 software. **Results:** The viruses that caused the fatal cases in humans in the Amur Region and Primorsky Krai share more than 90% identity to

Lyssavirus irkut detected in Russia and China. Together they form a separate monophyletic cluster with 100% bootstrap support. **Conclusion:** On the territory of Russia, monitoring of bat populations for infection with lyssaviruses is relevant. The material of people who died from encephalomyelitis of unknown etiology within 1015 days from the onset of the disease must be examined for lyssavirus infection. It is necessary to develop PCR assays that employ genus-specific primers. The use of molecular biological methods is promising for improving the diagnosis of rabies and epidemiological surveillance, as well as increasing the efficiency of the system of biological safety of the population of the Russian Federation.

Trachome

Water, Sanitation, and Hygiene (WASH) Factors Influencing the Effectiveness of Mass Drug Administration to Eliminate Trachoma as a Public Health Problem in Malawi.

Dyer CEF, Kalua K, Chisambi AB, Wand H, McManus H, Liu B, Kaldor JM, Vaz Nery S.

28-03-2023

Ophthalmic Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/36987395/>

Purpose: Following a national population-based trachoma survey in Malawi one round of azithromycin mass drug administration (MDA) was carried out, with a post-MDA impact survey showing TF prevalence below 5% and considered eliminated as a public health problem. However, active trachoma was still present in over 200 children. We assessed whether water, sanitation, and hygiene (WASH) factors were associated with ongoing presence of TF in children aged 1-9 years following MDA. **Methods:** A secondary analysis was performed on a subset of the post-MDA impact survey data for children aged 1-9 years. We used a logistic regression analysis, adjusted for clustering at the household and village level. **Results:** Among 16,142 children aged 1-9 years, 209 (1.3%) had TF after MDA. Factors associated with a significantly lower odds of TF after MDA were living in a household with a handwashing facility (aOR: 0.37) and living in a household where water for washing is located further away from the home (30 min away aOR: 0.39, $p = .034$, or more than 1 h away aOR: 0.31, $p = .018$) compared with water in the yard. **Conclusion:** The inverse association between a domestic handwashing facility and TF is consistent with previous findings, but the association of increasing distance to collect water for washing with a reduced risk of TF was unexpected and may reflect the impact of drought and unmeasured behavioural factors related to water usage. A more comprehensive collection of sociodemographic and WASH factor information in population-based trachoma surveys will provide insight into achieving and maintaining low levels of trachoma.

Preliminary assessment of *Onchocerca*-induced visual impairment using clinical

fundus camera in Gashaka local government area of Taraba state, north eastern Nigeria.

Olamiju FO, Mogaji HO, Bjørn MT, Marcus AJ, Oduwa V, Olamiju OJ, Nzunde M, Ikyerga DK, Hopkins A.
11-03-2023

Parasite Epidemiol Control.

<https://pubmed.ncbi.nlm.nih.gov/36969391/>

Introduction: Onchocerciasis is the world's second leading cause of infectious blindness and remains a major problem in parts of Africa. In light of the efforts targeted towards improving ongoing elimination program, this study assessed onchocerca-induced visual impairments in Gashaka local government areas (LGA) in Taraba State, north-eastern Nigeria. **Methods:** In 2019, we recruited 158 consenting visually impaired persons across three communities in Garbabi ward of Gashaka LGA. To avoid confusion with co-endemic trachoma, the integrity of the tarsal conjunctiva, eyelashes were assessed using direct light. The anterior segment of the eye was also examined using a torchlight with oblique illumination. However, the posterior segment of the eye was assessed using a fundus camera. Two photographic images for the left and right eye of each participant were captured using the clinical fundus camera. The photographic eye images that were too dark were discarded, and only clear images were analyzed by two ophthalmologists. An ocular manifestation report was recorded for each participant following consensus between the ophthalmologists. **Results:** Of the 316 photographic eye images, almost half 146 (46.2%) from 73 participants were just too destroyed for light to penetrate and was not included in the analysis. Only 170 from 85 participants were clear and examinable. A total of 33 (39%) participants had chorioretinitis suggestive of onchocerciasis, including 22(25.9%) with chorio-retinal atrophy, 7(8.2%) and 4(4.7%) had chorioretinal atrophy in combination with early cataract and signs of trachoma respectively. In addition, 3(3.5%) of the participant had eye images which showed lens opacities, 1(1.2%) showed signs of keratoconus and 1(1.2%) showed a scared and pigmented cornea, possibly due to onchocerciasis. Furthermore, 28 (32.9%) had some ill-defined changes and 19 (22.4%) showed poorly defined chorio-retinal atrophy. **Conclusion:** In a bid to sustain MDA gains towards elimination of onchocerciasis, this work highlights the need for continuous assessment of onchocerciasis induced visual impairment, strengthening of ivermectin delivery and optimizing compliance and patient care among affected populations. These would require resource acquisition and local capacity building. Our preliminary findings call for further operational research on ocular morbidity as well as future stakeholders' consultations in this important and understudied area.

Global trends in blindness and vision impairment due to corneal opacity 1984-2020: a meta-analysis.

Wang E, Kong X, Wolle M, Gasquet N, Ssekasanvu J, Mariotti SP, Bourne R, Taylor H, Resnikoff S, West S.
22-05-2023

Ophthalmology.

<https://pubmed.ncbi.nlm.nih.gov/36963570/>

Topic: We provide global estimates of the prevalence of corneal blindness and vision impairment in adults 40 years and older and examine the burden by age, gender, and geographic region from 1984-2020. **Clinical relevance:** Corneal opacities (CO) are among the top five causes of blindness worldwide, yet the global prevalence, regional differences, and risk factors are unclear. **Methods:** Abstracted data from the published literature and surveys were obtained from the Global Burden of Disease Vision Loss Expert Group. We supplemented this by an independent systematic literature search of PubMed, Embase, Web of Science, Scopus, and Cochrane. Studies that provided CO vision impairment data based on population-based surveys for subjects 40 years of age or older were included, for a total of 244. For each of the four outcomes of blindness and moderate to severe vision impairment (MSVI) caused by trachomatous and non-trachomatous CO (NTCO), time trends and differences in prevalence by region, age, and sex were evaluated using a Poisson log-linear model with a generalized estimating equation method. Age-standardized estimates of global prevalence of blindness and MSVI were calculated using the 2015 United Nations standard populations. **Results:** The global prevalence of blindness due to NTCO in those 40 years and older was 0.081% (95% CI=0.049% to 0.315%); MSVI was 0.130% (95% CI= 0.087% to 0.372%). There was a significant increase with age (prevalence rate ratio=2.15, 95% CI=1.99-2.32). Latin America and Europe had the lowest rates, with 2-8 fold higher rates of blindness/MSVI in the other regions. The global prevalence of blindness due to trachomatous CO in those 50 years and older was 0.013% (95% CI=0.006% to 0.043%); MSVI was 0.180% (95% CI=0.006% to 0.049%). Trachomatous CO blindness and MSVI increased with age and female gender, and rates were significantly higher in the African regions; a decrease in blindness rates over time was found (prevalence rate ratio estimate=0.91, 95% CI=0.86-0.96). **Conclusion:** An estimated 5.5 million persons worldwide are bilaterally blind or with MSVI due to CO, with an additional 6.2 million unilaterally blind. Trachomatous CO blindness is declining over time, likely due to the massive scaleup of the global trachoma elimination program and overall socioeconomic development.

Assessment of the status of improved F&E trachoma control practices among children of agro-pastoralists in Southern Ethiopia: a mixed design survey using theory of triadic influences.

Lakew S, Asefa G, Zerdo Z.

23-05-2023

BMC Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36959544/>

Ulcère de Buruli

Deep learning for AI-based diagnosis of skin-related neglected tropical diseases: a pilot study.

Yotsu R, Ding Z, Hamm J, Blanton R.

15-03-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993502/>

Background: Deep learning, which is a part of a broader concept of artificial intelligence (AI) and/or machine learning has achieved remarkable success in vision tasks. While there is growing interest in the use of this technology in diagnostic support for skin-related neglected tropical diseases (skin NTDs), there have been limited studies in this area and fewer focused on dark skin. In this study, we aimed to develop deep learning based AI models with clinical images we collected for five skin NTDs, namely, Buruli ulcer, leprosy, mycetoma, scabies, and yaws, to understand how diagnostic accuracy can or cannot be improved using different models and training patterns. **Methodology:** This study used photographs collected prospectively in Côte d'Ivoire and Ghana through our ongoing studies with use of digital health tools for clinical data documentation and for teledermatology. Our dataset included a total of 1,709 images from 506 patients. Two convolutional neural networks, ResNet-50 and VGG-16 models were adopted to examine the performance of different deep learning architectures and validate their feasibility in diagnosis of the targeted skin NTDs. **Principal findings:** The two models were able to correctly predict over 70% of the diagnoses, and there was a consistent performance improvement with more training samples. The ResNet-50 model performed better than the VGG-16 model. Model trained with PCR confirmed cases of Buruli ulcer yielded 1-3% increase in prediction accuracy over training sets including unconfirmed cases. **Conclusions:** Our approach was to have the deep learning model distinguish between multiple pathologies simultaneously - which is close to real-world practice. The more images used for training, the more accurate the diagnosis became. The percentages of correct diagnosis increased with PCR-positive cases of Buruli ulcer. This demonstrated that it may be better to input images from the more accurately diagnosed cases in the training models also for achieving better accuracy in the generated AI models. However, the increase was marginal which may be an indication that the accuracy of clinical diagnosis alone is reliable to an extent for Buruli ulcer. Diagnostic tests also have its flaws, and they are not always reliable. One hope for AI is that it will objectively resolve this gap between diagnostic tests and clinical diagnoses with addition of another tool. While there are still challenges to be overcome, there is a potential for AI to address the unmet needs where access to medical care is limited, like for those affected by skin NTDs.

A syndemic born of war: Combining intersectionality and structural violence to explore the biosocial interactions of neglected tropical diseases, disability and mental distress in Liberia.

Dean L, Theobald S, Nallo G, Bettee A, Kollie K, Tolhurst R.

29-06-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962440/>

The intersections between NTDs, disability, and mental ill-health are increasingly recognised globally. Chronic morbidity resultant from many NTDs, particularly those affecting the skin-including lymphatic filariasis (LF), leprosy, Buruli ulcer (BU) and onchocerciasis-is well known and largely documented from a medicalised perspective. However less is known about the complex biosocial interaction shaping interconnected morbidities. We apply syndemic theory to explain the biosocial relationship between NTDs and mental distress in the context of structural violence in Liberia. By advancing syndemic theory to include intersectional thought, it is apparent that structural violence becomes embodied in different ways through interacting multi-level (macro, meso and micro) processes. Through the use of in-depth qualitative methods, we explore the syndemic interaction of NTDs and mental distress from the vantage point of the most vulnerable and suggest that: 1) the post-conflict environment in Liberia predisposes people to the chronic effects of NTDs as well as other 'generalised stressors' as a consequence of ongoing structural violence; 2) people affected by NTDs are additionally exposed to stigma and discrimination that cause additional stressors and synergistically produce negative health outcomes in relation to NTDs and mental distress; and 3) the impact and experience of consequential syndemic suffering is shaped by intersecting axes of inequity such as gender and generation which are themselves created by unequal power distribution across multiple systems levels. Bringing together health systems discourse, which is focused on service integration and centred around disease control, with syndemic discourse that considers the biosocial context of disease interaction offers new approaches. We suggest that taking a syndemic-informed approach to care in the development of people-centred health systems is key to alleviating the burden of syndemic suffering associated with NTDs and mental distress currently experienced by vulnerable populations in resource-limited settings.

Pian

Deep learning for AI-based diagnosis of skin-related neglected tropical diseases: a pilot study.

Yotsu R, Ding Z, Hamm J, Blanton R.

15-03-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993502/>

Background: Deep learning, which is a part of a broader concept of artificial intelligence (AI) and/or machine learning has achieved remarkable success in vision tasks. While there is growing interest in the use of this technology in diagnostic support for skin-related neglected tropical diseases (skin NTDs), there have been limited studies in this area and fewer focused on dark skin.

In this study, we aimed to develop deep learning based AI models with clinical images we collected for five skin NTDs, namely, Buruli ulcer, leprosy, mycetoma, scabies, and yaws, to understand how diagnostic accuracy can or cannot be improved using different models and training patterns. **Methodology:** This study used photographs collected prospectively in Côte d'Ivoire and Ghana through our ongoing studies with use of digital health tools for clinical data documentation and for teledermatology. Our dataset included a total of 1,709 images from 506 patients. Two convolutional neural networks, ResNet-50 and VGG-16 models were adopted to examine the performance of different deep learning architectures and validate their feasibility in diagnosis of the targeted skin NTDs. **Principal findings:** The two models were able to correctly predict over 70% of the diagnoses, and there was a consistent performance improvement with more training samples. The ResNet-50 model performed better than the VGG-16 model. Model trained with PCR confirmed cases of Buruli ulcer yielded 1-3% increase in prediction accuracy over training sets including unconfirmed cases. **Conclusions:** Our approach was to have the deep learning model distinguish between multiple pathologies simultaneously - which is close to real-world practice. The more images used for training, the more accurate the diagnosis became. The percentages of correct diagnosis increased with PCR-positive cases of Buruli ulcer. This demonstrated that it may be better to input images from the more accurately diagnosed cases in the training models also for achieving better accuracy in the generated AI models. However, the increase was marginal which may be an indication that the accuracy of clinical diagnosis alone is reliable to an extent for Buruli ulcer. Diagnostic tests also have its flaws, and they are not always reliable. One hope for AI is that it will objectively resolve this gap between diagnostic tests and clinical diagnoses with addition of another tool. While there are still challenges to be overcome, there is a potential for AI to address the unmet needs where access to medical care is limited, like for those affected by skin NTDs.

Lèpre

B-lymphocytes deficiency results in altered immune response and increased susceptibility to *Mycobacterium leprae* in a murine leprosy model.

Azevedo MCS, Marques H, Binelli LS, Malange MSV, Devides AC, Fachin LRV, Soares CT, Belone AFF, Rosa PS, Garlet GP, Trombone APF.

28-03-2023

Cytokine.

<https://pubmed.ncbi.nlm.nih.gov/36996537/>

Leprosy is a chronic and infectious disease that primarily affects the skin and peripheral nervous system, presenting a wide spectrum of clinical forms with different degrees of severity. The distinct host immune response patterns developed in the response to the bacillus *Mycobacterium leprae*, the leprosy etiologic agent, are associated with the spectral clinical forms and outcome of the disease. In this context, B cells are allegedly involved in the disease

immunopathogenesis, usually as antibody-producing cells, but also as potential effector or regulatory elements. In order to determine the regulatory B cells role in experimental leprosy, this study evaluated the outcome of *M. leprae* infection in B cell deficient mice (BKO) and WT C57Bl/6 control, by means of microbiological/bacilloscopic, immunohistochemical and molecular analysis, performed 8 months after *M. leprae* inoculation. The results demonstrated that infected BKO showed a higher bacilli number when compared with WT animals, demonstrating the importance of these cells in experimental leprosy. The molecular analysis demonstrates that the expression of IL-4, IL-10 and TGF- β was significantly higher in the BKO footpads when compared to WT group. Conversely, there was no difference in IFN- γ , TNF- α and IL-17 expression levels in BKO and WT groups. IL-17 expression was significantly higher in the lymph nodes of WT group. The immunohistochemical analysis revealed that M1 (CD80⁺) cells counts were significantly lower in the BKO group, while no significant difference was observed to M2 (CD206⁺) counts, resulting a skewed M1/M2 balance. These results demonstrated that the absence of B lymphocytes contribute to the persistence and multiplication of *M. leprae*, probably due to the increased expression of the IL-4, IL-10 and TGF- β cytokines, as well as a decrease in the number of M1 macrophages in the inflammatory site.

Genetic diversity of *Mycobacterium leprae* in the state of São Paulo, an area of low-leprosy incidence in Brazil.

Finardi AJ, Oliveira NG, Moraes EB, Batista LCF, Bortolomai BE, Suffys PN, Baptista IMFD.

27-03-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/36995787/>

Lax skin and blurring of vision- A case report of pseudoxanthoma elasticum.

Narasimhan M, Ramachandran R, Cornelius Gnanadurai JS, Durai PCT, Kalaivani P, Nithila C.

Dec-2022

J Family Med Prim Care.

<https://pubmed.ncbi.nlm.nih.gov/36994043/>

Increased laxity of the skin can be caused by aging, significant weight loss, or defects in the elastic tissue. A 38-year-old female presented with increased laxity of the skin over the neck, thighs, and abdomen for 6 years, associated with headache and blurring of vision for a week. On cutaneous examination, prominent skin folds, laxity, and wrinkles were noted over the neck, abdomen, thighs, and groin, with yellowish papules along the neck creases. Ocular examination revealed features suggestive of angioid streaks. Skin biopsy showed fragmented elastic fibers and intervening calcium deposits on Verhoeff Van Gieson and Von Kossa stains. Based on these findings, a diagnosis of pseudoxanthoma elasticum (PXE) was made. The patient was started on oral and topical sunscreens and eye protection and advised regular follow-up. Diagnosing the condition early based on skin findings can help prevent

further multi-system manifestations by taking appropriate preventive measures as this condition is progressive and has no cure.

Linezolid-induced hematemesis, a rare and life-threatening adverse reaction. A case report of Karonga district in Malawi.

Chitsulo S, Omotayo D, Mbendera K, Sinyiza FW, Chisale M, Mbakaya BC.

25-03-2023

Oxf Med Case Reports.

<https://pubmed.ncbi.nlm.nih.gov/36993836/>

Early diagnosis of neural impairment in seropositive leprosy household contacts: The experience of a reference center in Brazil.

Dos Santos DF, Garcia LP, Borges IS, Oliveira TJ, Antunes DE, Luppi AM, Goulart IMB.

13-03-2023

Front Med (Lausanne).

<https://pubmed.ncbi.nlm.nih.gov/36993802/>

Multimodality imaging review of ulnar nerve pathologies.

Chaudhary RK, Karkala N, Nepal P, Gupta E, Kaur N, Batchala P, Sapire J, Alam SI.

24-03-2023

Neuroradiol J.

<https://pubmed.ncbi.nlm.nih.gov/36961518/>

The ulnar nerve is the second most commonly entrapped nerve after the median nerve. Although clinical evaluation and electrodiagnostic studies remain widely used for the evaluation of ulnar neuropathy, advancements in imaging have led to increased utilization of these newer / better imaging techniques in the overall management of ulnar neuropathy. Specifically, high-resolution ultrasonography of peripheral nerves as well as MRI has become quite useful in evaluating the ulnar nerve in order to better guide treatment. The caliber and fascicular pattern identified in the normal ulnar nerves are important distinguishing features from ulnar nerve pathology. The cubital tunnel within the elbow and Guyon's canal within the wrist are important sites to evaluate with respect to ulnar nerve compression. Both acute and chronic conditions resulting in deformity, trauma as well as inflammatory conditions may predispose certain patients to ulnar neuropathy. Granulomatous diseases as well as both neurogenic and non-neurogenic tumors can also potentially result in ulnar neuropathy. Tumors around the ulnar nerve can also lead to mass effect on the nerve, particularly in tight spaces like the aforementioned canals. Although high-resolution ultrasonography is a useful modality initially, particularly as it can be helpful for dynamic evaluation, MRI remains most reliable due to its higher resolution. Newer imaging techniques like sonoelastography and microneurography, as well as nerve-specific contrast agents, are currently being investigated for their usefulness and are not routinely being used currently.

Integrating interferon-gamma release assay testing into provision of tuberculosis preventive therapy is feasible in a tuberculosis high burden resource-limited setting: A mixed methods study.

Muchuro S, Makabayi-Mugabe R, Musaazi J, Mayito J, Zawedde-Muyanja S, Nakawooya M, Tugumisirize D, Semanda P, Wandiga S, Nabada-Ndidde S, Nkolo A, Turyahabwe S.

06-06-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962307/>

Accuracy of computer-aided chest X-ray in community-based tuberculosis screening: Lessons from the 2016 Kenya National Tuberculosis Prevalence Survey.

Mungai B, Ong'angò J, Ku CC, Henrion MYR, Morton B, Joekes E, Onyango E, Kiplimo R, Kirathe D, Masini E, Sitienei J, Manduku V, Mugi B, Squire SB, MacPherson P; IMPALA Consortium.

23-11-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962655/>

Community-based screening for tuberculosis (TB) could improve detection but is resource intensive. We set out to evaluate the accuracy of computer-aided TB screening using digital chest X-ray (CXR) to determine if this approach met target product profiles (TPP) for community-based screening. CXR images from participants in the 2016 Kenya National TB Prevalence Survey were evaluated using CAD4TBv6 (Delft Imaging), giving a probabilistic score for pulmonary TB ranging from 0 (low probability) to 99 (high probability). We constructed a Bayesian latent class model to estimate the accuracy of CAD4TBv6 screening compared to bacteriologically-confirmed TB across CAD4TBv6 threshold cut-offs, incorporating data on Clinical Officer CXR interpretation, participant demographics (age, sex, TB symptoms, previous TB history), and sputum results. We compared model-estimated sensitivity and specificity of CAD4TBv6 to optimum and minimum TPPs. Of 63,050 prevalence survey participants, 61,848 (98%) had analysable CXR images, and 8,966 (14.5%) underwent sputum bacteriological testing; 298 had bacteriologically-confirmed pulmonary TB. Median CAD4TBv6 scores for participants with bacteriologically-confirmed TB were significantly higher (72, IQR: 58-82.75) compared to participants with bacteriologically-negative sputum results (49, IQR: 44-57, $p < 0.0001$). CAD4TBv6 met the optimum TPP; with the threshold set to achieve a mean sensitivity of 95% (optimum TPP), specificity was 83.3%, (95% credible interval [CrI]: 83.0%-83.7%, CAD4TBv6 threshold: 55). There was considerable variation in accuracy by participant characteristics, with older individuals and those with previous TB having lowest specificity. CAD4TBv6 met the optimal TPP for TB community screening. To optimise screening accuracy and efficiency of confirmatory sputum testing, we recommend that an

adaptive approach to threshold setting is adopted based on participant characteristics.

Associations between occupation, leprosy disability and other sociodemographic factors in an endemic area of Brazil.

Cisneros J, Ferreira JA, de Faria Grossi MA, de Filippis T, de Oliveira ALG, Lyon S, Fairley JK.

12-09-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962742/>

Effectiveness of community-based burden estimation to achieve elimination of lymphatic filariasis: A comparative cross-sectional investigation in Côte d'Ivoire.

Simpson H, Konan DO, Brahima K, Koffi JD, Kashindi S, Edmiston M, Weiland S, Halliday K, Pullan RL, Meite A, Koudou BG, Timothy J.

31-08-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962795/>

For lymphatic filariasis (LF) elimination, endemic countries must document the burden of LF morbidity (LFM). Community-based screening (CBS) is used to collect morbidity data, but evidence demonstrating its reliability is limited. Recent pilots of CBS for LFM alongside mass drug administration (MDA) in Côte d'Ivoire suggested low LFM prevalence (2.1-2.2 per 10,000). We estimated LFM prevalence in Bongouanou District, Côte d'Ivoire, using a comparative cross-sectional design. We compared CBS implemented independently of MDA, adapted from existing Ministry of Health protocols, to a population-based prevalence survey led by formally trained nurses. We evaluated the reliability of case identification, coverage, equity, and cost of CBS. CBS identified 87.4 cases of LFM per 10,000; the survey identified 47.5 (39.4-56.3; prevalence ratio [PR] 1.84; 95% CI 1.64-2.07). CBS identified 39.7 cases of suspect lymphoedema per 10,000; the survey confirmed 35.1 (29.2-41.5) filarial lymphoedema cases per 10,000 (PR 1.13 [0.98-1.31]). CBS identified 96.5 scrotal swellings per 10,000; the survey found 91.3 (83.2-99.8; PR 1.06 [0.93-1.21]); including 33.9 (27.7-38.8) filarial hydrocoele per 10,000 (PR of suspect to confirmed hydrocoele 2.93 [2.46-3.55]). Positive predictive values for case identification through CBS were 65.0% (55.8-73.5%) for filarial lymphoedema; 93.7% (89.3-96.7%) for scrotal swellings; and 34.0% (27.3-41.2%) for filarial hydrocoele. Households of lower socioeconomic status and certain minority languages were at risk of exclusion. Direct financial costs were \$0.17 per individual targeted and \$69.62 per case confirmed. Our community-based approach to LFM burden estimation appears scalable and provided reliable prevalence estimates for LFM, scrotal swellings and LF-lymphoedema. The results represent a step-change improvement on CBS integrated with MDA, whilst remaining at programmatically feasible costs. Filarial hydrocoele cases were overestimated, attributable to the use of case definitions suitable for

mass-screening by informal staff. Our findings are broadly applicable to countries aiming for LF elimination using CBS. The abstract is available in French in the S1 File.

Non-tuberculous mycobacterial pulmonary disease: Awareness survey of front-desk healthcare workers in Northern Tanzania.

Maya T, Komba E, Mensah G, Mnyambwa N, Doulla B, Mfinanga S, Addo K, Kazwala R.

20-01-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36963008/>

Over the past decade, there have been increasing reports of non-tuberculous mycobacteria (NTM) species being implicated in tuberculosis (TB) treatment failure or misdiagnosed as TB. Inadequate awareness of NTM pulmonary disease among healthcare workers (HCWs) may contribute to a low index of suspicion for patients presenting to their hospitals. In this study, we assessed the awareness of NTM pulmonary disease (NTM-PD) among front desk HCWs in Northern Tanzania. A cross-sectional descriptive survey was carried out among front desk HCWs in four administrative regions of Northern Tanzania. A standardized questionnaire was administered to consented participants from four clusters; clinicians, laboratory scientists, nurses, and pharmacists serving TB patients from Regional and District Health Facilities. Each participant was asked a set of questions, scored and the total score for each participant was determined. An awareness score was used to measure the level of awareness. The average score for all participants was estimated including the 95% confidence interval (CI). The overall awareness score was 24.1%, 95% CI 22.0-26.2%. History of training, experience in TB care, level of health facilities, age group, and setting were found to be statistically associated with the level of awareness of study participants. More than two-thirds (67%) of participants believe that pulmonary NTM and TB are clinically similar and 60% are not aware that AFB Microscopy cannot distinguish between the two. Only 13% of participants could mention at least one risk factor for NTM pulmonary disease. The level of awareness of NTM pulmonary disease was poor among HCWs in the surveyed TB clinics. National TB Programs are advised to include a topic on NTM in various on-job TB training packages for HCWs.

The integration of tuberculosis and HIV testing on GeneXpert can substantially improve access and same-day diagnosis and benefit tuberculosis programmes: A diagnostic network optimization analysis in Zambia.

Girdwood S, Pandey M, Machila T, Warriar R, Gautam J, Mukumbwa-Mwenechanya M, Benade M, Nichols K, Shibemba L, Mwewa J, Mzyece J, Lungu P, Albert H, Nichols B, Choonga P.

25-01-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36963019/>

Thalidomide interaction with inflammation in idiopathic pulmonary fibrosis.

Dsouza NN, Alampady V, Baby K, Maity S, Byregowda BH, Nayak Y.

25-03-2023

Inflammopharmacology.

<https://pubmed.ncbi.nlm.nih.gov/36966238/>

The "Thalidomide tragedy" is a landmark in the history of the pharmaceutical industry. Despite limited clinical trials, there is a continuous effort to investigate thalidomide as a drug for cancer and inflammatory diseases such as rheumatoid arthritis, lepromatous leprosy, and COVID-19. This review focuses on the possibilities of targeting inflammation by repurposing thalidomide for the treatment of idiopathic pulmonary fibrosis (IPF). Articles were searched from the Scopus database, sorted, and selected articles were reviewed. The content includes the proven mechanisms of action of thalidomide relevant to IPF. Inflammation, oxidative stress, and epigenetic mechanisms are major pathogenic factors in IPF. Transforming growth factor- β (TGF- β) is the major biomarker of IPF. Thalidomide is an effective anti-inflammatory drug in inhibiting TGF- β , interleukins (IL-6 and IL-1 β), and tumour necrosis factor- α (TNF- α). Thalidomide binds cereblon, a process that is involved in the proposed mechanism in specific cancers such as breast cancer, colon cancer, multiple myeloma, and lung cancer. Cereblon is involved in activating AMP-activated protein kinase (AMPK)-TGF- β /Smad signalling, thereby attenuating fibrosis. The past few years have witnessed an improvement in the identification of biomarkers and diagnostic technologies in respiratory diseases, partly because of the COVID-19 pandemic. Hence, investment in clinical trials with a systematic plan can help repurpose thalidomide for pulmonary fibrosis.

Antibody seropositivity and endemicity of chikungunya and Zika viruses in Nigeria.

Mac PA, Airiohuodion PE, Zubair S, Tadele M, Aighobahi JO, Anyaie C, Kroeger A, Panning M.

2023

Anim Dis.

<https://pubmed.ncbi.nlm.nih.gov/36968287/>

Why and How Should Ethiopia Establish a Stem Cell Transplant Service? A Review Article.

Mekonnen S, Farris H.

20-03-2023

Biologics.

<https://pubmed.ncbi.nlm.nih.gov/36969332/>

Ethiopia is attempting to reduce cancer-related morbidity and mortality through a strategic national cancer control plan but according to Globocan 2020, hematologic malignancies particularly leukemia and non-Hodgkin's lymphoma rank among the top five leading causes of new cancer incidence and cause of death among all age groups in both sexes. Hematopoietic stem-cell transplantation

(HSCT) is an advanced treatment modality that makes the only effective treatment for cancer and non-cancer-related hematologic diseases unresponsive to conventional therapy. Patients who need stem cell transplants must travel to abroad countries to get the treatment. Meanwhile, the Ethiopian National Specialty and Subspecialty Roadmap sets the goal of establishing HSCT centers in 2020-2029 GC, yet leaders and planners must start taking steps to put the setup in place. Setting up an HSCT facility is challenging for developing countries due to the high costs, limited infrastructure, and need for intensive medical staff training; however, several nations have been able to start successful stem cell transplant programs. This review summarizes the basic steps and requirements of the program in light of guidelines recommendations and lessons learned from other developing countries. It also highlights possible cost-effective opportunities, bottlenecks, and areas that will require work and investment to make the objective reality in Ethiopia. Provides key information to assist administrators and policymakers to set priorities in planning and making informed decisions to establish and maintain the service.

Validation of a Simple Instrument of Fast Application to Track Disability in Leprosy Patients.

Pinho AB, Freitas MM, Fontes CJF.

27-06-2022

Rev Bras Ortop (Sao Paulo).

<https://pubmed.ncbi.nlm.nih.gov/36969776/>

Objective To evaluate a simple and fast diagnostic instrument to be used by any health professional to track the disability presented by leprosy patients. **Method** Validation study of a diagnostic test performed in a sample of 156 leprosy patients to track functional disability through the shortened disabilities of arm, shoulder, and hand (QuickDASH) questionnaire. The simplified neurological assessment proposed by the World Health Organization was used as a reference. A receiver operating characteristic (ROC) curve was constructed to determine the cutoff point of QuickDASH that best discriminated patients with functional disability caused by leprosy. **Results** We identified 86 (55.5%) patients with functional disability by simplified neurological evaluation. The performance of the QuickDASH instrument showed that, at a cut-off point of 30 points, the sensitivity and specificity were 72.1% and 68.1% (accuracy of 70.3%), respectively, to identify functional disability, with a positive predictive value of 73.8%. **Conclusion** The QuickDASH instrument showed good accuracy to track functional disability in leprosy patients, and it may be useful in clinical practice of primary and general outpatient care, with the goal of identifying patients who need specialized reference for the prevention and treatment of this condition.

Endoscopic Cubital Tunnel Release in Leprosy Neuritis of the Ulnar Nerve.

Leite JAD, Sampaio ACD, Leite CMGDS, Leite JGDS, Sampaio MV, Lima DA.

15-02-2022

Rev Bras Ortop (Sao Paulo).
<https://pubmed.ncbi.nlm.nih.gov/36969786/>

Allele-dependent interaction of LRRK2 and NOD2 in leprosy.

Dallmann-Sauer M, Xu YZ, da Costa ALF, Tao S, Gomes TA, Prata RBDS, Correa-Macedo W, Manry J, Alcaïs A, Abel L, Cobat A, Fava VM, Pinheiro RO, Lara FA, Probst CM, Mira MT, Schurr E.

27-03-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36972292/>

Leprosy, caused by *Mycobacterium leprae*, rarely affects children younger than 5 years. Here, we studied a multiplex leprosy family that included monozygotic twins aged 22 months suffering from paucibacillary leprosy. Whole genome sequencing identified three amino acid mutations previously associated with Crohn's disease and Parkinson's disease as candidate variants for early onset leprosy: LRRK2 N551K, R1398H and NOD2 R702W. In genome-edited macrophages, we demonstrated that cells expressing the LRRK2 mutations displayed reduced apoptosis activity following mycobacterial challenge independently of NOD2. However, employing co-immunoprecipitation and confocal microscopy we showed that LRRK2 and NOD2 proteins interacted in RAW cells and monocyte-derived macrophages, and that this interaction was substantially reduced for the NOD2 R702W mutation. Moreover, we observed a joint effect of LRRK2 and NOD2 variants on *Bacillus Calmette-Guérin* (BCG)-induced respiratory burst, NF- κ B activation and cytokine/chemokine secretion with a strong impact for the genotypes found in the twins consistent with a role of the identified mutations in the development of early onset leprosy.

Leprosy misdiagnosed as rheumatoid arthritis.

Qiang F, Sheng J.

Mar-2023

Intern Med J.

<https://pubmed.ncbi.nlm.nih.gov/36972991/>

150-year anniversary of leprosy bacillus.

Vollset M, Aavitsland P.

28-02-2023

Tidsskr Nor Lægeforen.

<https://pubmed.ncbi.nlm.nih.gov/36987907/>

Deep learning for AI-based diagnosis of skin-related neglected tropical diseases: a pilot study.

Yotsu R, Ding Z, Hamm J, Blanton R.

15-03-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993502/>

Is aggregated surveillance data a reliable method for constructing tuberculosis

care cascades? A secondary data analysis from Uganda.

White EB, Hernández-Ramírez RU, Majwala RK, Nalugwa T, Reza T, Cattamanchi A, Katamba A, Davis JL.

23-11-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962541/>

To accelerate tuberculosis (TB) control and elimination, reliable data is needed to improve the quality of TB care. We assessed agreement between a surveillance dataset routinely collected for Uganda's national TB program and a high-fidelity dataset collected from the same source documents for a research study from 32 health facilities in 2017 and 2019 for six measurements: 1) Smear-positive and 2) GeneXpert-positive diagnoses, 3) bacteriologically confirmed and 4) clinically diagnosed treatment initiations, and the number of people initiating TB treatment who were also 5) living with HIV or 6) taking antiretroviral therapy. We measured agreement as the average difference between the two methods, expressed as the average ratio of the surveillance counts to the research data counts, its 95% limits of agreement (LOA), and the concordance correlation coefficient. We used linear mixed models to investigate whether agreement changed over time or was associated with facility characteristics. We found good overall agreement with some variation in the expected facility-level agreement for the number of smear positive diagnoses (average ratio [95% LOA]: 1.04 [0.38-2.82]; CCC: 0.78), bacteriologically confirmed treatment initiations (1.07 [0.67-1.70]; 0.82), and people living with HIV (1.11 [0.51-2.41]; 0.82). Agreement was poor for Xpert positives, with surveillance data undercounting relative to research data (0.45 [0.099-2.07]; 0.36). Although surveillance data overcounted relative to research data for clinically diagnosed treatment initiations (1.52 [0.71-3.26]) and number of people taking antiretroviral therapy (1.71 [0.71-4.12]), their agreement as assessed by CCC was not poor (0.82 and 0.62, respectively). Average agreement was similar across study years for all six measurements, but facility-level agreement varied from year to year and was not explained by facility characteristics. In conclusion, the agreement of TB surveillance data with high-fidelity research data was highly variable across measurements and facilities. To advance the use of routine TB data as a quality improvement tool, future research should elucidate and address reasons for variability in its quality.

A syndemic born of war: Combining intersectionality and structural violence to explore the biosocial interactions of neglected tropical diseases, disability and mental distress in Liberia.

Dean L, Theobald S, Nallo G, Bettee A, Kollie K, Tolhurst R.

29-06-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962440/>

The intersections between NTDs, disability, and mental ill-health are increasingly recognised globally. Chronic morbidity resultant from many NTDs, particularly those

affecting the skin-including lymphatic filariasis (LF), leprosy, Buruli ulcer (BU) and onchocerciasis-is well known and largely documented from a medicalised perspective. However less is known about the complex biosocial interaction shaping interconnected morbidities. We apply syndemic theory to explain the biosocial relationship between NTDs and mental distress in the context of structural violence in Liberia. By advancing syndemic theory to include intersectional thought, it is apparent that structural violence becomes embodied in different ways through interacting multi-level (macro, meso and micro) processes. Through the use of in-depth qualitative methods, we explore the syndemic interaction of NTDs and mental distress from the vantage point of the most vulnerable and suggest that: 1) the post-conflict environment in Liberia predisposes people to the chronic effects of NTDs as well as other 'generalised stressors' as a consequence of ongoing structural violence; 2) people affected by NTDs are additionally exposed to stigma and discrimination that cause additional stressors and synergistically produce negative health outcomes in relation to NTDs and mental distress; and 3) the impact and experience of consequential syndemic suffering is shaped by intersecting axes of inequity such as gender and generation which are themselves created by unequal power distribution across multiple systems levels. Bringing together health systems discourse, which is focused on service integration and centred around disease control, with syndemic discourse that considers the biosocial context of disease interaction offers new approaches. We suggest that taking a syndemic-informed approach to care in the development of people-centred health systems is key to alleviating the burden of syndemic suffering associated with NTDs and mental distress currently experienced by vulnerable populations in resource-limited settings.

Correction: Association of NOD2 and IFNG single nucleotide polymorphisms with leprosy in the Amazon ethnic admixed population.

Leturiondo AL, Noronha AB, Mendonça CYR, Ferreira CO, Alvarado-Arnez LE, Manta FSN, Bezerra OCL, Carvalho EF, Moraes MO, Rodrigues FDC, Talhari C.

24-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36961805/>

A systematic review of caregivers' knowledge and related factors towards pressure ulcer prevention.

Farzan R, Yarali M, Mollaei A, Ghaderi A, Takasi P, Sarafi M, Samidoust P, Mahdiabadi MZ, Firooz M, Hosseini SJ, Vajargah PG, Karkhah S.

24-03-2022

Int Wound J.

<https://pubmed.ncbi.nlm.nih.gov/36960763/>

This systematic review aimed to examine the knowledge of caregivers regarding pressure ulcer (PU) prevention. A thorough, methodical search was conducted from the earliest date to February 1, 2023 using keywords extracted

from Medical Subject Headings such as "Caregivers", "Knowledge", and "Pressure ulcer" in various international electronic databases such as Scopus, PubMed, Web of Science, and Persian electronic databases such as Iranmedex and Scientific Information Database. The quality of the studies included in this systematic review was evaluated using an appraisal tool for cross-sectional studies (AXIS tool). In total, 927 caregivers participated in the eight studies. The average age of the participants was 40.50 (SD = 12.67). Among the participants, 61.87% were women. The average caregiver's knowledge of PU prevention was 53.70 (SD = 14.09) out of 100, which suggests a moderate level of knowledge. Factors such as level of education, age, occupation, information about PUs, attitude, and practice had a significant positive relationship with caregivers' knowledge related to the prevention of PUs. Knowledge had a significantly negative relationship with age. In addition, marital status, type of relationship, age, gender, occupation, level of education, and inpatient wards had a significant relationship with caregivers' knowledge regarding PUs prevention. Therefore, managers and policymakers in the medical field can help increase caregivers' knowledge by providing an online or in-person educational platform relevant to PU prevention.

Redefining tuberculosis: an interview with Lalita Ramakrishnan.

Ramakrishnan L.

01-03-2023

Dis Model Mech.

<https://pubmed.ncbi.nlm.nih.gov/36951140/>

Trypanosomes (trypanosomiasis et maladie de Chagas)

The Trypanosoma brucei MISP family of invariant proteins is co-expressed with BARP as triple helical bundle structures on the surface of salivary gland forms, but is dispensable for parasite development within the tsetse vector.

Casas-Sanchez A, Ramaswamy R, Perally S, Haines LR, Rose C, Aguilera-Flores M, Portillo S, Verbeelen M, Hussain S, Smithson L, Yunta C, Lehane MJ, Vaughan S, van den Abbeele J, Almeida IC, Boulanger MJ, Acosta-Serrano Á.

30-03-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36996244/>

Trypanosoma brucei spp. develop into mammalian-infectious metacyclic trypomastigotes inside tsetse salivary glands. Besides acquiring a variant surface glycoprotein (VSG) coat, little is known about the metacyclic expression of invariant surface antigens. Proteomic analyses of saliva from *T. brucei*-infected flies identified, in addition to VSG and Brucei Alanine-Rich Protein (BARP) peptides, a family of GPI-anchored surface

proteins herein named as Metacyclic Invariant Surface Proteins (MISP) because of its predominant expression on the surface of metacyclic trypomastigotes. The MISP family is encoded by five paralog genes with >80% protein identity, which are exclusively expressed by salivary gland stages of the parasite and peak in metacyclic stage, as shown by confocal microscopy and immuno-high resolution scanning electron microscopy. Crystallographic analysis of a MISP isoform (MISP360) and a high confidence model of BARP revealed a triple helical bundle architecture commonly found in other trypanosome surface proteins. Molecular modelling combined with live fluorescent microscopy suggests that MISP N-termini are potentially extended above the metacyclic VSG coat, and thus could be tested as a transmission-blocking vaccine target. However, vaccination with recombinant MISP360 isoform did not protect mice against a *T. brucei* infectious tsetse bite. Lastly, both CRISPR-Cas9-driven knock out and RNAi knock down of all MISP paralogues suggest they are not essential for parasite development in the tsetse vector. We suggest MISP may be relevant during trypanosome transmission or establishment in the vertebrate's skin.

Comparative Analysis of the Interaction of Silver Nanoparticles with Hexokinase from *Trypanosoma brucei* and Humans.

Mlozen MM, Van Marwijk J, Wilhelmi BS, Whiteley C.
23-03-2023

Int J Nanomedicine.

<https://pubmed.ncbi.nlm.nih.gov/36992823/>

Background: Regardless of the efforts to ease cases of human African trypanosomiasis (HAT), an increased number of cases get reported annually. This is because of drug resistant *Trypanosoma brucei* (Tb), the causative agent of the illness. This has renewed the need for creative methods to find new anti-trypanosomal drugs. The blood stream form (BSF) of the parasite depends exclusively on the glycolytic pathway for energy production while it is in the human host. Interruptions in this pathway efficiently kills the parasite. *Trypanosoma brucei* hexokinase (*TbHK*) is the first enzyme in glycolysis, and any effectors or inhibitors of *TbHK* would have potential as anti-trypanosomal agents. **Methods:** *TbHK* and human glucokinase (*hGCK*) were over-expressed with a 6 histidine-tag in *E. coli* BL21(DE3) cells having the pRARE2 plasmid. **Results:** *TbHK* had thermal and pH stability between 30°C and 55°C and 7.5 and 8.5, respectively, while *hGCK* exhibited thermal and pH stability between 30°C and 40°C and 7.0 and 8.0, respectively. Kinetically, *TbHK* had a K_m of 39.3 μM , V_{max} of 0.066 $\mu mol \cdot min^{-1} \cdot mL^{-1}$, k_{cat} of 2.05 min^{-1} and k_{cat}/K_m of 0.0526 $min^{-1} \cdot \mu mol^{-1}$. *hGCK* exhibited a K_m of 4.5 μM , V_{max} of 0.032 $\mu mol \cdot min^{-1} \cdot mL^{-1}$, k_{cat} of 11.25 min^{-1} , and k_{cat}/K_m of 2.5 $min^{-1} \cdot \mu mol^{-1}$. Interaction kinetic studies of silver nanoparticles (AgNPs) (0.1 μM) of average size of 6 nm with *TbHK* and *hGCK* were conducted. AgNPs selectively inhibited *TbHK* over *hGCK*. *TbHK* showed a non-competitive inhibition with a 50% and 28% decrease in V_{max} , and k_{cat}/K_m , respectively. *hGCK* showed a 33% increase in affinity, 9% decrease in V_{max} , and a 50% increase in enzyme efficiency. **Conclusion:** The observed pattern of *hGCK* and AgNPs falls under the

uncompetitive inhibition. The observed highly selective inhibitory effects of AgNPs between *TbHK* and *hGCK* may be used in development of new anti-trypanosomal drugs.

Dissecting the interstrand crosslink DNA repair system of *Trypanosoma cruzi*.

Martinez MZ, Olmo F, Taylor MC, Caudron F, Wilkinson SR.

16-03-2032

DNA Repair (Amst).

<https://pubmed.ncbi.nlm.nih.gov/36989950/>

Exploring Synthetic Dihydrobenzofuran and Benzofuran Neolignans as Antiprotozoal Agents against *Trypanosoma cruzi*.

Pagotti MC, Dias HJ, Candido ACBB, Oliveira TAS, Borges A, Oliveira ND, Lopes CD, Orenha RP, Parreira RLT, Crotti AEM, Magalhães LG.

24-02-2023

Pharmaceutics.

<https://pubmed.ncbi.nlm.nih.gov/36986617/>

Chagas disease is a neglected tropical disease that affects more than 8 million people. Although there are therapies against this disease, the search for new drugs is important because the current treatments show limited effectiveness and high toxicity. In this work, eighteen dihydrobenzofuran-type neolignans (DBNs) and two benzofuran-type neolignans (BNs) were synthesized and evaluated against amastigote forms of two *Trypanosoma cruzi* strains. The in vitro cytotoxicity and hemolytic activity of the most active compounds were also evaluated and their relationships with *T. cruzi* tubulin DBNs were investigated by an in silico approach. Four DBNs demonstrated activity against the *T. cruzi* Tulahuen lac-Z strain (IC₅₀ from 7.96 to 21.12 μM), and DBN **1** exhibited the highest activity against the amastigote forms of the *T. cruzi* Y strain (IC₅₀ 3.26 μM). Compounds **1-4** showed CC₅₀ values higher than antitrypanosomal activities, except for DBN **3**. All DBNs with antitrypanosomal activity demonstrated CH₅₀ higher than 100 μM . The in silico results indicated that DBNs **1**, **2**, and **4** are capable of destabilizing the dynamics of the tubulin-microtubule from the vinca site. These compounds displayed promising in vitro activity against *T. cruzi*, especially compound **1**, and can be considered molecular prototypes for the development of new antiparasitic drugs.

Trypanosoma cruzi Sirtuin 2 as a Relevant Druggable Target: New Inhibitors Developed by Computer-Aided Drug Design.

Ferreira GM, Kronenberger T, Maltarollo VG, Poso A, de Moura Gatti F, Almeida VM, Marana SR, Lopes CD, Tezuka DY, de Albuquerque S, da Silva Emery F, Trossini GHG.

10-03-2023

Pharmaceutics (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36986527/>

Trypanosoma cruzi, the etiological agent of Chagas disease, relies on finely coordinated epigenetic regulation during the transition between hosts. Herein we targeted the silent information regulator 2 (Sir2) enzyme, a NAD⁺-dependent class III histone deacetylase, to interfere with the parasites' cell cycle. A combination of molecular modelling with on-target experimental validation was used to discover new inhibitors from commercially available compound libraries. We selected six inhibitors from the virtual screening, which were validated on the recombinant Sir2 enzyme. The most potent inhibitor (CDMS-01, IC₅₀ = 40 µM) was chosen as a potential lead compound.

Inhibiting *Leishmania donovani* Sterol Methyltransferase to Identify Lead Compounds Using Molecular Modelling.

Sakyi PO, Kwofie SK, Tuekpe JK, Gwira TM, Broni E, Miller WA 3rd, Wilson MD, Amewu RK.

21-02-2023

Pharmaceuticals (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36986430/>

Vector-Borne Pathogens in Guard Dogs in Ibadan, Nigeria.

Gruenberger I, Liebich AV, Ajibade TO, Obebe OO, Ogbonna NF, Wortha LN, Unterköfler MS, Fuehrer HP, Ayinmode AB.

02-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986328/>

Canine vector-borne diseases are of great relevance not only regarding animal welfare but also in relation to the One Health concept. Knowledge concerning the most relevant vector-borne pathogens in dogs is scarce and limited to stray dogs in most western African regions, and there is virtually no information about the situation in kept dogs presenting (regularly) to vets. Therefore, the blood samples of 150 owned guard dogs in the Ibadan area in the southwest of Nigeria were collected and analyzed for the DNA of Piroplasmida (*Babesia*, *Hepatozoon*, *Theileria*), Filarioidea (e.g., *Dirofilaria immitis*, *Dirofilaria repens*), Anaplasmataceae (e.g., *Anaplasma*, *Ehrlichia*), Trypanosomatidae (e.g., *Leishmania*, *Trypanosoma*), *Rickettsia*, *Bartonella*, *Borrelia* and hemotropic *Mycoplasma* using molecular methods. Overall, samples from 18 dogs (12%) tested positive for at least one pathogen. *Hepatozoon canis* (6%) was the most prevalent blood parasite, followed by *Babesia rossi* (4%). There was a single positive sample each for *Babesia vogeli* (0.6%) and *Anaplasma platys* (0.6%). Moreover, one mixed infection with *Trypanosoma brucei/evansi* and *Trypanosoma congolense* kilifi was confirmed (0.67%). Generally, the prevalence of vector-borne pathogens in this sample group of owned dogs in southwest Nigeria was lower than in prior studies from the country and in other parts of Africa in total. This leads to the assumption that, firstly, the exact geographical location has a major influence on the incidence of vector-borne diseases, and, secondly, it seems to make a difference if the dogs are owned and, therefore, regularly checked at a veterinary clinic. This

study should raise awareness of the importance of routine health check-ups, tick and mosquito prophylaxis, and a well-managed infectious disease control program to prevent vector-borne diseases in canines.

An X-Domain Phosphoinositide Phospholipase C (PI-PLC-like) of *Trypanosoma brucei* Has a Surface Localization and Is Essential for Proliferation.

Negrão NW, Crowe LP, Mantilla BS, Baptista RP, King-Keller S, Huang G, Docampo R.

28-02-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986308/>

Trypanosoma brucei is the causative agent of African trypanosomiasis, a deadly disease that affects humans and cattle. There are very few drugs to treat it, and there is evidence of mounting resistance, raising the need for new drug development. Here, we report the presence of a phosphoinositide phospholipase C (TbPI-PLC-like), containing an X and a PDZ domain, that is similar to the previously characterized TbPI-PLC1. TbPI-PLC-like only possesses the X catalytic domain and does not have the EF-hand, Y, and C2 domains, having instead a PDZ domain. Recombinant TbPI-PLC-like does not hydrolyze phosphatidylinositol 4,5-bisphosphate (PIP₂) and does not modulate TbPI-PLC1 activity in vitro. TbPI-PLC-like shows a plasma membrane and intracellular localization in permeabilized cells and a surface localization in non-permeabilized cells. Surprisingly, knockdown of *TbPI-PLC-like* expression by RNAi significantly affected proliferation of both procyclic and bloodstream trypomastigotes. This is in contrast with the lack of effect of downregulation of expression of *TbPI-PLC1*.

The Low Variability of Tc24 in *Trypanosoma cruzi* TcI as an Advantage for Chagas Disease Prophylaxis and Diagnosis in Mexico.

Becker I, Miranda-Ortiz H, Fernández-Figueroa EA, Sánchez-Montes S, Colunga-Salas P, Grostieta E, Juárez-Gabriel J, Lozano-Sardaneta YN, Arce-Fonseca M, Rodríguez-Morales O, Meneses-Ruiz G, Pastén-Sánchez S, López Martínez I, González-Guzmán S, Paredes-Cervantes V, Moreira OC, Finamore-Araujo P, Canseco-Méndez JC, Coquis-Navarrete U, Rengifo-Correa L, González-Salazar C, Alfaro-Cortés MM, Falcón-Lezama JA, Tapia-Conyer R, Stephens CR.

23-02-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986290/>

Trypanosome Infections and Anemia in Cattle Returning from Transhumance in Tsetse-Infested Areas of Cameroon.

Farikou O, Simo G, Njiokou F, Kamé Ngassé GI, Achiri Fru M, Geiger A.

09-03-2023

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/36985285/>

The objective of this work was to assess the anemic status and the use of an immunological test and PCR-based methods to determine the infection rates of trypanosomes species. Transhumance aims to provide cattle with greener pastures and greater water resources than in the Djerem region during the dry season. Two criteria were used to assess the health status of the animals, the prevalence of trypanosomiasis and the level of anemia. In addition, we have evaluated the effectiveness, in trypanosomiasis detection, of the Very Diag Kit (CEVA Santé animale), a Rapid diagnosis test (RDT) based on immunological identification of *T. congolense* s.l. and *T. vivax*, responsible for AAT. Four trypanosome species (*Trypanosoma congolense* savannah type (Tcs), *T. congolense* forest type (Tcf), *T. brucei* s.l. (Tbr) and *T. vivax* (Txv)) were identified in cattle sampled in four villages. The overall infection rate determined by PCR (68.6%) was much higher than those generally reported in cattle from the Adamawa region (35 to 50%). Infections (including mixed infections) by Tc s.l. (Tcs + Tcf) were predominant (45.7%). The infection rates were also determined using the Very Diag Kit allowing us to identify Tc s.l. and Txv in the field in less than 20 min. This method provided, for the global infection, a higher rate (76.5%) than that determined by PCR (68.6%), although it is supposed to be less sensitive than PCR. Tc s.l. infection rate (37.8%) was similar to that (38.8%) determined by PCR (Tcs + Tcf single infections). In contrast, the prevalence of Txv single infections measured by RDT (18%) was nearly two-fold higher than that (9.4%) measured by PCR. Thus, further comparative analyses seem to be needed in order to more accurately assess the sensitivity and specificity of the Very Diag test under our conditions of use on blood samples. The mean PCVs in trypanosome-infected as well as in uninfected cattle were below 25%, the threshold below which an animal is considered anemic. Our study shows that cattle return from transhumance in poor health. It raises questions about its real benefit, especially since the herds are themselves likely to become vectors of trypanosomiasis and possibly of other diseases. At least, effective measures have to be undertaken to treat all cattle coming back from transhumance.

Synthetic Analogues of Gibbilibol B Induce Bioenergetic Damage and Calcium Imbalance in *Trypanosoma cruzi*.

Amaral M, Varela MT, Kant R, Christodoulides M, Fernandes JPS, Tempone AG.

28-02-2023

Life (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36983820/>

Chagas disease is an endemic tropical disease caused by the protozoan *Trypanosoma cruzi*, which affects around 7 million people worldwide, mostly in development countries. The treatment relies on only two available drugs, with severe adverse effects and a limited efficacy. Therefore, the search for new therapies is a legitimate need. Within this context, our group reported the anti-*Trypanosoma cruzi* activity of gibbilibol B, a natural alkylphenol isolated from the plant *Piper malacophyllum*. Two synthetic derivatives, LINS03018 (1) and LINS03024

(2), demonstrated a higher antiparasitic potency and were selected for mechanism of action investigations. Our studies revealed no alterations in the plasma membrane potential, but a rapid alkalization of the acidocalcisomes. Nevertheless, compound 1 exhibit a pronounced effect in the bioenergetics metabolism, with a mitochondrial impairment and consequent decrease in ATP and reactive oxygen species (ROS) levels. Compound 2 only depolarized the mitochondrial membrane potential, with no interferences in the respiratory chain. Additionally, no macrophages response of nitric oxide (NO) was observed in both compounds. Noteworthy, simple structure modifications in these derivatives induced significant differences in their lethal effects. Thus, this work reinforces the importance of the mechanism of action investigations at the early phases of drug discovery and support further developments of the series.

Nanopore-Based Direct RNA Sequencing of the *Trypanosoma brucei* Transcriptome Identifies Novel lncRNAs.

Kruse E, Göringer HU.

28-02-2023

Genes (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36980882/>

Trypanosomatids are single-cell eukaryotic parasites. Unlike higher eukaryotes, they control gene expression post-transcriptionally and not at the level of transcription initiation. This involves all known cellular RNA circuits, from mRNA processing to mRNA decay, to translation, in addition to a large panel of RNA-interacting proteins that modulate mRNA abundance. However, other forms of gene regulation, for example by lncRNAs, cannot be excluded. lncRNAs are poorly studied in trypanosomatids, with only a single lncRNA characterized to date. Furthermore, it is not clear whether the complete inventory of trypanosomatid lncRNAs is known, because of the inherent cDNA-recoding and DNA-amplification limitations of short-read RNA sequencing. Here, we overcome these limitations by using long-read direct RNA sequencing (DRS) on nanopore arrays. We analyze the native RNA pool of the two main lifecycle stages of the African trypanosome *Trypanosoma brucei*, with a special emphasis on the inventory of lncRNAs. We identify 207 previously unknown lncRNAs, 32 of which are stage-specifically expressed. We also present insights into the complexity of the *T. brucei* transcriptome, including alternative transcriptional start and stop sites and potential transcript isoforms, to provide a bias-free understanding of the intricate RNA landscape in *T. brucei*.

ECG Marker Evaluation for the Machine-Learning-Based Classification of Acute and Chronic Phases of *Trypanosoma cruzi* Infection in a Murine Model.

Haro P, Hevia-Montiel N, Perez-Gonzalez J.

04-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977158/>

Chagas disease (CD) is a neglected parasitic disease caused by the protozoan *Trypanosoma cruzi* (*T. cruzi*). The disease has two clinical phases: acute and chronic. In the acute phase, the parasite circulates in the blood. The infection can be asymptomatic or can cause unspecific clinical symptoms. During the chronic phase, the infection can cause electrical conduction abnormalities and progress to cardiac failure. The use of an electrocardiogram (ECG) has been a methodology for diagnosing and monitoring CD, but it is necessary to study the ECG signals to better understand the behavior of the disease. The aim of this study is to analyze different ECG markers using machine-learning-based algorithms for the classification of the acute and chronic phases of *T. cruzi* infection in a murine experimental model. The presented methodology includes a statistical analysis of control vs. infected models in both phases, followed by an automatic selection of ECG descriptors and the implementation of several machine learning algorithms for the automatic classification of control vs. infected mice in acute and/or chronic phases (binomial classification), as well as a multiclass classification strategy (control vs. the acute group vs. the chronic group). Feature selection analysis showed that P wave duration, R and P wave voltages, and the QRS complex are some of the most important descriptors. The classifiers showed good results in detecting the acute phase of infection (with an accuracy of 87.5%), as well as in multiclass classification (control vs. the acute group vs. the chronic group), with an accuracy of 91.3%. These results suggest that it is possible to detect infection at different phases, which can help in experimental and clinical studies of CD.

Optimizing XCMS parameters for GC-MS metabolomics data processing: a case study.

Dos Santos EKP, Canuto GAB.

28-03-2023

Metabolomics.

<https://pubmed.ncbi.nlm.nih.gov/36976375/>

Nanoformulation of a Trypanocidal Drug Isometamidium Chloride Ameliorates the Apurinic-Apyrimidinic DNA Sites/Genotoxic Effects in Horse Blood Cells.

Singh S, Kumar B, Dilbaghi N, Devi N, Prasad M, Manuja A.

02-03-2023

J Xenobiot.

<https://pubmed.ncbi.nlm.nih.gov/36976161/>

Isometamidium chloride (ISM) is a trypanocide for the prophylactic and therapeutic use against vector-borne animal trypanosomosis (mainly Surra caused by *Trypanosoma evansi*) and African animal trypanosomosis caused by *T. congolense*/*T. vivax*/*T. brucei*). ISM was found to be an efficient trypanocide for therapeutic/prophylactic use against trypanosomosis; however, it produces some local and systemic detrimental effects in animals. We synthesized isometamidium chloride-loaded alginate gum acacia nanoformulation (ISM SANPS) to lessen the

detrimental side effects of isometamidium chloride (ISM) while treating trypanosomal diseases. We intended to determine the cytocompatibility/toxicity, and DNA deterioration/chromosomal structural or number changes (genotoxicity) of ISM SANPs using mammalian cells in a concentration-dependent manner. Apurinic/aprimidinic (AP) sites are one of the major types of DNA lesions formed during base excision and repair of oxidized, deaminated, or alkylated bases. The intensity of the cellular AP site is an excellent marker of the deterioration of DNA quality. We thought it pertinent to quantify the AP sites in ISM SANPs-treated cells. Our investigations established a dose-dependent cyto-compatibility or toxicity and DNA impairment (genotoxicity) in ISM SANPs-treated horse peripheral blood mononuclear cells. ISM SANPs were biocompatible at various concentrations tested on the mammalian cells.

Natural Trypanosoma cruzi Infection and Climatic Season Influence the Developmental Capacity in Field-Caught Mepraia spinolai Nymphs.

Botzotz J, Méndez-Valdés G, Ortiz S, López A, Botto-Mahan C, Solari A.

09-03-2023

Insects.

<https://pubmed.ncbi.nlm.nih.gov/36975957/>

Efficacy and Safety of Nifurtimox in Pediatric Patients with Chagas Disease: Results at 4-Year Follow-Up in a Prospective, Historically Controlled Study (CHICO SECURE).

Altcheh J, Sierra V, Ramirez T, Pinto Rocha JJ, Grossmann U, Huang E, Moscatelli G, Ding O.

28-03-2023

Antimicrob Agents Chemother.

<https://pubmed.ncbi.nlm.nih.gov/36975790/>

Nifurtimox is recommended for the treatment of Chagas disease; however, long-term follow-up data are scarce. This prolonged follow-up phase of the prospective, historically controlled, CHICO clinical trial evaluated seronegative conversion in pediatric patients aged <18 years with Chagas disease who were followed for 4 years after nifurtimox treatment. Patients were randomly assigned 2:1 to nifurtimox 60-day or 30-day regimens comprising 10 to 20 mg/kg/day for patients aged <12 years and body weight <40 kg, and 8 to 10 mg/kg/day for those aged ≥12 years and body weight ≥40 kg. Anti-*Trypanosoma cruzi* antibodies decreased during the study period, achieving seronegative conversion in 16 (8.12%) and 8 (8.16%) patients in the 60-day and 30-day nifurtimox regimens, respectively, with corresponding incidence rates per 100 patients/year of seronegative conversion of 2.12 (95% confidence interval [CI]: 1.21 to 3.45) and 2.11 (95% CI: 0.91 to 4.16). Superiority of the 60-day nifurtimox regimen was confirmed by the lower limit of the 95% CI being higher than that (0%) in a historical placebo control group. Children aged <2 years at baseline were more likely to reach seronegative conversion during the 4-year follow-up than older children. At any annual follow-up visit, >90%

of evaluable patients had persistently negative quantitative PCR results for *T. cruzi* DNA. No adverse events potentially related to treatment or caused by protocol-required procedures were documented for either treatment regimen. This study confirms the effectiveness and safety of a pediatric formulation of nifurtimox administered in an age- and weight-adjusted regimen for 60 days to treat children with Chagas disease.

Treatment with benznidazole and pentoxifylline regulates microRNA transcriptomic profile in a murine model of Chagas chronic cardiomyopathy.

Silva Grijó Farani P, Iandra da Silva Ferreira B, Begum K, Vilar-Pereira G, Pereira IR, Figueroa EAF, Cardenas-Ovando RA, Almeida IC, Roy S, Lannes-Vieira J, Moreira OC.

27-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36972298/>

The usefulness of the exercise stress test to predict outcome in patients with chronic Chagas disease: a longitudinal cohort study.

Grassi LV, Neto AC, Nogueira PR, Silva EF, Bestetti RB.

27-03-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36970975/>

Background: Risk stratification is paramount for treatment of patients with chronic Chagas disease (CCD). The exercise stress test (EST) may be useful in the risk stratification of patients with this condition, but few studies have been performed in patients with CCD.

Methods: This was a longitudinal, retrospective cohort study. A total of 339 patients followed at our institution from January 2000 to December 2010 were screened. A total of 76 (22%) patients underwent the EST. The Cox proportional hazards model was used to identify independent predictors of all-cause mortality. **Results:** Sixty-five (85%) patients were alive and 11 (14%) patients died by the study's close. In the univariate analysis, decreased systolic blood pressure (BP) at the peak of exercise and the double product were associated with all-cause mortality. However, in the multivariate analysis, only systolic BP at the peak of exercise was independently associated with all-cause mortality [hazard ratio 0.97 (95% confidence interval 0.94 to 0.99), $p=0.02$].

Conclusion: Systolic BP at the peak of EST is an independent predictor of mortality in patients with CCD.

Murine colon organoids as a novel model to study *Trypanosoma cruzi* infection and interactions with the intestinal epithelium.

Daghero H, Pagotto R, Quiroga C, Medeiros A, Comini MA, Bollati-Fogolin M.

09-03-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36968103/>

Advanced polymeric metal/metal oxide bionanocomposite using seaweed *Laurencia dendroidea* extract for antiprotozoal, anticancer, and photocatalytic applications.

Amina M, Al Musayeib NM, Alterary S, F El-Tohamy M, A Alhwaiti S.

20-03-2023

PeerJ.

<https://pubmed.ncbi.nlm.nih.gov/36967991/>

Background: Biosynthesized nanoparticles are gaining popularity due to their distinctive biological applications as well as bioactive secondary metabolites from natural products that contribute in green synthesis. **Methodology:** This study reports a facile, ecofriendly, reliable, and cost-effective synthesis of silver nanoparticles (AgNPs), copper oxide nanoparticles (CuONPs), and polymeric PVP-silver-copper oxide nanocomposite using ethanol extract of seaweed *Laurencia dendroidea* and were evaluated for antiprotozoal, anticancer and photocatalytic potential. The nanostructures of the AgNPs, CuONPs, and polymeric PVP-Ag-CuO nanocomposite were confirmed by different spectroscopic and microscopic procedures. **Results:** The UV-vis spectrum displayed distinct absorption peaks at 440, 350, and 470 nm for AgNPs, CuONPs, and polymeric Ag-CuO nanocomposite, respectively. The average particles size of the formed AgNPs, CuONPs, and Ag-CuO nanocomposite was 25, 28, and 30 nm, respectively with zeta potential values -31.7 ± 0.6 mV, -17.6 ± 4.2 mV, and -22.9 ± 4.45 mV. The microscopic investigation of biosynthesized nanomaterials revealed a spherical morphological shape with average crystallite sizes of 17.56 nm (AgNPs), 18.21 nm (CuONPs), and 25.46 nm (PVP-Ag-CuO nanocomposite). The antiprotozoal potential of green synthesized nanomaterials was examined against *Leishmania amazonensis* and *Trypanosoma cruzi* parasites. The polymeric PVP-Ag-CuO nanocomposite exerted the highest antiprotozoal effect with IC_{50} values of 17.32 ± 1.5 and 17.48 ± 4.2 μ M, in contrast to AgNPs and CuONPs. The anticancer potential of AgNPs, CuONPs, and polymeric PVP-Ag-CuO nanocomposite against HepG2 cancer cell lines revealed that all the nanomaterials were effective and the highest anticancer potential was displayed by PVP-Ag-CuO nanocomposite with IC_{50} values 91.34μ g mL⁻¹ at 200 μ g mL⁻¹ concentration. Additionally, PVP-Ag-CuO nanocomposite showed strong photocatalytic effect. **Conclusion:** Overall, this study suggested that the biogenic synthesized nanomaterials AgNPs, CuONPs, and polymeric PVP-Ag-CuO nanocomposite using ethanol extract of seaweed *L. dendroidea* possesses promising antiprotozoal anticancer and photocatalytic effect and could be further exploited for the development of antiprotozoal and anticancer therapeutics agents.

Role of myeloid-derived suppressor cells during *Trypanosoma cruzi* infection.

Borgna E, Prochetto E, Gamba JC, Marcipar I, Cabrera G.

2023

Int Rev Cell Mol Biol.

<https://pubmed.ncbi.nlm.nih.gov/36967151/>

Incentivizing optimal risk map use for *Triatoma infestans* surveillance in urban environments.

Arevalo-Nieto C, Sheen J, Condori-Luna GF, Condori-Pino C, Shinnick J, Peterson JK, Castillo-Neyra R, Levy MZ.

03-08-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962496/>

In Arequipa, Peru, a large-scale vector control campaign has successfully reduced urban infestations of the Chagas disease vector, *Triatoma infestans*. In addition to preventing new infections with *Trypanosoma cruzi* (etiological agent of Chagas disease), the campaign produced a wealth of information about the distribution and density of vector infestations. We used these data to create vector infestation risk maps for the city in order to target the last few remaining infestations, which are unevenly distributed and difficult to pinpoint. Our maps, which are provided on a mobile app, display color-coded, individual house-level estimates of *T. infestans* infestation risk. Entomologic surveillance personnel can use the maps to select homes to inspect based on estimated risk of infestation, as well as keep track of which parts of a given neighborhood they have inspected to ensure even surveillance throughout the zone. However, the question then becomes, how do we encourage surveillance personnel to actually use these two functionalities of the risk map? As such, we carried out a series of rolling trials to test different incentive schemes designed to encourage the following two behaviors by entomologic surveillance personnel in Arequipa: (i) preferential inspections of homes shown as high risk on the maps, and (ii) even surveillance across the geographical distribution of a given area, which we term, 'spatial coverage.' These two behaviors together constituted what we termed, 'optimal map use.' We found that several incentives resulted in one of the two target behaviors, but just one incentive scheme based on the game of poker resulted in optimal map use. This poker-based incentive structure may be well-suited to improve entomological surveillance activities and other complex multi-objective tasks.

Leishmaniose

Can domestic dogs be considered a good reservoir of *Leishmania* (L.) *infantum* chagasi in an endemic area of nonulcerated cutaneous leishmaniasis in Southern Honduras?

Segura GBR, Ochoa WHS, Matta VLRD, Martínez M, Tercero CR, Gonzalez RR, Pacheco CMS, Flores GVA, Silveira FT, Henriquez MMR, Laurenti MD.

24-03-2023

Rev Inst Med Trop Sao Paulo.

<https://pubmed.ncbi.nlm.nih.gov/36995877/>

Dogs are considered to be the main domestic reservoir associated with the transmission of *Leishmania* (L.) *infantum* chagasi to humans in endemic areas of visceral leishmaniasis in America. However, little is known about the role of canines as a source of infection in endemic

areas of nonulcerated cutaneous leishmaniasis (NUCL). Therefore, the objective of the present study was to investigate the role of dogs as a possible reservoir of the parasite in Southern Honduras. Dogs (n = 107) living with individuals affected by NUCL were clinically examined and biological material was collected for parasitological and immunological diagnosis. Most animals showed a healthy appearance and a few presented slight weight loss (64%), alopecia (7%), onychogryphosis (5%) and skin lesions (1%). The overall seroprevalence of *Leishmania* infection based on the DDP® quick test and/or in-house ELISA serological test was 41%. The presence of the parasite's DNA was confirmed in 94% of the dogs; however, the average parasite load in the buffy coat was low at 6.09 parasites/μL, ranging between 0.221 and 50.2. The skin of seropositive dogs examined by histopathology using paraffin sections stained by hematoxylin and immunohistochemistry did not show cutaneous lesions or parasite amastigotes. Based on the absence of parasites in the skin and the low parasite load detected in the buffy coat, it seems that the dog does not represent a good source of infection for the vector in the endemic area of NUCL transmission in Southern Honduras. Other domestic and/or wild animals should be investigated.

DC-SIGN receptor is expressed by cells from cutaneous leishmaniasis lesions and differentially binds to *Leishmania* (Viannia) *braziliensis* and *L. (Leishmania) amazonensis* promastigotes.

Mendes-Aguiar CO, Kitahara-Oliveira MY, de Almeida ACO, Pereira-Oliveira M, de Oliveira Neto MP, Pirmez C, Sampaio EP, Gomes-Silva A, Da-Cruz AM.

27-03-2023

Mem Inst Oswaldo Cruz.

<https://pubmed.ncbi.nlm.nih.gov/36995847/>

Background: Dendritic cells (DCs) specific intercellular adhesion molecule (ICAM)-3-grabbing non integrin receptor (DC-SIGN) binds to subgenera *Leishmania* promastigotes mediating its interaction with DC and neutrophils, potentially influencing the infection outcome.

Objectives: In this work, we investigated whether DC-SIGN receptor is expressed in cells from cutaneous leishmaniasis (CL) lesions as well as the in vitro binding pattern of *Leishmania* (*Viannia*) *braziliensis* (Lb) and *L. (L.) amazonensis* (La) promastigotes. **Methods:** DC-SIGN receptor was labeled by immunohistochemistry in cryopreserved CL tissue fragments. In vitro binding assay with CFSE-labeled Lb or La promastigotes and RAJI-transfecting cells expressing DC-SIGN (DC-SIGNPOS) or mock-transfected (DC-SIGNNEG) were monitored by flow cytometry at 2 h, 24 h and 48 h in co-culture. **Results:** In CL lesion infiltrate, DC-SIGNPOS cells were present in the dermis and near the epidermis. Both Lb and La bind to DC-SIGNPOS cells, while binding to DC-SIGNNEG was low. La showed precocious and higher affinity to DC-SIGNhi population than to DC-SIGNlow, while Lb binding was similar in these populations. **Conclusion:** Our results demonstrate that DC-SIGN receptor is present in *L. braziliensis* CL lesions and interact with Lb promastigotes. Moreover, the differences in the binding pattern to Lb and

La suggest DC-SIGN can influence in a difference way the intake of the parasites at the first hours after Leishmania infection. These results raise the hypothesis that DC-SIGN receptor could participate in the immunopathogenesis of American tegumentary leishmaniasis accounting for the differences in the outcome of the Leishmania spp. infection.

Blood parasite load by qPCR as therapeutic monitoring in visceral leishmaniasis patients in Brazil: a case series study.

Aquino SR, Diniz LFB, Nunes SLP, Silva RLO, Gouveia GV, Gouveia JJS, Sales KGDS, Dantas-Torres F, Carmo RFD.
27-03-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/36995785/>

Parasite hybridization promotes spreading of endosymbiotic viruses.

Heeren S, Maes I, Sanders M, Lye LF, Arevalo J, Llanos-Cuentas A, Garcia L, Lemey P, Beverley SM, Cotton JA, Dujardin JC, Van den Broeck F.
25-03-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993291/>

Viruses are the most abundant biological entities on Earth and play a significant role in the evolution of many organisms and ecosystems. In pathogenic protozoa, the presence of endosymbiotic viruses has been linked to an increased risk of treatment failure and severe clinical outcome. Here, we studied the molecular epidemiology of the zoonotic disease cutaneous leishmaniasis in Peru and Bolivia through a joint evolutionary analysis of *Leishmania braziliensis* parasites and their endosymbiotic *Leishmania* RNA virus. We show that parasite populations circulate in isolated pockets of suitable habitat and are associated with single viral lineages that appear in low prevalence. In contrast, groups of hybrid parasites were geographically and ecologically dispersed, and commonly infected from a pool of genetically diverse viruses. Our results suggest that parasite hybridization, likely due to increased human migration and ecological perturbations, increased the frequency of endosymbiotic interactions known to play a key role in disease severity.

ULK4 and Fused/STK36 interact to mediate assembly of a motile flagellum.

McCoy CJ, Paupelin-Vaucelle H, Gorilak P, Beneke T, Varga V, Gluenz E.
29-03-2023

Mol Biol Cell.

<https://pubmed.ncbi.nlm.nih.gov/36989043/>

The Bioactivity of Xylene, Pyridine, and Pyrazole Aza Macrocyces against Three Representative Leishmania Species.

Martín-Montes Á, Martínez-Camarena Á, Lopera A, Bonastre-Sabater I, Clares MP, Verdejo B, García-España E, Marín C.

20-03-2023

Pharmaceutics.

<https://pubmed.ncbi.nlm.nih.gov/36986853/>

Due to the urgent need for finding effective and free of secondary effect treatments for every clinical form of Leishmaniasis, a series of synthetic xylene, pyridine and, pyrazole azamacrocycles were tested against three *Leishmania* species. A total of 14 compounds were tested against J774.2 macrophage cells which were models for host cells, and against promastigote and amastigote forms of each studied *Leishmania* parasite. Amongst these polyamines, one proved effective against *L. donovani*, another one for *L. braziliensis* and *L. infantum*, and another one was selective solely for *L. infantum*. These compounds showed leishmanicidal activity and reduced parasite infectivity and dividing ability. Action mechanism studies gave a hint that compounds were active against *Leishmania* due to their ability to alter parasite metabolic pathways and reduce (except Py33333) parasitic Fe-SOD activity.

Emetic Tartar-Loaded Liposomes as a New Strategy for Leishmaniasis Treatment.

Coelho LD, Souza MMD, Cassali GD, Silva RA, Paiva MJN, Barros ALB, Teixeira EM, Silveira JN, Coelho PMZ, Aguiar MMG, Oliveira MC.
10-03-2023

Pharmaceutics.

<https://pubmed.ncbi.nlm.nih.gov/36986765/>

Virtual Screening of Benzimidazole Derivatives as Potential Triose Phosphate Isomerase Inhibitors with Biological Activity against Leishmania mexicana.

Vázquez-Jiménez LK, Juárez-Saldivar A, Chan-Bacab MJ, Delgado-Maldonado T, González-Morales LD, Palos I, Ortiz-Pérez E, Lara-Ramírez EE, Ramírez-Moreno E, Rivera G.
03-03-2023

Pharmaceutics (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36986489/>

Leishmania mexicana (*L. mexicana*) is a causal agent of cutaneous leishmaniasis (CL), a "Neglected disease", for which the search for new drugs is a priority. Benzimidazole is a scaffold used to develop antiparasitic drugs; therefore, it is interesting molecule against *L. mexicana*. In this work, a ligand-based virtual screening (LBVS) of the ZINC15 database was performed. Subsequently, molecular docking was used to predict the compounds with potential binding at the dimer interface of triosephosphate isomerase (TIM) of *L. mexicana* (*LmTIM*). Compounds were selected on binding patterns, cost, and commercial availability for in vitro assays against *L. mexicana* blood promastigotes. The compounds were analyzed by molecular dynamics simulation on *LmTIM* and its homologous human TIM. Finally, the physicochemical and pharmacokinetic properties were determined *in silico*. A total of 175 molecules with docking scores between -10.8 and -9.0 Kcal/mol were obtained. Compound E2 showed

the best leishmanicidal activity ($IC_{50} = 4.04 \mu M$) with a value similar to the reference drug pentamidine ($IC_{50} = 2.23 \mu M$). Molecular dynamics analysis predicted low affinity for human TIM. Furthermore, the pharmacokinetic and toxicological properties of the compounds were suitable for developing new leishmanicidal agents.

Antileishmanial Activity of Cinnamic Acid Derivatives against *Leishmania infantum*.

de Moraes MC, Medeiros GA, Almeida FS, Rocha JDC, Perez-Castillo Y, Keesen TSL, de Sousa DP.

21-03-2023

Molecules.

<https://pubmed.ncbi.nlm.nih.gov/36985814/>

Leishmania infantum is the etiological agent of visceral leishmaniasis (VL) in South America, the Mediterranean basin, and West and Central Asia. The most affected country, Brazil, reported 4297 VL cases in 2017. *L. infantum* is transmitted by female phlebotomine sand flies during successive blood meals. There are no validated vaccines to prevent the infection and the treatment relies on drugs that often present severe side effects, which justify the efforts to find new antileishmanial drugs. Cinnamic acid derivatives have shown several pharmacological activities, including antiparasitic action. Therefore, in the present study, the biological evaluation of cinnamic acid and thirty-four derivatives against *L. infantum* is reported. The compounds were prepared by several synthesis methods and characterized by spectroscopic techniques and high-resolution mass spectrometry. The results revealed that compound **32** (N-(4-isopropylbenzyl)cinnamamide) was the most potent antileishmanial agent ($IC_{50} = 33.71 \mu M$) with the highest selectivity index ($SI > 42.46$), followed by compound **15** (piperonyl cinnamate) with an $IC_{50} = 42.80 \mu M$ and $SI > 32.86$. Compound **32** was slightly less potent and nineteen times more selective for the parasite than amphotericin B ($MIC = 3.14 \mu M$; $SI = 2.24$). In the molecular docking study, the most likely target for the compound in *L. infantum* was aspartyl aminopeptidase, followed by aldehyde dehydrogenase, mitochondrial. The data obtained show the antileishmanial potential of this class of compounds and may be used in the search for new drug candidates against *Leishmania* species.

Antileishmanial and Antiplasmodial Activities of Secondary Metabolites from the Root of *Antrocaryon klaineana* Pierre (Anacardiaceae).

Amang À Ngnoung GA, Sidjui LS, Leutcha PB, Nganso Ditchou YO, Tchokouaha LRY, Herbette G, Baghdikian B, Kowa TK, Soh D, Kemzeu R, Poka M, Demana PH, Siwe Noundou X, Tchinda AT, Fekam Boyom F, Lannang AM, Nyassé B.

17-03-2023

Molecules.

<https://pubmed.ncbi.nlm.nih.gov/36985700/>

Constituents of the Stem Bark of *Symphonia globulifera* Linn. f. with

Antileishmanial and Antibacterial Activities.

Nguengang RT, Tchegnitegni BT, Nono ECN, Bellier Tabekoueng G, Fongang YSF, Bankeu JJK, Chouna JR, Nkenfou CN, Fekam FB, Sewald N, Lenta BN.

08-03-2023

Molecules.

<https://pubmed.ncbi.nlm.nih.gov/36985446/>

The chemical investigation of the *n*-hexane fraction from the methanol extract of the stem bark of *Symphonia globulifera* Linn f., which displayed good in vitro activity against *Leishmania donovani* NR-48822 promastigotes ($IC_{50} 43.11 \mu g/mL$), led to the isolation of three previously unreported polyprenylated benzophenones, guttiferone U (**1**), V (**2**)/W (**3**), and a new tocotrienol derivative named globuliferanol (**4**), along with 11 known compounds (**5-15**). Their structures were elucidated based on their NMR and MS data. Some isolated compounds were assessed for both their antileishmanial and cytotoxic activities against *L. donovani* and Vero cells, respectively. Guttiferone K (**5**) exhibited the best potency ($IC_{50} 3.30 \mu g/mL$), but with low selectivity to Vero cells. The *n*-hexane fraction and some compounds were also assessed in vitro for their antibacterial activity against seven bacterial strains. All the samples exhibited moderate to potent antibacterial activity ($MICs \leq 15.6 \mu g/mL$) against at least one of the tested strains.

Advances in Leishmania Research: From Basic Parasite Biology to Disease Control.

Santarém N, Cardoso L, Cordeiro-da-Silva A.

08-03-2023

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/36985269/>

Gene Signatures of Symptomatic and Asymptomatic Clinical-Immunological Profiles of Human Infection by *Leishmania (L.) chagasi* in Amazonian Brazil.

da Matta VLR, Gonçalves AN, Gomes CMC, Chouman IH, Ferreira FM, Campos MB, Lima LV, Vasconcelos Dos Santos T, Ramos PK, Furtado RR, Laurenti MD, Corbett CEP, Nakaya HI, Silveira FT.

03-03-2023

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/36985226/>

Data Independent Acquisition Reveals In-Depth Serum Proteome Changes in Canine Leishmaniosis.

Martinković F, Popović M, Smolec O, Mrljak V, Eckersall PD, Horvatić A.

28-02-2023

Metabolites.

<https://pubmed.ncbi.nlm.nih.gov/36984805/>

Comprehensive profiling of serum proteome provides valuable clues of health status and pathophysiological processes, making it the main strategy in biomarker

discovery. However, the high dynamic range significantly decreases the number of detectable proteins, obstructing the insights into the underlying biological processes. To circumvent various serum enrichment methods, obtain high-quality proteome wide information using the next-generation proteomic, and study host response in canine leishmaniosis, we applied data-independent acquisition mass spectrometry (DIA-MS) for deep proteomic profiling of clinical samples. The non-depleted serum samples of healthy and naturally *Leishmania*-infected dogs were analyzed using the label-free 60-min gradient sequential window acquisition of all theoretical mass spectra (SWATH-MS) method. As a result, we identified 554 proteins, 140 of which differed significantly in abundance. Those were included in lipid metabolism, hematological abnormalities, immune response, and oxidative stress, providing valuable information about the complex molecular basis of the clinical and pathological landscape in canine leishmaniosis. Our results show that DIA-MS is a method of choice for understanding complex pathophysiological processes in serum and serum biomarker development.

Inhibiting *Leishmania donovani* Sterol Methyltransferase to Identify Lead Compounds Using Molecular Modelling.

Sakyi PO, Kwofie SK, Tuekpe JK, Gwira TM, Broni E, Miller WA 3rd, Wilson MD, Amewu RK.

21-02-2023

Pharmaceuticals (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36986430/>

The recent outlook of leishmaniasis as a global public health concern coupled with the reportage of resistance and lack of efficacy of most antileishmanial drugs calls for a concerted effort to find new leads. The study combined *In silico* and in vitro approaches to identify novel potential synthetic small-molecule inhibitors targeting the *Leishmania donovani* sterol methyltransferase (*LdSMT*). The *LdSMT* enzyme in the ergosterol biosynthetic pathway is required for the parasite's membrane fluidity, distribution of membrane proteins, and control of the cell cycle. The lack of *LdSMT* homologue in the human host and its conserved nature among all *Leishmania* parasites makes it a viable target for future antileishmanial drugs. Initially, six known inhibitors of *LdSMT* with $IC_{50} < 10 \mu M$ were used to generate a pharmacophore model with a score of 0.9144 using LigandScout. The validated model was used to screen a synthetic library of 95,630 compounds obtained from InterBioScreen limited. Twenty compounds with pharmacophore fit scores above 50 were docked against the modelled three-dimensional structure of *LdSMT* using AutoDock Vina. Consequently, nine compounds with binding energies ranging from -7.5 to -8.7 kcal/mol were identified as potential hit molecules. Three compounds comprising STOCK6S-06707, STOCK6S-84928, and STOCK6S-65920 with respective binding energies of -8.7, -8.2, and -8.0 kcal/mol, lower than 22,26-azasterol (-7.6 kcal/mol), a known *LdSMT* inhibitor, were selected as plausible lead molecules. Molecular dynamics simulation studies and molecular mechanics Poisson-Boltzmann surface area calculations showed that the residues Asp25 and Trp208 were critical for ligand binding.

The compounds were also predicted to have antileishmanial activity with reasonable pharmacological and toxicity profiles. When the antileishmanial activity of the three hits was evaluated in vitro against the promastigotes of *L. donovani*, mean half-maximal inhibitory concentrations (IC_{50}) of $21.9 \pm 1.5 \mu M$ (STOCK6S-06707), $23.5 \pm 1.1 \mu M$ (STOCK6S-84928), and $118.3 \pm 5.8 \mu M$ (STOCK6S-65920) were obtained. Furthermore, STOCK6S-84928 and STOCK6S-65920 inhibited the growth of *Trypanosoma brucei*, with IC_{50} of $14.3 \pm 2.0 \mu M$ and $18.1 \pm 1.4 \mu M$, respectively. The identified compounds could be optimised to develop potent antileishmanial therapeutic agents.

Behind Base J: The Roles of JBP1 and JBP2 on Trypanosomatids.

Assis LHC, de Paiva SC, Cano MIN.

16-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986389/>

Chalcone Derivative Induces Flagellar Disruption and Autophagic Phenotype in *Phytomonas serpens* In Vitro.

Santos TAC, Silva KP, Souza GB, Alves PB, Menna-Barreto RFS, Scher R, Fernandes RPM.

07-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986345/>

Phytomonas serpens is a trypanosomatid phytoparasite, found in a great variety of species, including tomato plants. It is a significant problem for agriculture, causing high economic loss. In order to reduce the vegetal infections, different strategies have been used. The biological activity of molecules obtained from natural sources has been widely investigated to treat trypanosomatids infections. Among these compounds, chalcones have been shown to have anti-parasitic and anti-inflammatory effects, being described as having a remarkable activity on trypanosomatids, especially in *Leishmania* species. Here, we evaluated the antiprotozoal activity of the chalcone derivative (NaF) on *P. serpens* promastigotes, while also assessing its mechanism of action. The results showed that treatment with the derivative NaF for 24 h promotes an important reduction in the parasite proliferation ($IC_{50}/24 h = 23.6 \pm 4.6 \mu M$). At $IC_{50}/24 h$ concentration, the compound induced an increase in reactive oxygen species (ROS) production and a shortening of the unique flagellum of the parasites. Electron microscopy evaluation reinforced the flagellar phenotype in treated promastigotes, and a dilated flagellar pocket was frequently observed. The treatment also promoted a prominent autophagic phenotype. An increased number of autophagosomes were detected, presenting different levels of cargo degradation, endoplasmic reticulum profiles surrounding different cellular structures, and the presence of concentric membranar structures inside the mitochondrion. Chalcone derivatives may present an opportunity to develop a treatment for the *P. serpens* infection, as they

are easy to synthesize and are low in cost. In order to develop a new product, further studies are still necessary.

Vector-Borne Pathogens in Guard Dogs in Ibadan, Nigeria.

Gruenberger I, Liebich AV, Ajibade TO, Obebe OO, Ogbonna NF, Wortha LN, Unterköfler MS, Fuehrer HP, Ayinmode AB.

02-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986328/>

A New Strategy for Mapping Epitopes of LACK and PEPCK Proteins of *Leishmania amazonensis* Specific for Major Histocompatibility Complex Class I.

Ferreira-Sena EP, Haridoim DJ, Cardoso FO, d'Escoffier LN, Soares IF, Carvalho JPRDS, Angnes RA, Fragoso SP, Alves CR, De-Simone SG, Lima-Junior JDC, Bertho AL, Zaverucha-do-Valle T, da Silva FS, Calabrese KDS.

22-03-2023

Int J Mol Sci.

<https://pubmed.ncbi.nlm.nih.gov/36983046/>

Characterization and Proteomic Analysis of Plasma EVs Recovered from Healthy and Diseased Dogs with Canine Leishmaniosis.

Esteves S, Lima C, Costa I, Osório H, Fernandez-Becerra C, Santarém N, Cordeiro-da-Silva A.

13-03-2023

Int J Mol Sci.

<https://pubmed.ncbi.nlm.nih.gov/36982564/>

Dogs are highly valued companions and work animals that are susceptible to many life-threatening conditions such as canine leishmaniosis (CanL). Plasma-derived extracellular vesicles (EVs), exploited extensively in biomarker discovery, constitute a mostly untapped resource in veterinary sciences. Thus, the definition of proteins associated with plasma EVs recovered from healthy and diseased dogs with a relevant pathogen would be important for biomarker development. For this, we recovered, using size-exclusion chromatography (SEC), EVs from 19 healthy and 20 CanL dogs' plasma and performed proteomic analysis by LC-MS/MS to define their core proteomic composition and search for CanL-associated alterations. EVs-specific markers were identified in all preparations and also non-EVs proteins. Some EVs markers such as CD82 were specific to the healthy animals, while others, such as the Integrin beta 3 were identified in most samples. The EVs-enriched preparations allowed the identification of 529 canine proteins that were identified in both groups, while 465 and 154 were only identified in healthy or CanL samples, respectively. A GO enrichment analysis revealed few CanL-specific terms. *Leishmania* spp. protein identifications were also found, although with only one unique peptide. Ultimately, CanL-associated proteins of interest were identified and a core proteome was revealed that will be available for intra- and inter-species comparisons.

A RP-HPLC-DAD method for analysis of Brazilian southeast brown propolis and its leishmanicidal properties.

Ribeiro VP, Aldana-Mejia JA, Arruda C, Candido ACBB, Magalhães LG, Oliveira ND, Veneziani RCS, Bastos JK, Ambrósio SR.

28-03-2023

Biomed Chromatogr.

<https://pubmed.ncbi.nlm.nih.gov/36977284/>

A Calcium- and GTP-Dependent Transglutaminase in *Leishmania infantum*.

Almugadam SH, Trentini A, Maritati M, Contini C, Manfrinato MC, Cervellati C, Bellini T, Hanau S.

20-03-2023

Vet Sci. 2023

<https://pubmed.ncbi.nlm.nih.gov/36977273/>

Leishmanicidal Activity of Guanidine Derivatives against *Leishmania infantum*.

Almeida FS, Moreira VP, Silva EDS, Cardoso LL, de Sousa Palmeira PH, Cavalcante-Silva LHA, Araújo DAM, Amaral IPGD, González ERP, Keesen TSL.

25-02-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977142/>

Leishmaniasis is a neglected tropical infectious disease with thousands of cases annually; it is of great concern to global health, particularly the most severe form, visceral leishmaniasis. Visceral leishmaniasis treatments are minimal and have severe adverse effects. As guanidine-bearing compounds have shown antimicrobial activity, we analyzed the cytotoxic effects of several guanidine-bearing compounds on *Leishmania infantum* in their promastigote and amastigote forms in vitro, their cytotoxicity in human cells, and their impact on reactive nitrogen species production. LQOFG-2, LQOFG-6, and LQOFG-7 had IC₅₀ values of 12.7, 24.4, and 23.6 μ M, respectively, in promastigotes. These compounds exhibited cytotoxicity in axenic amastigotes at 26.1, 21.1, and 18.6 μ M, respectively. The compounds showed no apparent cytotoxicity in cells from healthy donors. To identify mechanisms of action, we evaluated cell death processes by annexin V and propidium iodide staining and nitrite production. Guanidine-containing compounds caused a significant percentage of death by apoptosis in amastigotes. Independent of *L. infantum* infection, LQOFG-7 increased nitrite production in peripheral blood mononuclear cells, which suggests a potential mechanism of action for this compound. Therefore, these data suggest that guanidine derivatives are potential anti-microbial molecules, and further research is needed to fully understand their mechanism of action, especially in anti-leishmanial studies.

Knowledge, attitude, and practice of the rural community about cutaneous leishmaniasis in Wolaita zone, southern Ethiopia.

Alemayehu B, Kelbore AG, Alemayehu M, Adugna C, Bibo T, Megaze A, Leirs H.

28-03-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/36976758/>

Background: Cutaneous leishmaniasis (CL) is a neglected tropical disease that is caused by a *Leishmania* parasite and transmitted by the bite of infected female sandflies. Community awareness is an essential component of disease control and prevention. Therefore, this study aimed to assess the community's knowledge, attitude, and practice toward CL in Wolaita zone, southern Ethiopia.

Methods: A community-based cross-sectional study design was employed to include 422 study subjects selected using a systematic sampling technique from two districts, Kindo Didaye and Sodo Zuria. A pretested structured questionnaire was used to collect data from the household heads. Bivariate and multivariate logistic regression analyses were performed to determine the relationship between the participants' knowledge about CL and socio-demographic characteristics. **Results:** Out of the 422 study participants, only 19% had good knowledge of CL in general. Most (67.1%) of the respondents knew CL by its local name ("bolbo" or "moora") though this knowledge varied highly over the study districts. The majority (86.3%) of respondents did not know how CL is acquired, though they considered CL a health problem. Most (62.8%) respondents believed that CL was an untreatable disease. Most (77%) participants responded that CL patients preferred to go to traditional healers for treatment. Herbal treatment was the most (50.2%) used to treat CL. Knowledge about CL was significantly associated with sex, age, and study districts.

Conclusion: The overall knowledge, attitude, and practice about CL and its prevention in the study area were low. This emphasizes the need to implement health education and awareness campaign to reduce the risk of CL infection. Policymakers and stakeholders should also give due attention to the prevention and treatment of CL in the study area.

Advanced polymeric metal/metal oxide bionanocomposite using seaweed *Laurencia dendroidea* extract for antiprotazoal, anticancer, and photocatalytic applications.

Amina M, Al Musayeib NM, Alterary S, F El-Tohamy M, A Alhwaiti S.

20-03-2023

PeerJ. 2023

<https://pubmed.ncbi.nlm.nih.gov/36967991/>

Towards effective natural anthraquinones to mediate antimicrobial photodynamic therapy of cutaneous leishmaniasis.

Dimmer JA, Cabral FV, Núñez Montoya SC, Ribeiro MS.

24-03-2023

Photodiagnosis Photodyn Ther.

<https://pubmed.ncbi.nlm.nih.gov/36966867/>

Background: Cutaneous leishmaniasis (CL) is an important tropical neglected disease with broad geographical dispersion. The lack of effective drugs has raised an urgent need to improve CL treatment, and antimicrobial photodynamic therapy (APDT) has been investigated as a new strategy to face it with positive outcomes. Natural compounds have emerged as promising photosensitizers (PSs), but their use in vivo remains unexplored. **Purpose:** In this work, we investigated the potential of three natural anthraquinones (AQs) on CL induced by *Leishmania amazonensis* in BALB/c mice. **Study design/methods:** ANIMALS WERE INFECTED AND RANDOMLY DIVIDED INTO FOUR GROUPS: : CG (control, non-treated group), G5ClSor-gL (treated with 5-chlorosoranjidiol and green LED, 520±10 nm), GSor-bL and GBisor-bL (treated with soranjidiol and bisoranjidiol, respectively, exposed to violet-blue LED, 410±10 nm). All AQs were assayed at 10 µM and LEDs delivered a radiant exposure of 45 J/cm² with an irradiance of 50 mW/cm². We assessed the parasite burden in real time for three consecutive days. Lesion evolution and pain score were assessed over 3 weeks after a single APDT session. **Results:** G5ClSor-gL was able to sustain low levels of parasite burden over time. Besides, GSor-bL showed a smaller lesion area than the control group, inhibiting the disease progression. **Conclusion:** Taken together, our data demonstrate that monoAQs are promising compounds for pursuing the best protocol for treating CL and helping to face this serious health problem. Studies involving host-pathogen interaction as well as monoAQ-mediated PDT immune response are also encouraged.

Updated diagnosis and graft involvement for visceral leishmaniasis in kidney transplant recipients: a case report and literature review.

Busutti M, Deni A, De Pascali AM, Ortalli M, Attard L, Granozzi B, Fabbri B, La Manna G, Comai G, Varani S.

Apr-2023

Infection.

<https://pubmed.ncbi.nlm.nih.gov/36329343/>

Purpose: Visceral leishmaniasis (VL) has become a rising concern to transplantation teams, being associated with graft dysfunction and reduced survival of renal transplant recipients. Here, we describe a case of VL occurring in a kidney transplant (KT) recipient in Italy, a country in which *Leishmania infantum* is endemic and we reviewed the literature on the clinical course and diagnosis of VL in KT recipients residing or travelling to southern Europe. **Results:** The VL case was diagnosed 18 months after transplant and 28 days after the onset of symptoms by quantitative PCR (qPCR) on peripheral blood. A graft biopsy showed renal involvement, and PCR performed on graft tissue displayed the presence of *Leishmania* DNA. The retrospective confirmation of *Leishmania*-positive serology in a serum sample collected before transplantation, as well as the absence of anti-*Leishmania* IgG in the graft donor strongly suggest that reactivation of a latent parasitic infection caused VL in the current case. **Conclusion:** VL is often underdiagnosed in transplant recipients, despite the presence of latent *Leishmania* infection being reported in endemic countries. This case

report, as well as the literature review on leishmaniasis in KT recipients, underline the importance of rapid VL diagnosis to promptly undergo treatment. Serology is scarcely sensitive in immunocompromised patients, thus molecular tests in peripheral blood should be implemented and standardized for both VL identification and follow-up.

Infectious diseases in German military personnel after predominantly tropical deployments: a retrospective assessment over 13 years.

Schawaller M, Wiemer D, Hagen RM, Frickmann H.

Apr-2023

BMJ Mil Health.

<https://pubmed.ncbi.nlm.nih.gov/33257519/>

Evasion of the complement system by *Leishmania* through the uptake of C4bBP, a complement regulatory protein, and probably by the action of GP63 on C4b molecules deposited on parasite surface.

Pereira-Filho AA, Queiroz DC, Saab NAA, D'Ávila Pessoa GC, Koerich LB, Pereira MH, Sant'Anna MRV, Araújo RN, Bartholomeu DC, Gontijo NF.

22-03-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36963597/>

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

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

22-03-2023

Int J Biol Macromol.

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

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

dynamics simulations. Altogether, our study presents a promising scaffold to explore small molecules to target the enzymatic activity of leishmanial SerRS to develop the specific therapeutics.

Real Time PCR-based diagnosis of human visceral leishmaniasis using urine samples.

Rahim S, Sharif MM, Amin MR, Rahman MT, Karim MM.

29-12-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962767/>

Editorial: *Leishmania* genome variability: Impacts on parasite evolution, parasitism and leishmaniases control.

Tosi LRO, Denny PW, De Oliveira CI, Damasceno JD.

06-03-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36949811/>

Retinoic acid shows direct parasitocidal activity by targeting ergosterol pathway in *Leishmania donovani*: a potential therapeutic advancement.

Prakash S, Rai AK.

28-03-2023

J Biomol Struct Dyn.

<https://pubmed.ncbi.nlm.nih.gov/36974957/>

Visceral leishmaniasis (VL) is an infectious disease caused by *Leishmania donovani* parasite in Indian subcontinent and is life-threatening. It primarily inflicts the malnourished population. There is little therapeutic advancement in the last one decade or more, as the available drugs show adverse effects, complex long treatment, high cost and drug resistance. Here, in a concerted approach, we intended to address the malnutrition as well as the parasite load with a single modality. Our earlier findings show the protective effects of retinoic acid (RA) in controlling the parasite load in infected macrophages (mφ) and restores their M1 phenotype. RA also restores the levels of cellular cholesterol in infected mφ. In this process, we observed loss of ergosterol in the parasite upon treatment with RA. Hence, we hypothesized that RA, besides boosting the parasitocidal mechanism in mφ, may also target the sterol pathway in the parasite by targeting sterol 24-C methyltransferase (SMT). SMT plays an essential role in the formation of ergosterol, required for growth and viability in *Leishmania* species. Therefore, we predicted as well as validated the 3D structure of SMT protein and performed the quality check. RA showed -9.9 free binding energy towards SMT which is higher than any of its derivatives. The molecular dynamics showed stable conjugate and the *in vitro* testing showed a reduction by ~ twofold in the parasite number upon RA treatment. Importantly, it showed a loss of ergosterol possibly due to the inhibition of SMT protein. Our finding showed direct parasitocidal function of RA which is of significance in terms

of therapeutic advancement. Communicated by Ramaswamy H. Sarma.

Comparing Dermatoscopic Features With Slit Skin Smear and Histopathology in Diagnosis of Cutaneous Leishmaniasis.

Memon S, Ahmed N, Shah SA, Bari AU, Rahim M, Farooq O, Nasir Memon M.

22-02-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36974240/>

Retraction Note: Role of inhibitors of serine peptidases in protecting *Leishmania donovani* against the hydrolytic peptidases of sand fly midgut.

Verma S, Das S, Mandal A, Ansari MY, Kumari S, Mansuri R, Kumar A, Singh R, Saini S, Abhishek K, Kumar V, Sahoo GC, Das P.

27-03-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36973726/>

MCP-1/IL-12 ratio expressions correlated with adventitial collagen depositions in renal vessels and IL-4/IFN- γ expression correlated with interstitial collagen depositions in the kidneys of dogs with canine leishmaniasis.

Verçosa BLA, Muniz-Junqueira MI, Menezes-Souza D, Fujiwara RT, Borges LF, Melo MN, Vasconcelos AC.

Apr-2023

Mol Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36889187/>

Collagen deposition is a common event in chronic inflammation, and canine Leishmaniosis (CanL) is generally associated with a long and chronic evolution. Considering that the kidney shows fibrinogenic changes during CanL, and the balance of cytokines/chemokines regulates the profibrinogenic and antifibrinogenic immune responses differently, it can be hypothesized that the balance of cytokines/chemokines can be differentially expressed in the renal tissue in order to determine the expression of collagen depositions in the kidneys. This study aimed to measure collagen deposition and to evaluate cytokine/chemokine expressions in the kidney by means of qRT-PCR in sixteen *Leishmania*-infected dogs and six uninfected controls. Kidney fragments were stained with hematoxylin & eosin (H&E), Masson's Trichrome, Picrosirius Red, and Gomori's reticulin. Intertubular and adventitial collagen depositions were evaluated by the morphometric approach. Cytokine RNA expressions were measured by means of qRT-PCR to identify molecules involved in chronic collagen depositions in kidneys with CanL. Collagen depositions were related to the presence of clinical signs, and more intense intertubular collagen depositions occurred in infected dogs. Adventitial collagen deposition, as morphometrically measured by the average

area of the collagen, was more intense in clinically affected dogs than in subclinically infected dogs. TNF- α /TGF- β , MCP1/IL-12, CCL5/IL-12, IL-4/IFN- γ , and IL-12/TGF- β expressions were associated with clinical manifestations in dogs with CanL. The IL-4/IFN- α ratio was more commonly expressed and upregulated in clinically affected dogs, and downregulated in subclinically infected dogs. Furthermore, MCP-1/IL-12 and CCL5/IL-12 were more commonly expressed in subclinically infected dogs. Strong positive correlations were detected between morphometric values of interstitial collagen depositions and MCP-1/IL-12, IL-12, and IL-4 mRNA expression levels in the renal tissues. Adventitial collagen deposition was correlated with TGF- β , IL-4/IFN- γ , and TNF- α /TGF- β . In conclusion, our results showed the association of MCP-1/IL-12 and CCL5/IL-12 ratios with an absence of clinical signs, as well as an IL-4/IFN- α ratio with adventitial and intertubular collagen depositions in dogs with visceral leishmaniosis.

Epoxy- α -lapachone (2,2-Dimethyl-3,4-dihydro-spiro[2H-naphtho[2,3-b]pyran-10,2'-oxirane]-5(10H)-one): a promising molecule to control infections caused by protozoan parasites.

Peixoto JF, Oliveira ADS, Gonçalves-Oliveira LF, Souza-Silva F, Alves CR.

Mar-Apr2023

Braz J Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36731538/>

Exploration of aminoacyl-tRNA synthetases from eukaryotic parasites for drug development.

Gill J, Sharma A.

Mar-2023

J Biol Chem.

<https://pubmed.ncbi.nlm.nih.gov/36596362/>

Parasitic diseases result in considerable human morbidity and mortality. The continuous emergence and spread of new drug-resistant parasite strains is an obstacle to controlling and eliminating many parasitic diseases. Aminoacyl-tRNA synthetases (aaRSs) are ubiquitous enzymes essential for protein synthesis. The design and development of diverse small molecule, drug-like inhibitors against parasite-encoded and expressed aaRSs have validated this enzyme family as druggable. In this work, we have compiled the progress to date towards establishing the druggability of aaRSs in terms of their biochemical characterization, validation as targets, inhibitor development, and structural interpretation from parasites responsible for malaria (*Plasmodium*), lymphatic filariasis (*Brugia*, *Wuchereria bancrofti*), giardiasis (*Giardia*), toxoplasmosis (*Toxoplasma gondii*), leishmaniasis (*Leishmania*), cryptosporidiosis (*Cryptosporidium*), and trypanosomiasis (*Trypanosoma*). This work thus provides a robust framework for the systematic dissection of aaRSs from these pathogens and will facilitate the cross-usage of potential inhibitors to jump-start anti-parasite drug development.

Cysticercose

Financial Losses Arising from Cattle Organ and Carcass Condemnation at Lokoloko Abattoir in Wau, South Sudan.

Taha A, Saad S, Jubara A, Wani C, Phiri AM, Simuunza M, Munyeme M, Hang'ombe B, Mumba C.

Mar-2023

Adv Prev Med.

<https://pubmed.ncbi.nlm.nih.gov/36993140/>

Slaughterhouses in South Sudan mirror the economic losses resulting from cattle organs and carcass condemnation due to zoonotic and epizootic diseases of livestock, such as tuberculosis, cysticercosis, and hydatidosis in cattle. However, due to the war, slaughterhouse record keeping has been inconsistent in South Sudan, and thus the estimation of diseases in cattle and their impact may be underestimated. Therefore, this study was conducted to estimate the major causes of carcasses and organ condemnation of cattle slaughtered at Lokoloko abattoir and the resulting financial losses. A cross-sectional active abattoir survey involving antemortem and postmortem examinations was conducted on 310 cattle between January 2021 and March 2021. Furthermore, five-year (September 2015-September 2020) retrospective data on meat inspection records were also collected and analyzed. During the antemortem inspection of the active abattoir survey, 103 (33.2%) cattle had signs of disease. These signs included herniam 17 (5.5%), local swelling 16 (5.2%), lameness 15 (4.8%), emaciation 13 (4.2%), blindness 12 (3.9%), depression 11 (3.5%), pale mucus membrane 7 (2.3%), nasal discharge 5 (1.6%), lacrimation 4 (1.3%), and salivation 03 (0.97%). Postmortem inspection revealed gross pathological findings on 180 (58.6%) carcasses, out of which 47 (26.1%) livers and 31 (17.2%) hearts were condemned due to various causes. The active abattoir survey and the retrospective data revealed that tuberculosis, fascioliasis, hydatidosis, and heart cysticercosis were the leading causes of condemnation of carcasses and organs. In the active abattoir survey, a total of 19,592,508 South Sudanese Pounds, equivalent to US\$29,686 was lost from organ condemnation, while in the retrospective data; the overall direct financial loss during the five years was estimated to be 299,225,807 South Sudanese Pounds equivalent to US\$453,372. This study revealed that bacterial and parasitic diseases were the common causes of carcass and organ condemnations and caused significant financial losses at Lokoloko abattoir in Wau, South Sudan. Therefore, there is a need for training farmers on cattle disease management, heightened meat inspections, and proper disposal of condemned meat.

Clinical Implications for the Comprehensive Interpretation of Radiologic and Immunodiagnostic Tests in Patients Suspected of Parasitic Hepatic Cyst, a Rare Case in Korea.

Yoo JS, Kang MK, Park JG, Kim HJ, Choi JH.

Mar-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977156/>

Cystic echinococcosis (CE) is a representative neglected tropical disease (NTD) with increased morbidity and mortality but is ignored and overlooked in developed countries. Serological and radiographic findings are helpful in distinguishing these parasites; however, conflicting results of these can make it difficult to diagnose if medical knowledge of hepatic parasitic disease, including the etiology, features of imaging, and immunodiagnostic test, is not acquired. We report the case of a male patient with dyspepsia and right epigastric pain who had positive results for cysticercosis antibodies on immunodiagnostic examination. Abdominal ultrasonography revealed two huge communicating cystic lesions measuring 8-11 cm. Further evaluations for cysticercosis of the brain (neurocysticercosis) and eyes (intraocular cysticercosis) were unremarkable throughout the brain imaging test and fundus examination. A laparoscopic right hemihepatectomy was performed for diagnosis and treatment. On histopathological examination, diverse stages of *Echinococcus granulosus* were identified. Albendazole was administered postoperatively, and the patient was also followed up. We should be aware of the etiologies that have been prevalent in parasite infection thought to be the cause of hepatic cysts. Moreover, we make an effort to ascertain the patient's nationality, past travel experiences, and immediate environment, including any animals and pets. We present the case of a patient who was worried about the possibility of liver invasion of cysticercus due to the positivity of the cysticercosis antibody and was ultimately diagnosed with CE.

[A case with severe neurocysticercosis].

Huang L, Chen X, Liu Y, Li T.

May-2022

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36974025/>

[Temporal trends in disease burden of major human parasitic diseases in China from 1990 to 2019].

Zeng T, Lü S, Tian L, Li S, Sun L, Jia T.

06-03-2023

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36974009/>

Objective: To analyze the temporal trends in the disease burden of major human parasitic diseases in China from 1990 to 2019, so as to provide the evidence for improving the parasitic disease control strategy in China. **Methods:** The disability-adjusted life years (DALYs) of malaria, intestinal nematode infections, schistosomiasis, food-borne trematodiasis, cysticercosis and echinococcosis in China from 1990 to 2019 were captured from the Global Burden of Disease Study 2019 (GBD 2019), and age- and gender-specific DALYs of parasitic diseases were estimated. The temporal trends in DALYs of malaria, intestinal nematode infections, schistosomiasis, food-borne trematodiasis, cysticercosis and echinococcosis were evaluated in China from 1990 to 2019 using average annual percent change (AAPC) with Joinpoint regression

analysis. **Results:** The DALYs were 643 836.42 person-years due to food-borne trematodiasis, 156 853.03 person-years due to cysticercosis, 79 764.62 person-years due to schistosomiasis, 70 989.73 person-years due to intestinal nematode infections, 4 258.61 person-years due to echinococcosis and 264.86 person-years due to malaria in China in 2019, respectively. The overall DALYs of six parasitic diseases were higher among men (546 441.93 person-years) than among women (409 525.33 person-years), and were greater among adults at ages of 14 to 65 years (684 780.84 person-years) than among children at 14 years and lower (35 437.38 person-years) and the elderly at ages of 65 years and older (235 749.04 person-years). During the period from 1990 to 2019, food-borne trematodiasis were the leading cause of DALYs among the six parasitic diseases, and cysticercosis shifted from the fourth leading cause in 1990 to the second leading cause of DALYs in China in 2019, while intestinal nematode infections shifted from the second leading cause in 1990 to the fourth leading cause of DALYs in 2019. The DALYs of major human parasitic diseases appeared an overall tendency towards a decline in China from 1990 to 2019, with the fastest drop seen in DALYs due to malaria (AAPC = -19.6%, $P = 0.003$), followed by due to intestinal nematode infections (AAPC = -8.2%, $P < 0.001$) and schistosomiasis (AAPC = -3.1%, $P < 0.001$), and a slow decline was seen in the DALYs of food-borne trematodiasis (AAPC = -1.0%, $P < 0.001$), while there were no significant decrease in the DALYs of echinococcosis (AAPC = -0.5%, $P = 0.264$) and the DALYs of cysticercosis appeared a tendency towards a rise (AAPC = 0.7%, $P < 0.001$). **Conclusions:** The disease burden of major human parasitic diseases appeared an overall tendency towards a decline in China from 1990 to 2019, with a high disease burden seen due to food-borne parasitic diseases, no remarkable reduction seen in echinococcosis, and a tendency towards a rise seen in cysticercosis. It is recommended to focus on echinococcosis control, and continue to consolidate the control achievements of other major human parasitic diseases in China; meanwhile, the surveillance and prevention of food-borne parasitic diseases should be reinforced.

Knowledge and practices about taeniasis/cysticercosis complex within the framework of the national plan for its elimination in Colombia, 2019.

Rueda RG, Ospina RAK, Másmela LAO, López NG, Calambas AIO, Díaz LFN, Ippolito NGA, Fernández-Niño JA, Pérez MCL.

22-03-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36963599/>

The taeniasis/cysticercosis complex (TCC) belongs to the group of neglected infectious diseases with a multifactorial transmission that includes hosts such as humans and pigs of the parasitic tapeworm (*Taenia solium*) and environmental factors. This study represents the first phase of the National and Cross-sectoral Plan for TCC Elimination. **Objectives:** To obtain data about knowledge and practices in relation to the TCC from knowledge, attitudes, and practices (KAP) surveys applied

in two pilot localities for building a baseline of the potential risk factors related to identification, prevention, and control of TCC in Colombia. **Methods:** A descriptive cross-sectional survey from October to November in 2019 was carried out using a structured questionnaire and random sampling by single-stage conglomerates in the municipalities of Mahates, Bolívar (n=152) (Atlantic Region) and Mercaderes, Cauca (n=152) (Andean Region). **Results:** Respondents in Mahates showed moderate knowledge about TCC compared to those in Mercaderes, however, risky practices were identified in both places (consumption of pork with cysts and defecation in places other than the bathroom or latrine). Deficiency in infrastructure and failure in basic services were observed as potential risk factors for TCC transmission in both municipalities. **Conclusion:** Based on the framework of the National and Cross-sectoral Plan for TCC Elimination, adequate knowledge on identification, prevention, and control of the disease must be reinforced; cultural and ecological differences should be considered when designing communication and knowledge transmission tools. We consider that major investment should be made in improving basic services and creating sustainable modernized pig farming in Mahates and Mercaderes.

Food- and vector-borne parasitic zoonoses: Global burden and impacts.

Anisuzzaman, Hossain MS, Hatta T, Labony SS, Kwofie KD, Kawada H, Tsuji N, Alim MA.

2023

Adv Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36948728/>

An epidemiological survey of porcine cysticercosis in Rungwe District, Tanzania.

Sanga TA, Maganira JD, Kidima WB.

Apr-2023

Prev Vet Med.

<https://pubmed.ncbi.nlm.nih.gov/36736267/>

Taeniasis/cysticercosis caused by tapeworms belonging to the genus *Taenia*, poses serious veterinary and public health problems, resulting in economic burden in endemic low-income countries worldwide. However, little epidemiological data exist on infection status among pigs in many areas in Tanzania. We conducted a cross-sectional survey in Rungwe District, Mbeya Region, Tanzania, to define the prevalence and risk factors associated with porcine cysticercosis transmission. One-hundred sixty-nine pigs from 152 households were examined for circulating taeniid antigens by cysticercosis antigen (Ag) enzyme-linked immunosorbent assay (ELISA). Agarose gel electrophoresis was used to differentially diagnose *Taenia* species-specific cysticerci DNA bands. Structured questionnaires were administered in the surveyed households to collect information on risk factors for porcine cysticercosis transmission. Sera from eleven household pigs tested positive for porcine cysticercosis in the Ag-ELISA with an apparent prevalence of 6.5 % (95 % C.I. 3.8-11.3 %) and estimated true prevalence of 6.1 % (95 % C.I. 3.3-10.9 %). DNA Gel electrophoresis confirmed that

100 % of cysticerci isolated amongst pigs slaughtered in the study area belonged to *T. solium*. Of the five surveyed wards, positive household pigs were from Bulyaga, Kiwira, and Mpuguso. Lack of knowledge on porcine cysticercosis among household members was found to be significantly associated with positivity of *Taenia* species antigen in pigs sera (OR = 7.742, $p = 0.017$). Our results show that porcine cysticercosis is prevalent in Rungwe. There is a definite need to establish control measures against this potential zoonosis to safeguard veterinary and public health in the Rungwe District.

Dracunculose

Curcumin inhibits the pruritus in mice through mast cell MrgprB2 receptor.

Jiang Y, Zong Y, Du Y, Zhang M, Ye F, Zhang J, Yang Y, Zhu C, Tang Z.

30-03-2023

Inflamm Res.

<https://pubmed.ncbi.nlm.nih.gov/36997814/>

Background: Curcumin is a diketone compound extracted from the rhizomes of some plants in the Zingiberaceae and Araceae family. It possesses a variety of biological activities, including antioxidant, anti-inflammatory and anti-cancer properties. However, the cellular and molecular antipruritic mechanisms of curcumin remain to be explored. **Objective:** Our objective was to study the role of curcumin in pruritus and determine whether its antipruritic effect is related to MrgprB2 receptor. **Methods:** The effect of curcumin on pruritus in mice was examined by scratching behavior test. The antipruritic mechanism of curcumin was explored by using transgenic mice (MrgprB2^{-/-} mice, MrgprB2Cre^{Td/tomato} mice), histological analysis, western blot and immunofluorescence. In addition, the relationship between curcumin and MrgprB2/X2 receptor was studied in vitro by using calcium imaging, plasmid transfection and molecular docking. **RESULTS:** In the current study, we found that curcumin had obvious antipruritic effect. Its antipruritic effect was related to the regulation of MrgprB2 receptor activation and mast cells tryptase release. In vitro, mouse peritoneal mast cells activated by compound 48/80 could be inhibited by curcumin. In addition, curcumin was also found to suppress the calcium flux in MrgprX2 or MrgprB2-overexpression HEK cells induced by compound 48/80, substance P, and PAMP 9-20, displaying the specific relation with the MrgprB2/X2 receptor. Moreover, molecular docking results showed that curcumin had affinity to MrgprX2 protein. **Conclusions:** Overall, these results indicated that curcumin has the potential to treat pruritus induced by mast cell MrgprB2 receptor.

The Effect of Quinolones on Common Duckweed *Lemna minor* L., a Hydrophyte Bioindicator of Environmental Pollution.

Sikorski Ł, Bęś A, Warmiński K.

14-03-2032

Int J Environ Res Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36981998/>

Modulation of MRSA virulence gene expression by the wall teichoic acid enzyme TarO.

Lu Y, Chen F, Zhao Q, Cao Q, Chen R, Pan H, Wang Y, Huang H, Huang R, Liu Q, Li M, Bae T, Liang H, Lan L.

22-03-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/36949052/>

Phenol-soluble modulins (PSMs) and Staphylococcal protein A (SpA) are key virulence determinants for community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA), an important human pathogen that causes a wide range of diseases. Here, using chemical and genetic approaches, we show that inhibition of TarO, the first enzyme in the wall teichoic acid (WTA) biosynthetic pathway, decreases the expression of genes encoding PSMs and SpA in the prototypical CA-MRSA strain USA300 LAC. Mechanistically, these effects are linked to the activation of VraRS two-component system that directly represses the expression of accessory gene regulator (*agr*) locus and *spa*. The activation of VraRS was due in part to the loss of the functional integrity of penicillin-binding protein 2 (PBP2) in a PBP2a-dependent manner. TarO inhibition can also activate VraRS in a manner independent of PBP2a. We provide multiple lines of evidence that accumulation of lipid-linked peptidoglycan precursors is a trigger for the activation of VraRS. In sum, our results reveal that WTA biosynthesis plays an important role in the regulation of virulence gene expression in CA-MRSA, underlining TarO as an attractive target for anti-virulence therapy. Our data also suggest that acquisition of PBP2a-encoding *mecA* gene can impart an additional regulatory layer for the modulation of key signaling pathways in *S. aureus*.

Polyploidy impacts population growth and competition with diploids: multigenerational experiments reveal key life-history trade-offs.

Anneberg TJ, O'Neill EM, Ashman TL, Turcotte MM.

May-2023

New Phytol.

<https://pubmed.ncbi.nlm.nih.gov/36740596/>

Ecological theory predicts that early generation polyploids ('neopolyploids') should quickly go extinct owing to the disadvantages of rarity and competition with their diploid progenitors. However, polyploids persist in natural habitats globally. This paradox has been addressed theoretically by recognizing that reproductive assurance of neopolyploids and niche differentiation can promote establishment. Despite this, the direct effects of polyploidy at the population level remain largely untested despite establishment being an intrinsically population-level process. We conducted population-level experiments where life-history investment in current and future growth was tracked in four lineage pairs of diploids and synthetic autotetraploids of the aquatic plant *Spirodela polyrrhiza*. Population growth was evaluated with and without competition between diploids and neopolyploids across a

range of nutrient treatments. Although neopolyploid populations produce more biomass, they reach lower population sizes and have reduced carrying capacities when growing alone or in competition across all nutrient treatments. Thus, contrary to individual-level studies, our population-level data suggest that neopolyploids are competitively inferior to diploids. Conversely, neopolyploid populations have greater investment in dormant propagule production than diploids. Our results show that neopolyploid populations should not persist based on current growth dynamics, but high potential future growth may allow polyploids to establish in subsequent seasons.

Echinococcoses

Popliteal Echinococcosis: A Long Journey from the Liver.

Erginöz E, Ergün S, Tunç E, Pekmezci S.

30-03-2023

Acta Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36995509/>

Complication of Hepatic Hydatid Cyst Surgery Presenting as Obstructive Jaundice.

Ahire P, Iyer N, Gada PB.

24-03-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36994267/>

The liver is the commonest organ affected by hydatid disease. We report a rare case of a 25-year-old female patient who was treated surgically for hepatic echinococcosis two weeks ago with laparoscopic excision of hepatic hydatid cyst with marsupialization and omentoplasty. She then presented with features of obstructive jaundice, which is a known complication following hydatid endocystectomy. Cholangiogram revealed a communication of the residual hydatid cyst with right segmental intrahepatic biliary radicals. She was treated with endoscopic retrograde cholangiopancreatography (ERCP)-guided stenting. ERCP is regarded as an important therapeutic strategy for hydatid cysts occurring in the extra biliary tree either as primary or as complications of liver cysts. It facilitates the clearing of hydatid debris from the biliary tree, and the closure of fistulas and bile leaks followed by laparoscopic cholecystectomy when the hydatid cysts are also located in the gallbladder.

Ruptured pulmonary hydatid cyst and lophomoniasis comorbidity in a young man: a rare case.

Jalayeri MHT, Zakariaei Z, Fakhar M, Sharifpour A, Banimostafavi ES, Soleymani M.

25-03-2023

Oxf Med Case Reports.

<https://pubmed.ncbi.nlm.nih.gov/36993831/>

Hydatidosis is a parasitic and zoonotic infection caused by the larval stage of *Echinococcus granulosus*. Cysts of this parasite involve almost all the organs of the human body, especially the liver and lungs. Asymptomatic cases may develop into symptomatic pulmonary hydatidosis due to the rupture of hydatid cysts. *Lophomonas*, as causative agents of pulmonary lophomoniasis, is an emerging protozoan that mostly infects the lower respiratory airways. Clinical symptoms of these two diseases can mostly be overlapped. Herein, we describe the rare case of comorbidity of a ruptured cystic echinococcosis and lophomoniasis in a 38-year-old male farmer with a history of opium addiction from northern Iran.

Anti-Tumor Effect of Protoscolex Hydatid Cyst Somatic Antigen on Inhibition Cell Growth of K562.

Asouli A, Sadr S, Mohebalian H, Borji H.

29-03-2023

Acta Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36991291/>

Response of wild rodents to red fox feces: implication for the echinococcus infection.

Sasaki R, Okuma I, Asari Y.

29-03-2023

J Vet Med Sci.

<https://pubmed.ncbi.nlm.nih.gov/36990791/>

Echinococcus multilocularis causes zoonotic disease, alveolar echinococcosis. The life cycle of *E. multilocularis* is maintained by the predator-prey relationship between red foxes and rodents. Infection to red fox (*Vulpes vulpes*) of *E. multilocularis* is considered that rodents take eggs of *E. multilocularis*, then red fox forage the rodents. However, it has been not known how to take eggs by rodents. On infection process of *E. multilocularis* from red foxes to rodents, we predicted that rodents would forage or touch with feces of red fox to use undigested materials within the feces. We monitored rodent's response to fox feces and their distance to the feces by using camera trap from May to October 2020. *Myodes* spp. and *Apodemus* spp. touched fox feces, and touch rate of *Apodemus* spp. was significantly higher than that of *Myodes* spp. We found smelling and passing as contact behaviors to fox feces by *Myodes* spp., while *Apodemus* spp. showed behaviors which oral directly contacted feces. There was no significant difference on the shortest distance between *Apodemus* spp. and *Myodes* spp. The distance between 0 cm and 5 cm was mostly observed for both rodents. The results that *Myodes* spp. did not forage feces and their contact to feces was low frequency suggested that the infection from red foxes to *Myodes* spp., the main intermediate host, was to be other pathways. The approach to feces and the act near feces might increase the probability attached with eggs.

Basic Operative Tactics for Pulmonary Echinococcosis in the Era of Endostaplers and Energy Devices.

Bakinowska E, Kostopanagiotou K, Wojtyś ME, Kiełbowski K, Ptasiński K, Gajić D, Ruszel N, Wójcik J, Grodzki T, Tomos P.
10-03-2023
Medicina (Kaunas).
<https://pubmed.ncbi.nlm.nih.gov/36984545/>

Hydatid Disease: A Radiological Pictorial Review of a Great Neoplasms Mimicker.

Alshoabi SA, Alkalady AH, Almas KM, Magram AO, Algaberi AK, Alareqi AA, Hamid AM, Alhazmi FH, Qurashi AA, Abdulaal OM, Aloufi KM, Alsharif WM, Alsultan KD, Omer AM, Gareeballah A.
16-03-2023
Diagnostics (Basel).
<https://pubmed.ncbi.nlm.nih.gov/36980435/>

Hydatid cyst is a common name for the larval stage of a tapeworm species of *Echinococcus granulosus*, which is transmitted from animals to humans via the fecal-oral route. Hydatid cysts predominantly affect the liver (75%), followed by the lung (15%), and they can affect many organs in the human body. Medical imaging modalities are the keystone for the diagnosis of hydatid cysts with high sensitivity and specificity. Ultrasound imaging with high resolution is the first choice for diagnosis, differential diagnosis, staging, establishing a role in interventional management, and follow-up, and it can differentiate Type I hydatid cysts from simple liver cysts. Unenhanced computed tomography (CT) is indicated where or when an ultrasound is unsatisfactory, such as with chest or brain hydatid cysts, when detecting calcification, and in obese patients. Magnetic resonance imaging (MRI) is superior for demonstrating cyst wall defects, biliary communication, neural involvement, and differentiating hydatid cysts from simple cysts using diffusion-weighted imaging (DWI) sequences. According to the phase of growth, hydatid cysts occur in different sizes and shapes, which may mimic benign or malignant neoplasms and may create diagnostic challenges in some cases. Hydatid cysts can mimic simple cysts, choledochal cysts, Caroli's disease, or mesenchymal hamartomas of the liver. They can mimic lung cystic lesions, mycetoma, blood clots, Rasmussen aneurysms, and even lung carcinomas. Differential diagnosis can be difficult for arachnoid cysts, porencephalic cysts, pyogenic abscesses, and even cystic tumors of the brain, and can create diagnostic dilemmas in the musculoskeletal system.

Seroprevalence of Strongyloides stercoralis in Patients about to Receive Immunosuppressive Treatment in Gran Canaria (Spain).

Carranza-Rodríguez C, López-Delgado L, Granados-Magan Á, Pérez-Arellano JL.
20-03-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/36977182/>

Clinical Implications for the Comprehensive Interpretation of Radiologic and Immunodiagnostic Tests

in Patients Suspected of Parasitic Hepatic Cyst, a Rare Case in Korea.

Yoo JS, Kang MK, Park JG, Kim HJ, Choi JH.
02-03-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/36977156/>

Renal Hydatid Cyst in a Child Managed with Albendazole.

Pandey U, Timilsina BR, Acharya S, Paudel U, Kc SR, Pradhan S.
10-03-2023
J Nepal Health Res Council.
<https://pubmed.ncbi.nlm.nih.gov/36974879/>

Primary Renal hydatid cyst is a rare entity. We report a case of isolated right renal hydatid cyst in a 13-year-old female who presented with pain in the right lumbar region for 4-5 months and a palpable mass in the right upper quadrant. The radiological features were suggestive of a hydatid cyst in the right kidney with no cyst in the liver, lungs, or left kidney. She was managed medically with oral Albendazole tablets (400 mg twice daily). A total of 6 cycles of Albendazole were given with each cycle lasting for 4 weeks and a drug-free period of 2 weeks in between two consecutive cycles and kept on follow-up for a year. Her condition improved with no recurrence on follow-up after one year. Keywords: Albendazole; echinococcus granulosus; renal hydatid cyst.

[Progress of researches on albendazole for treatment of alveolar echinococcosis].

Cui Z, Ye G, Yu W, Wang Z, Kong F, Ren L.
30-08-2022
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
<https://pubmed.ncbi.nlm.nih.gov/36974024/>

Alveolar echinococcosis, caused by *Echinococcus multilocularis* infection, is a highly deadly zoonotic parasitic disease. As a benzimidazole compound, albendazole has a strong and broad-spectrum anti-parasitic action. For alveolar echinococcosis patients that are unwilling to receive surgical treatment, lose the timing for surgery, or are intolerant to surgery due to poor physical status, administration of albendazole may delay disease progression. Recently, a large number of advances have been achieved in experimental studies on alveolar echinococcosis. In order to increase the understanding of the therapeutic efficacy of albendazole for alveolar echinococcosis, this review summarizes the advances in albendazole treatment for alveolar echinococcosis, so as to provide insights into the clinical treatment of alveolar echinococcosis with albendazole.

Tension Hydropneumothorax Caused by a Ruptured Hydatid Cyst in the Pleural Cavity: Case Report.

Messaoud O, El Haddad S, Cherraji A, Allali N, Chat L.
20-03-2023
Glob Pediatr Health.
<https://pubmed.ncbi.nlm.nih.gov/36968457/>

Ruptured hydatid cyst presenting with a hydropneumothorax in a 16-year-old boy: A case report from Syria.

Ataya J, Hanifa H, Ismail A, Ismail A.

23-03-2023

Int J Surg Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36965441/>

Findings of a community screening programme for human cystic echinococcosis in a non-endemic area.

Mutwiri T, Magambo J, Zeyhle E, Muigai AWT, Alumasa L, Amanyia F, Fèvre EM, Falzon LC.

15-08-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962714/>

Cystic Echinococcosis (CE) is a zoonosis caused by infection with the larval stages of the taeniid cestodes of the species complex *Echinococcus granulosus sensu lato*. It is prevalent among transhumant communities in East Africa, including those residing in northern Kenya. The movement of livestock from these regions of high incidence to areas of low incidence creates an indirect risk of disease spill-over to humans. To assess possible establishment of the CE life cycle outside known endemic regions, we used a portable ultrasound scanner to screen for the presence of human CE in Bungoma County of western Kenya, an area which imports substantial numbers of cattle for slaughter from neighbouring pastoralist regions. Eight sentinel sites were purposively selected based on their proximity to slaughterhouses handling animals introduced from pastoralist regions, and necessary permissions to conduct the study were sought. Regression analyses were conducted to identify risk factors associated with the presence of abdominal and cystic lesions (CL). In total, 1002 participants were screened; of these, 654 (65.3%) were female and the median age was 43. Farming ($n = 403$; 43.4%) was the most frequent occupation, followed by professional (i.e. on regular salary) ($n = 215$; 23.1%), and business ($n = 207$; 22.3%) categories. Sixty-seven participants (6.7%) had abnormal ultrasound findings, of these, 7 (1.1%) had simple liver cysts/CL, as per WHO classification. As such, their outcome was inconclusive and they were not put on treatment but advised to attend follow-up investigations in a referral health facility. Other abnormal findings included splenomegaly ($n = 14$), ovarian cysts ($n = 14$), uterine fibroids ($n = 10$), polycystic kidneys ($n = 6$), and benign prostatic hyperplasia ($n = 6$). Age was unconditionally associated with the presence of presumptive CL. These results contribute to CE baseline data while providing insights on the implementation of ultrasound diagnosis in the field, as recommended by the WHO for targeted control of echinococcosis by 2030.

Complete excision of giant clavicular hydatid cyst: a case report.

Wang X, Huang J, Su L, Ma Q, Ma C, Xie Z.

22-03-2023

BMC Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36949399/>

Background: Echinococcosis, also known as hydatid disease, is a zoonotic parasitic disease prevalent in pastoral areas, mainly involving the liver and lungs, and less frequently the bones and surrounding soft tissues. Diagnosis and treatment of bone hydatid disease is a challenge, and because of the insidious course of the disease, the lesions are often widely disseminated by the time patients seek medical attention. **Case presentation:** A 29-year-old woman presented with a painless mass that was gradually increasing in size in the cervical thorax. Imaging revealed an enlarged clavicle with multiple bone cortical defects and the existence of cysts in the soft tissues surrounding the clavicle, for which complete excision of the clavicle and the attached cysts was performed. There was no recurrence of the cyst within one year after the operation, and the patient felt well and had normal shoulder joint movement. **Conclusions:** Bone hydatid may appear in bones throughout the body, and cysts that leak from the bone into the surrounding soft tissues may spread at a relatively rapid rate. Prompt surgical removal of the affected bone and surrounding cysts is necessary for treatment.

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

Peptide derived from progranulin of the carcinogenic liver fluke, *Opisthorchis viverrini* stimulates cell hyperproliferation and proinflammatory cytokine production.

Hembasat T, Chaipayet S, Ittiprasert W, Smout MJ, Young ND, Loukas A, Brindley PJ, Laha T.

14-03-2032

Res Sq.

<https://pubmed.ncbi.nlm.nih.gov/36993607/>

Purpose Progranulin (PGRN) is a secreted glycoprotein growth factor with roles in wound healing, inflammation, angiogenesis and malignancy. An orthologue of the gene encoding human PGRN was identified in the carcinogenic liver fluke *Opisthorchis viverrini*. Methods Sequence structure, general characteristics and possible function of *O. viverrini* PGRN was analyzed using bioinformatics. Expression profiles were investigated with quantitative RT-PCR, western blot and immunolocalization. A specific peptide of Ov-PGRN was used to investigate a role for this molecule in pathogenesis. Results The structure of the gene coding for *O. viverrini* PGRN was 36,463 bp in length, and comprised of 13 exons, 12 introns, and a promoter sequence. The *Ov-pgrn* mRNA is 2,768 bp in length and encodes an 846 amino acids with a predicted molecular mass of 91.61 kDa. *Ov*-PGRN exhibited one half and seven complete granulin domains. Phylogenetic analysis revealed that *Ov*-PGRN formed its closest relationship

with PGRN of liver flukes in the Opisthorchiidae. Transcripts of *Ov - pgrn* were detected in several developmental stages, with highest expression in the metacercaria, indicating that *Ov*-PGRN may participate as a growth factor in the early development of *O. viverrini*. Western blot analysis revealed the presence of detected *Ov*-PGRN in both soluble somatic or excretory/secretory products, and immunolocalization indicated high levels of expression in the tegument and parenchyma of the adult fluke. Co-culture of a human cholangiocyte cell line and a peptide fragment of *Ov*-PGRN stimulated proliferation of cholangiocytes and upregulation of expression of the cytokines IL6 and IL8. Conclusion *Ov*-PGRN is expressed throughout the life cycle of liver fluke, and likely plays a key role in development and growth.

Type I Cystatin Derived from *Fasciola gigantica* Suppresses Macrophage-Mediated Inflammatory Responses.

Chantree P, Tarasuk M, Prathaphan P, Ruangtong J, Jamklang M, Chumkiew S, Martviset P.

01-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986318/>

Helminth Infections in Dairy Sheep Found in an Extensive Countrywide Study in Greece and Potential Predictors for Their Presence in Faecal Samples.

Lianou DT, Arsenopoulos KV, Michael CK, Mavrogiani VS, Papadopoulos E, Fthenakis GC.

24-03-2023

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/36985144/>

The aims of the present study were: (a) to describe the prevalence of helminth infections from pooled faecal samples from sheep flocks across Greece and (b) to evaluate flock-related factors potentially associated with the presence of these infections in the flocks. An extensive countrywide study was performed on 325 sheep farms throughout Greece; faecal samples were collected from ewes and processed for the identification of helminth parasites. Helminths were detected in samples from 92.9% of flocks; these included *Dicrocoelium dendriticum* (16.7% of flocks), *Fasciola hepatica* (0.6%), *Paramphistomum cervi* (2.2%), *Moniezia* spp. (18.8%), *Trichostrongylidae* (85.5%), *Nematodirus* spp. (18.8%), *Strongyloides papillosus* (7.1%), *Trichuris* spp. (20.0%) and lungworms (17.8%). Mean *Trichostrongylidae* counts across all flocks in the study were 215 epg. Specifically, for *Trichostrongylidae*, there were differences between flocks that had or had not received anthelmintics during the two months prior to sampling, as well as between flocks located in various areas of the country. In multivariable analyses, for the outcome 'high (>300) epg counts in faecal samples', the month into the lactation period at sampling and the application of reproductive control practices on the farm emerged as significant factors; for the outcome 'high proportion (>63%) of *Teladorsagia* spp. in faecal samples', the availability of straw bedding emerged as a significant factor; and for the outcome 'high proportion (>63%) of

Haemonchus contortus in faecal samples', the age of the farmer emerged as a significant factor. For the outcome 'presence of *Trichuris* spp. in faecal samples', the provision of finished feed (concentrate) to animals emerged as a significant factor, whilst, finally, for the outcomes 'presence of *D. dendriticum* in faecal samples' and 'presence of lungworms in faecal samples,' no significant factors emerged.

Omega-Class Glutathione Transferases Protect DNA from Oxidative Stress in Pathogenic Helminth Reproductive Cells.

Kim JG, Kang I, Ahn CS, Sohn WM, Kong Y.

23-02-2023

Antioxidants (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36978808/>

Pathogenic helminths have evolved mechanisms to preserve reproductive function while surviving long-term in the host via robust protective responses. A protective role of antioxidant enzymes in preventing DNA degradation has long been proposed, but little evidence has been provided. Here, we show that omega-class glutathione transferases (GSTOs) are critical for maintaining viability by protecting the reproductive cell DNA of the carcinogenic liver fluke, *Clonorchis sinensis*. *Clonorchis sinensis* GSTO (CsGSTO) activities modified by changes in the GSH/GSSG and NADPH/NADP⁺ molar ratios suppressed the overproduction of reactive oxygen species. CsGSTO1 and CsGSTO2 catalyzed deglutathionylation under physiologic and low-stress conditions (GSH/GSSG ratio of 6:1 or higher) but promoted glutathionylation under high-stress conditions (GSH/GSSG ratio of 3:1 or lower). Gliotoxin-induced functional disruption of CsGSTOs in living *C. sinensis* reduced the GSH/GSSG molar ratio and increased the production of protein glutathionylation (PSSG) under physiologic and low-stress conditions, indicating that suppression of GSTO function did not affect deglutathionylation. However, the perturbation of CsGSTOs decreased the GSH/GSSG ratio but also reduced PSSG production under high oxidative stress, demonstrating that glutathionylation was impeded. In response to oxidative stimuli, *C. sinensis* decreased GSTO-specific dehydroascorbate reductase and thiol transferase activities and the GSH/GSSG ratio, while it increased the NADPH/NADP⁺ ratio and PSSG. CsGSTOs utilized GSH to regulate GSH/GSSG and NADPH/NADP⁺ recycling and triggered a redox signal leading to nuclear translocation. Nuclear-imported CsGSTOs were modified by glutathionylation to prevent DNA damage. Antibodies specific to CsGSTOs dose-dependently inhibited this process. Disruption of CsGSTOs or the depletion of GSH caused glutathionylation defects, leading to DNA degradation. Our results demonstrate that CsGSTOs and the GSH system play a previously unappreciated role in protecting DNA from oxidative stress.

Gastrointestinal Polyparasitism in Bushmeat in Zadié Department in Northeast Gabon.

Maganga GD, Makouloutou-Nzassi P, Boundenga L, Maganga Landjekpo HN, Bangueboussa F, Ndong Mebaley T, Mounioko F, Gbati OB.
17-03-2023
Vet Sci.
<https://pubmed.ncbi.nlm.nih.gov/36977268/>

Seasonal Occurrence of Cattle Fascioliasis in Kelantan, Malaysia.

Muhammad Faez A, Ahmad Najib M, Noraini AG, Weng Kin W, Abd Rahman A, Wan Nor Amilah WAW, Noor Izani NJ.
07-03-2023
Vet Sci.
<https://pubmed.ncbi.nlm.nih.gov/36977241/>

Fasciola gigantica Cathepsin L1H: High Sensitivity and Specificity of Immunochromatographic Strip Test for Antibody Detection.

Suksomboon P, Kueakhai P, Changklungmoa N.
11-03-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/36977165/>

Fasciolosis is a zoonotic disease caused by *Fasciola gigantica* or *F. hepatica* infections, which are frequently occurring parasites in animals and humans. The present gold-standard diagnostic technique involves finding parasite eggs through microscopy. However, this method is also restricted due to low specificity and low sensitivity. An alternative to coprological diagnosis is the immunochromatographic strip (ICS) test, which is rapid, simple, convenient, and cost-effective, with high sensitivity and high specificity. Cathepsin L1H (CathL1H) is a cysteine protease secreted by *F. gigantica*, which is found in high amounts in newly excysted juvenile (NEJ) and juvenile stages. Cathepsin L1H plays an important role in both the immune response to invading pathogens and in the ability of some pathogens to evade the host immune system. The present study aims to develop an ICS test and detect antibodies against CathL1H in mice and cattle serum using the recombinant *F. gigantica* Cathepsin L1H (rFgCathL1H) and rabbit anti-rFgCathL1H antibody. The *F. gigantica*-infected serum and non-infected serum of mice and cattle were tested using the ICS test. Moreover, the strip results were confirmed with an indirect enzyme-linked immunosorbent assay (indirect ELISA). The relative sensitivity, specificity, and accuracy of the ICS strip were 97.5, 99.99, and 99.00%, respectively. Therefore, these data suggest that the ICS method could be used to detect *F. gigantica* antibodies to highly enhance throughput, reduce costs, and determine the best alternative on-site method.

Production and Immunological Characterization of scFv Specific to Epitope of Opisthorchis viverrini Rophilin-Associated Tail Protein 1-like (OvROPN1L).

Geadkaew-Krenc A, Krenc D, Thanongsaksrikul J, Grams R, Phadungsil W, Glab-Ampai K, Chantree P, Martviset P.

06-03-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/36977161/>

Effects of Land-Use and Environmental Factors on Snail Distribution and Trematode Infection in Ethiopia.

Mereta ST, Abaya SW, Tulu FD, Takele K, Ahmednur M, Melka GA, Nanyingi M, Vineer HR, Graham-Brown J, Caminade C, Mor SM.
01-03-2023
Trop Med Infect Dis.
<https://pubmed.ncbi.nlm.nih.gov/36977155/>

Freshwater snails are intermediate hosts for several snail-borne diseases affecting humans and animals. Understanding the distribution of snail intermediate hosts and their infection status is very important to plan and implement effective disease prevention and control interventions. In this study, we determined the abundance, distribution, and trematode infection status of freshwater snails in two agro-ecological zones of Ethiopia. We sampled snails from 13 observation sites and examined them for trematode infections using a natural cercarial shedding method. A redundancy analysis (RDA) was used to examine the relationship between snail abundance and environmental variables. Overall, a total of 615 snails belonging to three species were identified. *Lymnaea natalensis* and *Bulinus globosus* were the dominant snail species, representing 41% and 40% of the total collection, respectively. About one-third of the total snail population (33%) shed cercariae. The cercariae species recorded were *Xiphidiocercaria*, *Brevifurcata apharyngeate distome* (BAD), *Echinostome*, and *Fasciola*. Snail species were found in high abundance in aquatic habitats located in the agricultural landscape. Therefore, land-use planning and protection of aquatic habitats from uncontrolled human activities and pollution can be considered as important strategies to prevent and control the spread of snail-borne diseases in the region.

[Establishment and evaluation of a method for extracting exogenous short DNA fragments of Schistosoma japonicum from urine samples].

Zhang Q, Zhao S, Ye Y, Bi N, Wang X, Zhang J, Li W, Yang K.
09-03-2023
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
<https://pubmed.ncbi.nlm.nih.gov/36974010/>

Objective: To establish the method for extracting exogenous short DNA fragments of *Schistosoma japonicum* from urine samples, and to evaluate the efficiency of this method for extraction from urine samples treated with various methods. **Methods:** The *S. japonicum* SjG28 gene fragment was selected as a target sequence, and the 81 bp short DNA fragment was amplified on the target sequence using PCR assay. Following characterization using sequencing, the short DNA fragment was added into the urine samples as an exogenous short DNA fragment. Primers and probes were designed with SjG28 as a target gene, to establish the real-

time fluorescent quantitative PCR (qPCR) assay. The sensitivity of this qPCR assay was evaluated with exogenous short DNA fragments that were diluted at a 1:10 dilution ratio as the DNA template, and the specificity of the qPCR assay was evaluated with the genomic DNA of *S. mansoni*, *S. haematobium*, *Babesia*, *Ancylostoma duodenale*, *Clonorchis sinensis*, and *Paragonimus westermani* as DNA templates. Exogenous short DNA fragments were added into artificial and healthy volunteers' urine samples, followed by pH adjustment, centrifugation and concentration, and the efficiency of extracting exogenous short DNA fragments from urine samples was compared with the QIAmp Viral RNA Mini Kit (Qiagen kit) and BIOG cfDNA easy kit (BIOG kit). **Results:** An 81 bp small DNA fragment of *S. japonicum* was successfully prepared, and the lowest detection limit of the established qPCR assay was 100 copies/ μ L of the 81 bp small DNA fragment of *S. japonicum*. If the genomic DNA of *S. japonicum*, *S. mansoni*, *S. haematobium*, *Babesia*, *A. duodenale*, *C. sinensis*, and *P. westermani* served as DNA templates, the qPCR assay only detected fluorescent signals with *S. japonicum* genomic DNA as the DNA template. If the pH values of artificial urine samples were adjusted to 5, 6, 7 and 8, the recovery rates were $(49.12 \pm 2.09)\%$, $(84.52 \pm 4.96)\%$, $(89.38 \pm 3.32)\%$ and $(87.82 \pm 3.90)\%$ for extracting the exogenous short DNA fragment of *S. japonicum* with the Qiagen kit, and were $(2.30 \pm 0.07)\%$, $(8.11\% \pm 0.26)\%$, $(13.35 \pm 0.61)\%$ and $(20.82 \pm 0.68)\%$ with the BIOG kit, respectively ($t = 38.702$, 26.955 , 39.042 and 29.571 ; all P values < 0.01). If the Qiagen kit was used for extracting the exogenous short DNA fragment from artificial urine samples, the lowest recovery rate was seen from urine samples with a pH value of 5 (all P values < 0.05), and there were no significant differences in the recovery rate from urine samples with pH values of 6, 7 and 8 (all P values > 0.05). Following centrifugation of artificial $[(64.30 \pm 1.00)\%$ vs. $(58.87 \pm 0.26)\%$; $t = 12.033$, $P < 0.05$] and healthy volunteers' urine samples $[(31\ 165 \pm 1\ 017)$ copies/ μ L vs. $(28\ 471 \pm 818)$ copies/ μ L; $t = 23.164$, $P < 0.05$]. In addition, concentration of artificial urine samples with the 10 kDa Centrifugal Filter and concentration of healthy volunteers' urine samples with the 100 kDa Centrifugal Filter were both effective to increase the recovery of the Qiagen kit for extracting the exogenous short DNA fragment of *S. japonicum* (both P values < 0.01). **Conclusions:** A method for extracting exogenous short DNA fragments of *S. japonicum* from urine samples has been successfully established, and the Qiagen kit has a high extraction efficiency. Adjustment of urine pH to 6 to 8 and concentration of healthy volunteers' urine samples with the 100 kDa Centrifugal Filter are both effective to increase the efficiency of extracting exogenous short DNA fragments of *S. japonicum*.

A case of spontaneous pneumothorax due to paragonimiasis in North America with literature review.

Kang SA, Patel PK, Patil S, Bran-Acevedo A, Layfield L, Wiesemann S, Roland W.

09-03-2023

IDCases.

<https://pubmed.ncbi.nlm.nih.gov/36968306/>

A review of tuberculosis and parasitic disease co-infection in ungulates, with regard to the potential threat to European bison (*Bison bonasus*).

Gałązka M, Didkowska A, Anusz K, Pyziel-Serafin A.

Mar-2023

Pol J Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/36961266/>

Bovine tuberculosis (BTB) is a dangerous zoonosis which presents a serious problem for endangered species such as European bison (*Bison bonasus*). Little is known about the influence of parasitic co-infections on the course and diagnosis of tuberculosis in animals. The best known co-infection in cattle is *Fasciola hepatica* and *Mycobacterium bovis*. The aim of this study was to review the most recent literature regarding tuberculosis and parasite co-infection in ungulates and relate the results to European bison. Our findings indicate that any comprehensive diagnosis of BTB should include parasitological monitoring, and the possible impact of such invasions on cellular response-based tuberculosis tests should be taken into account. The diagnosis of BTB is complex, as is its pathogenesis, and parasitic infestations can have a significant impact on both. This should be taken into account during further research and monitoring of tuberculosis in European bison.

Co-infection of hepatitis E virus, *Clonorchis sinensis*, and *Escherichia coli*: A case report.

Zhang L, Wang X, Zhang J, Wang Z, Cai D.

07-03-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36960040/>

Hepatitis E virus (HEV) is a common cause of acute hepatitis that threatens human health worldwide. With the popularization of detection technology, the reports of hepatitis E have gradually increased. Here, we present a rare case of co-infection with hepatitis E viruses, *Clonorchis sinensis* and *Escherichia coli*. A 52-year-old man was hospitalized because of fatigue, jaundice, and nausea for more than 2 weeks. Laboratory tests showed elevated bilirubin, aminotransferase (ALT), and aspartate aminotransferase (AST); HEV-IgM was positive, and HEV-RNA could be detected. Moreover, parasites were found in the biliary drainage and the biliary culture, which suggested *Escherichia coli*. The patient was effectively treated with praziquantel, imipenem, and hepatoprotective drugs and his clinical symptoms were relieved after 2 months; total bilirubin decreased to 85.1 μ mol/L, ALT decreased to 92.4 U/L, and AST decreased to 102 U/L.

An evolutionary molecular adaptation of an unusual stefin from the liver fluke *Fasciola hepatica* redefines the cystatin superfamily.

Buša M, Matoušková Z, Bartošová-Sojčková P, Páchl P, Řezáčová P, Eichenberger RM, Deplazes P, Horn M, Štefanič S, Mareš M.

Mar-2023

J Biol Chem.

<https://pubmed.ncbi.nlm.nih.gov/36736427/>

Filariose lymphatique

Construction and validation of a multi-epitope in silico vaccine model for lymphatic filariasis by targeting *Brugia malayi*: a reverse vaccinology approach.

Madanagopal P, Muthusamy S, Pradhan SN, Prince PR. 2023

Bull Natl Res Cent.

<https://pubmed.ncbi.nlm.nih.gov/36987521/>

Background: Lymphatic filariasis (LF), often referred to as elephantiasis, has been identified as one of the 17 neglected tropical diseases by the World Health Organization. Currently, there are no vaccines available to treat this infection in humans. Therefore, with the objective of devising a novel preventive measure, we exploited an immunoinformatics approach to design a multi-epitope-based subunit vaccine for LF, that can elicit a variety of immune responses within the host. In this study, different B cell, T_C cell, and T_H cell-binding epitopes were screened from the antigenic proteins of *Brugia malayi* and they were passed through several immunological filters to determine the optimal epitopes.

Results: As a result, 15 CD8+, 3 CD4+, and 3 B cell epitopes were found to be prominent, antigenic, non-toxic, immunogenic and non-allergenic. The presence of conformational B cell epitopes and cytokine-inducing epitopes confirmed the humoral and cell-mediated immune response that would be triggered by the constructed vaccine model. Following that, the selected epitopes and TLR-4-specific adjuvant were ligated by appropriate peptide linkers to finalize the vaccine construct. Protein-protein docking of the vaccine structure with the TLR4 receptor predicted strong binding affinity and hence putatively confirms its ability to elicit an immune response. Further, the efficiency of the vaccine candidate to provide a long-lasting protective immunity was assessed by in silico immune simulation. The reverse translated vaccine sequence was also virtually cloned in the pET28a (+) plasmid after the optimization of the gene sequence. **Conclusion:** So taken together, by monitoring the overall in silico assessment, we hypothesize that our engineered peptide vaccine could be a viable prophylactic approach in the development of vaccines against the threat of human lymphatic filariasis.

Monitoring the Status of Soil-Transmitted Helminthiases in Non-Endemic Implementation Units: A Case Study of Borgu in Northcentral Nigeria.

Adewale B, Mogaji H, Balogun J, Balogun E, Olamiju F, Herbert D.

21-03-2032

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986413/>

Increased HIV Incidence in *Wuchereria bancrofti* Microfilaria Positive Individuals in Tanzania.

Mnkai J, Ritter M, Maganga L, Maboko L, Olomi W, Clowes P, Minich J, Lelo AE, Kariuki D, Debrah AY, Geldmacher C, Hoelscher M, Saathoff E, Chachage M, Pfarr K, Hoerauf A, Kroidl I.

28-02-202

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986309/>

Background: Infections with *Wuchereria bancrofti* are associated with reduced immunity against concomitant infections. Indeed, our previous study described a 2.3-fold increased HIV incidence among individuals with *W. bancrofti* infection, as measured by the circulating filarial antigen of the adult worm. This new study aimed to retrospectively determine microfilariae status of the participants to assess if the previously described increased HIV susceptibility was associated with the presence of MF in the same cohort. **Methods:** CFA positive but HIV negative biobanked human blood samples ($n = 350$) were analyzed for *W. bancrofti* MF chitinase using real time PCR.

Results: The PCR provided a positive signal in 12/350 (3.4%) samples. During four years of follow-up (1109 person years (PY)), 22 study participants acquired an HIV infection. In 39 PY of *W. bancrofti* MF chitinase positive individuals, three new HIV infections occurred (7.8 cases per 100 PY), in contrast to 19 seroconversions in 1070 PY of *W. bancrofti* MF chitinase negative individuals (1.8 cases per 100 PY, $p = 0.014$). **Conclusions:** In the subgroup of MF-producing Wb-infected individuals, the HIV incidence exceeded the previously described moderate increased risk for HIV seen in all Wb-infected individuals (regardless of MF status) compared with uninfected persons from the same area.

Mosquito-Borne Diseases and Their Control Strategies: An Overview Focused on Green Synthesized Plant-Based Metallic Nanoparticles.

Onen H, Luzala MM, Kigozi S, Sikumbili RM, Muanga CK, Zola EN, Wendji SN, Buya AB, Balciunaitiene A, Viškelis J, Kaddumukasa MA, Memvanga PB.

23-02-2023

Insects.

<https://pubmed.ncbi.nlm.nih.gov/36975906/>

Mosquitoes act as vectors of pathogens that cause most life-threatening diseases, such as malaria, Dengue, Chikungunya, Yellow fever, Zika, West Nile, *Lymphatic filariasis*, etc. To reduce the transmission of these mosquito-borne diseases in humans, several chemical, biological, mechanical, and pharmaceutical methods of control are used. However, these different strategies are facing important and timely challenges that include the rapid spread of highly invasive mosquitoes worldwide, the development of resistance in several mosquito species, and the recent outbreaks of novel arthropod-borne viruses (e.g., Dengue, Rift Valley fever, tick-borne encephalitis, West Nile, yellow fever, etc.). Therefore, the development of novel and effective methods of control is urgently needed to manage mosquito vectors. Adapting

the principles of nanobiotechnology to mosquito vector control is one of the current approaches. As a single-step, eco-friendly, and biodegradable method that does not require the use of toxic chemicals, the green synthesis of nanoparticles using active toxic agents from plant extracts available since ancient times exhibits antagonistic responses and broad-spectrum target-specific activities against different species of vector mosquitoes. In this article, the current state of knowledge on the different mosquito control strategies in general, and on repellent and mosquitocidal plant-mediated synthesis of nanoparticles in particular, has been reviewed. By doing so, this review may open new doors for research on mosquito-borne diseases.

Community engagement in health services research on elimination of lymphatic filariasis: A systematic review.

Naing C, Htet NH, Aung HH, Whittaker MA.

17-01-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36963022/>

Effectiveness of community-based burden estimation to achieve elimination of lymphatic filariasis: A comparative cross-sectional investigation in Côte d'Ivoire.

Simpson H, Konan DO, Brahima K, Koffi JD, Kashindi S, Edmiston M, Weiland S, Halliday K, Pullan RL, Meite A, Koudou BG, Timothy J.

31-08-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962795/>

Sociodemographic characteristics as predictors of knowledge regarding mode of transmission of Lymphatic Filariasis among population of Nepal.

Adhikari R, Acharya D, Wagle A.

11-10-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962552/>

Introduction: The majority of the districts of Nepal (63 out of 77) were detected as prevalent of Lymphatic Filariasis (LF), with an average prevalence of 13 percent ranging from less than one to 39 percent in Nepal. Despite people's ignorance about the LF, the government has a target to eliminate LF by 2020. The study aimed to assess the association between sociodemographic characteristics and knowledge of the mode of transmission of LF. **Materials and methods:** The study used a cross-sectional design. Secondary data from Nepal Demographic and Health Survey 2016 were analysed. Altogether, 11040 participants participated in the study. Sociodemographic characteristics were the independent variables, whereas household heads' knowledge of LF transmission was the dependent variable. Descriptive, bivariate, and multivariate analyses were performed to assess the association between sociodemographic characteristics and knowledge of the mode of transmission. **Results:**

Findings showed that only 28 percent of household-heads correctly identified the mode of transmission of Lymphatic Filariasis in the study. Household head's age, sex, wealth status, place of residence in terms of areas, geo-belt and province, migration history, and household assets such as bed nets, Radio, TV were significantly associated with the knowledge of the mode of transmission of Lymphatic Filariasis. Variables: wealth status, sex, residence, eco-belts, possessing bed nets, and Radio appeared as significant predictors for knowledge of the mode of transmission of Lymphatic Filariasis. The richest to the poorest people had lower odds ranging from 0.22 to 0.53 for knowing the mode of transmission of Lymphatic Filariasis compared to the richest people ($p = 0.001$).

Conclusion: The study identified the population groups with a low level of knowledge of modes of transmission of Lymphatic Filariasis. Thus, it can be inferred from the study that relevant programs need to focus on women, people residing in the mountains and Terai, and those belonging to the middle and poor wealth index. The study also emphasizes that information, education, and communication materials can effectively impart knowledge of Lymphatic Filariasis.

A mixed-methods exploration into the resilience of community drug distributors conducting mass drug administration for preventive chemotherapy of lymphatic filariasis and onchocerciasis in Côte d'Ivoire and Uganda.

Dillio D, Addiss D, Thickstun C, Djima AM, Comoe E, Thompson L, Neema S, Amuyunzu-Nyamongo M, Wung-Buh A, McFarland D, Gyapong M, Krentel A.

15-06-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962463/>

A syndemic born of war: Combining intersectionality and structural violence to explore the biosocial interactions of neglected tropical diseases, disability and mental distress in Liberia.

Dean L, Theobald S, Nallo G, Bettee A, Kollie K, Tolhurst R.

29-06-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962440/>

Seaweed *Sargassum wightii* mediated preparation of TiO_2 nanoparticles, larvicidal activity against malaria and filariasis vectors, and its effect on non-target organisms.

Mathivanan D, Kamaraj C, Suseem SR, Gandhi PR, Malafaia G.

25-05-2023

Environ Res.

<https://pubmed.ncbi.nlm.nih.gov/36848976/>

Volunteer community drug distributors (CDDs) have been vital to progress made in the elimination of onchocerciasis and lymphatic filariasis; two neglected tropical diseases amenable to preventive chemotherapy (PC-NTDs). However, formative work in Côte d'Ivoire and Uganda revealed that CDDs can encounter considerable challenges during mass drug administration (MDA). CDDs must be resilient to overcome these challenges, yet little is known about their resilience. This mixed-methods study explored the resilience of CDDs in Côte d'Ivoire and Uganda. The characteristics and experiences of 248 CDDs involved in the 2018 MDAs in Côte d'Ivoire (N = 132) and Uganda (N = 116) were assessed using a micronarrative survey. Thematic analysis of CDDs' micronarratives was used to identify challenges they encountered during MDA. Resilience was assessed using the Connor-Davidson Resilience Scale 25 (CD-RISC-25). Variables from the micronarrative survey found to be individually associated with mean CD-RISC-25 score ($P < 0.05$) through bivariate analyses were included in a multiple linear regression model. Post-hoc, country-specific analyses were then conducted. Thematic analysis showed that CDDs encountered a wide range of challenges during MDA. The aggregate model revealed that CDDs who had positive relationships or received support from their communities scored higher on the CD-RISC-25 on average ($P < 0.001$ for both), indicating higher resilience. These trends were also observed in the country-specific analyses. Mean CD-RISC-25 scores were unaffected by variations in district, age, gender, and length of involvement with the NTD program. Community support during MDA and positive community-CDD relationships appear to be associated with CDDs' personal capacity to overcome adversity. Involving communities and community leadership in the selection and support of CDDs has the potential to benefit their well-being. This study establishes the CD-RISC-25 as a useful tool for assessing the resilience of CDDs. Further research is needed to understand, promote, and support the resilience of this valuable health workforce, upon which NTD programs depend.

Exploration of aminoacyl-tRNA synthetases from eukaryotic parasites for drug development.

Gill J, Sharma A.

Mar-2023

J Biol Chem.

<https://pubmed.ncbi.nlm.nih.gov/36596362/>

Malaria and Lymphatic filariasis are considered significant public health concerns in several countries. As a researcher, controlling those mosquitos using safe and eco-friendly insecticides is essential. Thus, we aimed to explore the potential use of seaweed *Sargassum wightii* for the biosynthesis of TiO_2 NPs and evaluate its efficiency in controlling disease-transmitting mosquito larvae (using *Anopheles subpictus* and *Culex quinquefasciatus* larvae as model systems (in vivo)) as well as its potential effect on non-target organisms (using *Poecilia reticulata* fish as an experimental model). XRD, FT-IR, SEM-EDAX, and TEM carried out the characterization of TiO_2 NPs. It evaluated the larvicidal activity against the fourth instar larvae of *A. subpictus* and *C. quinquefasciatus*. The larvicidal mortality

was observed after 24 h of exposure to *S. wightii* extract and TiO_2 NPs. *S. wightii* synthesized TiO_2 NPs show excellent activity against *A. subpictus* and *C. quinquefasciatus* ($\text{LC}_{50} = 4.37$ and 4.68 ; $\text{LC}_{90} = 8.33$ and 8.97 ; $\chi^2 = 5.741$ and 4.531) mg/L respectively. The GC-MS results indicate the presence of some important long-chain phytoconstituents like linoleic acid, palmitic acid, oleic acid methyl ester, and stearic acid, among others. Furthermore, when testing the possible toxicity of biosynthesized NPs in a non-target organism, no adverse effects were observed in *Poecilia reticulata* fish exposed for 24 h, considering the evaluated biomarkers. Thus, overall, our study results reveal that biosynthesized TiO_2 NPs are an effective and exciting eco-friendly approach to controlling the *A. subpictus* and *C. quinquefasciatus*.

Mycétome

Pulmonary Mycetoma With a Concomitant Reactivation of Pulmonary Tuberculosis Infection: A Case Report and Clinical Pathological Review.

Ortiz WJ, McKowen RL, Cervantes M.

25-02-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36994297/>

Tuberculosis is a bacterial infection caused by *Mycobacterium tuberculosis*. It primarily affects the lungs but can also spread to other body parts. One of the possible symptoms of pulmonary tuberculosis (TB) is hemoptysis. In the case of TB, aspergillomas can develop in the cavitary lesions of TB and result in a deteriorating clinical situation. The current case report describes a 63-year-old female previously treated for TB who presented with hemoptysis, fever, and a 4 cm focal density in the right upper lobe on chest X-ray. The patient was found to have concomitant TB and aspergillosis, manifesting as a pulmonary aspergilloma. The co-occurrence of TB and aspergillosis can occur, particularly in patients with weakened immune systems. This case report highlights the importance of considering concomitant TB and pulmonary mycetoma in patients with a history of treated TB who present with pulmonary symptoms.

Deep learning for AI-based diagnosis of skin-related neglected tropical diseases: a pilot study.

Yotsu R, Ding Z, Hamm J, Blanton R.

15-03-2032

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993502/>

Background: Deep learning, which is a part of a broader concept of artificial intelligence (AI) and/or machine learning has achieved remarkable success in vision tasks. While there is growing interest in the use of this technology in diagnostic support for skin-related neglected tropical diseases (skin NTDs), there have been limited studies in this area and fewer focused on dark skin. In this study, we aimed to develop deep learning based AI models with clinical images we collected for five skin NTDs,

namely, Buruli ulcer, leprosy, mycetoma, scabies, and yaws, to understand how diagnostic accuracy can or cannot be improved using different models and training patterns. **Methodology:** This study used photographs collected prospectively in Côte d'Ivoire and Ghana through our ongoing studies with use of digital health tools for clinical data documentation and for teledermatology. Our dataset included a total of 1,709 images from 506 patients. Two convolutional neural networks, ResNet-50 and VGG-16 models were adopted to examine the performance of different deep learning architectures and validate their feasibility in diagnosis of the targeted skin NTDs. **Principal findings:** The two models were able to correctly predict over 70% of the diagnoses, and there was a consistent performance improvement with more training samples. The ResNet-50 model performed better than the VGG-16 model. Model trained with PCR confirmed cases of Buruli ulcer yielded 1-3% increase in prediction accuracy over training sets including unconfirmed cases. **Conclusions:** Our approach was to have the deep learning model distinguish between multiple pathologies simultaneously - which is close to real-world practice. The more images used for training, the more accurate the diagnosis became. The percentages of correct diagnosis increased with PCR-positive cases of Buruli ulcer. This demonstrated that it may be better to input images from the more accurately diagnosed cases in the training models also for achieving better accuracy in the generated AI models. However, the increase was marginal which may be an indication that the accuracy of clinical diagnosis alone is reliable to an extent for Buruli ulcer. Diagnostic tests also have its flaws, and they are not always reliable. One hope for AI is that it will objectively resolve this gap between diagnostic tests and clinical diagnoses with addition of another tool. While there are still challenges to be overcome, there is a potential for AI to address the unmet needs where access to medical care is limited, like for those affected by skin NTDs.

Hydatid Disease: A Radiological Pictorial Review of a Great Neoplasms Mimicker.

Alshoabi SA, Alkalady AH, Almas KM, Magram AO, Algaberi AK, Alareqi AA, Hamid AM, Alhazmi FH, Qurashi AA, Abdulaal OM, Aloufi KM, Alsharif WM, Alsultan KD, Omer AM, Gareeballah A.

16-03-2023

Diagnostics (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36980435/>

Hydatid cyst is a common name for the larval stage of a tapeworm species of *Echinococcus granulosus*, which is transmitted from animals to humans via the fecal-oral route. Hydatid cysts predominantly affect the liver (75%), followed by the lung (15%), and they can affect many organs in the human body. Medical imaging modalities are the keystone for the diagnosis of hydatid cysts with high sensitivity and specificity. Ultrasound imaging with high resolution is the first choice for diagnosis, differential diagnosis, staging, establishing a role in interventional management, and follow-up, and it can differentiate Type I hydatid cysts from simple liver cysts. Unenhanced computed tomography (CT) is indicated where or when an ultrasound is unsatisfactory, such as with chest or brain

hydatid cysts, when detecting calcification, and in obese patients. Magnetic resonance imaging (MRI) is superior for demonstrating cyst wall defects, biliary communication, neural involvement, and differentiating hydatid cysts from simple cysts using diffusion-weighted imaging (DWI) sequences. According to the phase of growth, hydatid cysts occur in different sizes and shapes, which may mimic benign or malignant neoplasms and may create diagnostic challenges in some cases. Hydatid cysts can mimic simple cysts, choledochal cysts, Caroli's disease, or mesenchymal hamartomas of the liver. They can mimic lung cystic lesions, mycetoma, blood clots, Rasmussen aneurysms, and even lung carcinomas. Differential diagnosis can be difficult for arachnoid cysts, porencephalic cysts, pyogenic abscesses, and even cystic tumors of the brain, and can create diagnostic dilemmas in the musculoskeletal system.

Histopathology in the Diagnosis of Tinea Capitis: When to Do, How to Interpret?

Elmas ÖF, Durdu M.

28-03-2023

Mycopathologia.

<https://pubmed.ncbi.nlm.nih.gov/36976441/>

The diagnosis of tinea capitis is usually made by clinical signs and direct microscopic examination. Early diagnosis of this dermatophytic infection, which may cause permanent hair loss if not treated appropriately, is very crucial. In recent years, the use of dermoscopy has helped with early diagnosis. However, when tinea capitis has an atypical course and develops in adulthood, it can be confused with several diseases, such as psoriasis, seborrheic dermatitis, folliculitis decalvans, acne keloidalis, and dissecting cellulitis. Due to the different treatment approaches and prognoses, it is important to distinguish tinea capitis from invasive dermatoses on the scalp. In this article, histopathological findings of tinea capitis and several advantages and disadvantages of histopathology in the diagnosis of fungal infections are also reviewed and updated.

Onchocercose

Preliminary assessment of Onchocerca-induced visual impairment using clinical fundus camera in Gashaka local government area of Taraba state, north eastern Nigeria.

Olamiju FO, Mogaji HO, Bjørn MT, Marcus AJ, Oduwa V, Olamiju OJ, Nzunde M, Ikyerga DK, Hopkins A.

11-03-2023

Parasite Epidemiol Control.

<https://pubmed.ncbi.nlm.nih.gov/36969391/>

Introduction: Onchocerciasis is the world's second leading cause of infectious blindness and remains a major problem in parts of Africa. In light of the efforts targeted towards improving ongoing elimination program, this study assessed onchocerca-induced visual impairments in Gashaka local government areas (LGA) in Taraba State, north-eastern Nigeria. **Methods:** In 2019, we recruited 158 consenting visually impaired persons across three

communities in Garbabi ward of Gashaka LGA. To avoid confusion with co-endemic trachoma, the integrity of the tarsal conjunctiva, eyelashes were assessed using direct light. The anterior segment of the eye was also examined using a torchlight with oblique illumination. However, the posterior segment of the eye was assessed using a fundus camera. Two photographic images for the left and right eye of each participant were captured using the clinical fundus camera. The photographic eye images that were too dark were discarded, and only clear images were analyzed by two ophthalmologists. An ocular manifestation report was recorded for each participant following consensus between the ophthalmologists. **Results:** Of the 316 photographic eye images, almost half 146 (46.2%) from 73 participants were just too destroyed for light to penetrate and was not included in the analysis. Only 170 from 85 participants were clear and examinable. A total of 33 (39%) participants had chorioretinitis suggestive of onchocerciasis, including 22(25.9%) with chorio-retinal atrophy, 7(8.2%) and 4(4.7%) had chorioretinal atrophy in combination with early cataract and signs of trachoma respectively. In addition, 3(3.5%) of the participant had eye images which showed lens opacities, 1(1.2%) showed signs of keratoconus and 1(1.2%) showed a scared and pigmented cornea, possibly due to onchocerciasis. Furthermore, 28 (32.9%) had some ill-defined changes and 19 (22.4%) showed poorly defined chorio-retinal atrophy. **Conclusion:** In a bid to sustain MDA gains towards elimination of onchocerciasis, this work highlights the need for continuous assessment of onchocerciasis induced visual impairment, strengthening of ivermectin delivery and optimizing compliance and patient care among affected populations. These would require resource acquisition and local capacity building. Our preliminary findings call for further operational research on ocular morbidity as well as future stakeholders' consultations in this important and understudied area.

A new key-player for onchocerciasis elimination.

Jesudason T.

Apr-2023

Lancet Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36965498/>

Unraveling cross-reactivity of anti-glycan IgG responses in filarial nematode infections.

Petralia LMC, van Diepen A, Nguyen DL, Lokker LA, Sartono E, Bennuru S, Nutman TB, Pfarr K, Hoerauf A, Wanji S, Foster JM, Hokke CH.

06-03-2023

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36949937/>

Parasitic nematodes responsible for filarial diseases cause chronic disablement in humans worldwide. Elimination programs have substantially reduced the rate of infection in certain areas, but limitations of current diagnostics for population surveillance have been pointed out and improved assays are needed to reach the elimination

targets. While serological tests detecting antibodies to parasite antigens are convenient tools, those currently available are compromised by the occurrence of antibodies cross-reactive between nematodes, as well as by the presence of residual antibodies in sera years after treatment and clearance of the infection. We recently characterized the N-linked and glycosphingolipid derived glycans of the parasitic nematode *Brugia malayi* and revealed the presence of various antigenic structures that triggered immunoglobulin G (IgG) responses in infected individuals. To address the specificity of IgG binding to these glycan antigens, we screened microarrays containing *Brugia malayi* glycans with plasma from uninfected individuals and from individuals infected with *Loa loa*, *Onchocerca volvulus*, *Mansonella perstans* and *Wuchereria bancrofti*, four closely related filarial nematodes. IgG to a restricted subset of cross-reactive glycans was observed in infection plasmas from all four species. In plasma from *Onchocerca volvulus* and *Mansonella perstans* infected individuals, IgG binding to many more glycans was additionally detected, resulting in total IgG responses similar to the ones of *Brugia malayi* infected individuals. For these infection groups, *Brugia malayi*, *Onchocerca volvulus* and *Mansonella perstans*, we further studied the different IgG subclasses to *Brugia malayi* glycans. In all three infections, IgG1 and IgG2 appeared to be the major subclasses involved in response to glycan antigens. Interestingly, in *Brugia malayi* infected individuals, we observed a marked reduction in particular in IgG2 to parasite glycans post-treatment with anthelmintic, suggesting a promising potential for diagnostic applications. Thus, we compared the IgG response to a broad repertoire of *Brugia malayi* glycans in individuals infected with various filarial nematodes. We identified broadly cross-reactive and more specific glycan targets, extending the currently scarce knowledge of filarial nematode glycosylation and host anti-glycan antibody response. We believe that our initial findings could be further exploited to develop disease-specific diagnostics as part of an integrated approach for filarial disease control.

Onchocerca sp. in an imported Zangersheide gelding causing suspensory ligament desmitis.

Brown KA, Johnson AL, Bender SJ, Nolan TJ, Pfisterer B, Slack J, Willis E, Rule EK.

Mar-2023

J Vet Intern Med.

<https://pubmed.ncbi.nlm.nih.gov/36821075/>

A 5-year-old imported Zangersheide gelding was evaluated for SC swellings over both forelimbs and lameness localized to the distal metacarpus. Ultrasound examination of the SC masses was compatible with verminous granulomas. Linear hyperechoic foci were present within the suspensory ligament branches of both forelimbs, suggestive of ligamentous parasitic infiltrates. A diagnosis of onchocerciasis was confirmed on biopsy of a SC mass. The gelding was treated with ivermectin and a tapering course of PO dexamethasone but was eventually euthanized. Necropsy confirmed the presence of SC eosinophilic granulomas and degenerative suspensory

ligament desmitis, both with intralesional nematodes. Given the location and appearance of the nematode, a diagnosis of *Onchocerca* sp., most likely *O. reticulata*, was made. Onchocerciasis should be included as a differential diagnosis for multifocal suspensory ligament desmitis with these sonographic characteristics when paired with SC masses in imported European Warmbloods.

Schistosomiasis

A randomized, controlled Phase 1b trial of the Sm-TSP-2 Vaccine for intestinal schistosomiasis in healthy Brazilian adults living in an endemic area.

Diemert DJ, Correa-Oliveira R, Fraga CG, Talles F, Silva MR, Patel SM, Galbiati S, Kennedy JK, Lundeen JS, Gazzinelli MF, Li G, Hoeweler L, Deye GA, Bottazzi ME, Hotez PJ, El Sahly HM, Keitel WA, Bethony J, Atmar RL. 30-03-202

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36996185/>

Detection of cytological abnormalities in urothelial cells from individuals previously exposed or currently infected with *Schistosoma haematobium*.

Smith-Togobo C, Mprah R, Yeboah EA, Anyidoho HK, Asigbe D, Afernorfe JK, Ayroo F, Duedu KO. 30-03-202

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/36996097/>

Urinary schistosomiasis has long been associated with bladder cancer, but it is still not clear the mechanisms involved. *Schistosoma haematobium* causes injury and disruptions in the integrity of the urothelium. The cellular and immunologic responses to the infection lead to the formation of granulomata. The ability to use cellular morphological changes to predict the risk of developing bladder cancer following *S. haematobium* infection is thus important. This study assessed the cellular changes in the urine associated with schistosomiasis and the potential of routine urine being used as a risk predictor of the development of bladder cancer. Urine samples (160) were screened for the presence of *S. haematobium* ova. Smears stained with the Papanicolaou method were evaluated using light microscopy to determine the cell populations. A high prevalence (39.9%) of urinary schistosomiasis and haematuria (46.9%) was found among the participants. Polymorphonuclear cells, normal and reactive urothelial cells and lymphocytes were characteristic of *S. haematobium* infection. Squamous metaplastic cells (SMCs) were found in 48% and 47.1% of participants who have had past or current *S. haematobium* infection respectively, but were not found in participants who had no exposure to *S. haematobium*. These squamous metaplastic cells are in transition and are prone to malignant transformation when exposed to a carcinogenic agent. There is still a high burden of schistosomiasis in endemic communities in Ghana. By examining urine, one can find metaplastic cells and dysplastic cells and thus

predict cancer in SH-infested patients. Thus, routine urine cytology as a tool to monitor the risk of bladder cancer development is recommended.

Differential Analysis of Key Proteins Related to Fibrosis and Inflammation in Soluble Egg Antigen of *Schistosoma mansoni* at Different Infection Times.

Chen YC, Chen IA, Peng SY, Cheng PC.

11-03-2023

Pathogens.

<https://pubmed.ncbi.nlm.nih.gov/36986363/>

Schistosomiasis is a major global health problem. Schistosomes secrete antigens into the host tissue that bind to chemokines or inhibit immune cell receptors, regulating the immune responses to allow schistosome development. However, the detailed mechanism of chronic schistosome infection-induced liver fibrosis, including the relationship between secreted soluble egg antigen (SEA) and hepatic stellate cell (HSC) activation, is still unknown. We used mass spectrometry to identify the SEA protein sequences from different infection weeks. In the 10th and 12th infection weeks, we focused on the SEA components and screened out the special protein components, particularly fibrosis- and inflammation-related protein sequences. Our results have identified heat shock proteins, phosphorylation-associated enzymes, or kinases, such as Sm16, GSTA3, GPCRs, EF1- α , MMP7, and other proteins linked to schistosome-induced liver fibrosis. After sorting, we found many special proteins related to fibrosis and inflammation, but studies proving their association with schistosomiasis infection are limited. Follow-up studies on MICOS, MATE1, 14-3-3 epsilon, and CDCP1 are needed. We treated the LX-2 cells with the SEA from the 8th, 10th, and 12th infection weeks to test HSC activation. In a trans-well cell model in which PBMCs and HSCs were co-cultured, the SEA could significantly induce TGF- β secretion, especially from the 12th week of infection. Our data also showed that TGF- β secreted by PBMC after the SEA treatment activates LX-2 and upregulates hepatic fibrotic markers α -SMA and collagen 1. Based on these results, the CUB domain-containing protein 1 (CDCP1) screened at the 12th infection week could be investigated further. This study clarifies the trend of immune mechanism variation in the different stages of schistosome infection. However, how egg-induced immune response transformation causes liver tissue fibrosis needs to be studied further.

Knocking Down Gm16685 Decreases Liver Granuloma in Murine Schistosomiasis Japonica.

Zhao R, Tang X, Lin H, Xing C, Xu N, Dai B, Wang P, Shao W, Liu M, Shen J, Deng S, Ren C.

21-03-202

Microorganisms.

<https://pubmed.ncbi.nlm.nih.gov/36985369/>

Effects of Age, Gender and Soil-Transmitted Helminth Infection on Prevalence of Plasmodium Infection

among Population Living in Bata District, Equatorial Guinea.

Meñe GR, Mpina MG, Lopelo A, Nyakarungu EL, Bijeri JR, Elo AME, Ondo FA, Garcia GA, Phiri WP, Ali AM, Agobé JCD, Adegnika AA, Abdulla SM.

27-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977150/>

Introduction: Malaria and soil-transmitted helminth (STH) co-infection is an important parasitic infection affecting populations in co-endemic countries including Equatorial Guinea. To date, the health impact of STH and malaria co-infection is inconclusive. The current study aimed to report the malaria and STH infection epidemiology in the continental region of Equatorial Guinea. **Methods:** We performed a cross-sectional study between October 2020 and January 2021 in the Bata district of Equatorial Guinea. Participants aged 1-9 years, 10-17 years and above 18 were recruited. Fresh venous blood was collected for malaria testing via mRDTs and light microscopy. Stool specimens were collected, and the Kato-Katz technique was used to detect the presence of *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm spp. and intestinal *Schistosoma* eggs. **Results:** A total of 402 participants were included in this study. An amount of 44.3% of them lived in urban areas, and only 51.9% of them reported having bed nets. Malaria infections were detected in 34.8% of the participants, while 50% of malaria infections were reported in children aged 10-17 years. Females had a lower prevalence of malaria (28.8%) compared with males (41.7%). Children of 1-9 years carried more gametocytes compared with other age groups. An amount of 49.3% of the participants infected with *T. trichiura* had malaria parasites compared with those infected with *A. lumbricoides* (39.6%) or both (46.8%). **Conclusions:** The overlapping problem of STH and malaria is neglected in Bata. The current study forces the government and other stakeholders involved in the fight against malaria and STH to consider a combined control program strategy for both parasitic infections in Equatorial Guinea.

Geographical Influence on Morphometric Variability of Genetically "Pure" *Schistosoma haematobium* Eggs from Sub-Saharan Migrants in Spain.

Reguera-Gómez M, Valero MA, Artigas P, De Elías-Escribano A, Fantozzi MC, Luzón-García MP, Salas-Coronas J, Boissier J, Mas-Coma S, Bargues MD.

27-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977146/>

Infectious diseases in German military personnel after predominantly tropical deployments: a retrospective assessment over 13 years.

Schawaller M, Wiemer D, Hagen RM, Frickmann H.

Apr-2023

BMJ Mil Health.

<https://pubmed.ncbi.nlm.nih.gov/33257519/>

Objectives: Military deployments to the tropics are associated with specific infection risks. To add to the available epidemiological information, infectious disease risks in German military personnel returning from predominantly tropical deployments were assessed. **Methods:** Since 2006, German soldiers returning from predominantly tropical deployments have been offered the opportunity of returnee screenings at the Department of Tropical Medicine and Infectious Diseases of the Bundeswehr Hospital Hamburg. Case files and diagnostic results recorded between 2006 and 2018 were retrospectively assessed to identify deployment-associated infectious disease risks. **Results:** Along with high enteric colonisation rates with apathogenic protozoa and resistant *Enterobacteriaceae*, direct or indirect proof of infections among the 764 assessed cases comprised *Plasmodium* spp (n=37), *Giardia duodenalis* (n=21), *Schistosoma* spp (n=14), *Yersinia enterocolitica* (n=5), *Strongyloides stercoralis* (n=3), *Campylobacter jejuni* (n=1), *Leishmania* spp (n=1) and *Salmonella enterica* (n=1), as well as latent infections with *Mycobacterium tuberculosis* complex (n=8). The infections were mainly imported from the African region and Eastern Mediterranean region and high proportions of cases lacked typical symptoms. Reported side effect rates of antimalarial chemoprophylaxis for mefloquine (n=121), atovaquone/proguanil (n=49) and doxycycline (n=6) were 36.3%, 19.3% and 11.8%, respectively, while non-compliance rates were 12.9%, 13.0% and 5.9%, respectively. **Conclusions:** Considerable rates of infections with sometimes atypical or absent symptoms confirm a need for returnee screenings after tropical deployments. High reported side effect rates for mefloquine support its replacement by atovaquone/proguanil or doxycycline for antimalarial chemoprophylaxis.

MicroRNA dysregulation in schistosomiasis-induced hepatic fibrosis: a systematic review.

Nóbrega DND, Carvalho TL, do Ó KP, Lima RE, Farias ICC, Souza RDS, Pereira JB, Maranhão ACN, Lima VFDS, Melo ALTM, Silva TCG, Belmont TFM, Gomes ECS, Vasconcelos LRS.

Mar-2023

Expert Rev Mol Diagn.

<https://pubmed.ncbi.nlm.nih.gov/36803616/>

Increased hepatic interleukin-1, arachidonic acid, and reactive oxygen species mediate the protective potential of peptides shared by gut cysteine peptidases against *Schistosoma mansoni* infection in mice.

Tallima H, El Ridi R.

15-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36920999/>

A genome sequence for *Biomphalaria pfeifferi*, the major vector snail for the

human-infecting parasite *Schistosoma mansoni*.

Bu L, Lu L, Laidemitt M, Zhang SM, Mutuku M, Mkoji G, Steinauer M, Loker ES.

24-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36961841/>

Background: *Biomphalaria pfeifferi* is the world's most widely distributed and commonly implicated vector snail species for the causative agent of human intestinal schistosomiasis, *Schistosoma mansoni*. In efforts to control *S. mansoni* transmission, chemotherapy alone has proven insufficient. New approaches to snail control offer a way forward, and possible genetic manipulations of snail vectors will require new tools. Towards this end, we here offer a diverse set of genomic resources for the important African schistosome vector, *B. pfeifferi*. **Methodology/principal findings:** Based largely on PacBio High-Fidelity long reads, we report a genome assembly size of 772 Mb for *B. pfeifferi* (Kenya), smaller in size than known genomes of other planorbid schistosome vectors. In a total of 505 scaffolds (N50 = 3.2Mb), 430 were assigned to 18 large linkage groups inferred to represent the 18 known chromosomes, based on whole genome comparisons with *Biomphalaria glabrata*. The annotated *B. pfeifferi* genome reveals a divergence time of 3.01 million years with *B. glabrata*, a South American species believed to be similar to the progenitors of *B. pfeifferi* which undertook a trans-Atlantic colonization < five million years ago. **Conclusions/significance:** The genome for this preferentially self-crossing species is less heterozygous than related species known to be preferential out-crossers; its smaller genome relative to congeners may similarly reflect its preference for selfing. Expansions of gene families with immune relevance are noted, including the FReD gene family which is far more similar in its composition to *B. glabrata* than to *Bulinus truncatus*, a vector for *Schistosoma haematobium*. Provision of this annotated genome will help better understand the dependencies of trematodes on snails, enable broader comparative insights regarding factors contributing to susceptibility/ resistance of snails to schistosome infections, and provide an invaluable resource with respect to identifying and manipulating snail genes as potential targets for more specific snail control programs.

"Female genital schistosomiasis is a sexually transmitted disease": Gaps in healthcare workers' knowledge about female genital schistosomiasis in Tanzania.

Mazigo HD, Samson A, Lambert VJ, Kosia AL, Ngoma DD, Murphy R, Matungwa DJ.

23-03-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962298/>

Female Genital Schistosomiasis is a gynecological disease that is a complication of parasitic *Schistosoma haematobium* infection and affects at least 40 million girls and women, mostly in sub-Saharan Africa. Little is known about how healthcare workers in endemic areas perceive

and manage (diagnose and treat) Female Genital Schistosomiasis. We conducted cross-sectional focus group discussions and key informant interviews among healthcare workers in northwestern Tanzania. Healthcare workers, particularly those working in areas where *S. haematobium* is highly endemic, were purposively sampled to participate in the study. Discussions and interviews were digitally recorded, transcribed, and analyzed using NVivo version 12. Most healthcare workers lacked knowledge and skills to manage Female Genital Schistosomiasis. They also had multiple misconceptions about its aetiology, modes of transmission, symptoms, and management. Healthcare workers did not consider Female Genital Schistosomiasis in differential diagnoses of women presenting with gynecologic symptoms except sometimes in patients who did not respond to the initial therapy for sexually transmitted infections. Healthcare facilities had limited capacity to manage Female Genital Schistosomiasis. Our findings show critical gaps in both the knowledge of healthcare workers to manage Female Genital Schistosomiasis and in the capacity of healthcare facilities to manage it. To fill these gaps, two urgent needs must be fulfilled: first, training healthcare workers (particularly those working in schistosomiasis-endemic settings) on Female Genital Schistosomiasis, and second, stocking healthcare facilities with necessary medical equipment and supplies for managing this disease.

Occurrence of urinary schistosomiasis and associated bacteria in parts of Ondo State, Nigeria.

Kone KJ, Onifade AK, Dada EO.

12-10-2022

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36962613/>

Toxicological effects of Saponin on the free larval stages of *Schistosoma mansoni*, infection rate, some biochemical and molecular parameters of *Biomphalaria alexandrina* snails.

Ibrahim AM, Gad El-Karim RM, Ali RE, Nasr SM.

Apr-2023

Pestic Biochem Physiol.

<https://pubmed.ncbi.nlm.nih.gov/36963932/>

Saponins have been used as biopesticides. The objective of the present study is to investigate the toxic effects of Saponin against *Biomphalaria alexandrina* snails. Results showed that Saponin exhibited a molluscicidal activity against adult *B. alexandrina* snails at LC₅₀ (70.05 mg/l) and had a larvicidal effect on the free larval stages of *Schistosoma mansoni*. To evaluate the lethal effects, snails were exposed to either LC₁₀ (51.8 mg/l) or LC₂₅ (60.4 mg/l) concentrations of Saponin. The survival, the infection rates, protein, albumin, and total fat levels were decreased, while glucose levels were increased in exposed snails compared to control snails. Also, these concentrations significantly raised Malondialdehyde (MDA) and Glutathione S Transferase (GST) levels, whereas reduced Superoxide dismutase (SOD) activity and the total antioxidant capacity (TAC) in exposed snails.

Furthermore, these concentrations resulted in endocrine disruptions where it caused a significant increase in testosterone (T) level; while a significant decrease in Estradiol (E2) levels were noticed. As for Estrogen (E) level, it was increased after exposure to LC₁₀ Saponin concentration while after exposure to LC₂₅ concentration, it was decreased. Also, LC₁₀ and LC₂₅ concentrations of Saponin caused a genotoxic effect and down-regulation of metabolic cycles in the snails. In conclusion, Saponins caused deleterious effects on the intermediate host of schistosomiasis mansoni. Therefore, *B. alexandrina* snails could be used as models to screen the toxic effects of Saponins in the aquatic environment and if it was used as a molluscicide, it should be used cautiously and under controlled circumstances.

Salmonella typhimurium exacerbates injuries but resolves fibrosis in liver and spleen during Schistosoma mansoni infection.

Lam HYP, Wu WJ, Liang TR, Li HC, Chang KC, Peng SY.

13-03-2023

J Microbiol Immunol Infect.

<https://pubmed.ncbi.nlm.nih.gov/36964051/>

Schistosoma mansoni Infections and Morbidities Among School Children in Hotspot Areas of Jimma Town, Southwest Ethiopia: A Cross-Sectional Study.

Tiruneh A, Zemene E, Abdissa Mizana B, Girma H, Dereje E, Sharew B, Ayana M, Mekonnen Z.

22-03-2023

Environ Health Insights.

<https://pubmed.ncbi.nlm.nih.gov/36969091/>

CRISPR-assisted test for Schistosoma haematobium.

Cherkaoui D, Mesquita SG, Huang D, Lugli EB, Webster BL, McKendry RA.

27-03-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/36973334/>

Schistosomiasis is a major neglected tropical disease targeted for elimination as a public health issue by 2030, however there is an urgent need for more sensitive and specific diagnostic tests suitable to resource-limited settings. Here we developed CATSH, a CRISPR-assisted diagnostic test for *Schistosoma haematobium*, utilising recombinase polymerase amplification, Cas12a-targeted cleavage and portable real-time fluorescence detection. CATSH showed high analytical sensitivity, consistent detection of a single parasitic egg and specificity for urogenital *Schistosoma* species. Thanks to a novel CRISPR-compatible sample preparation developed using simulated urine samples containing parasitic eggs, CATSH had a sample-to-result within 2 h. The components of CATSH can be lyophilised, reducing cold chain dependence and widening access to lower and middle-income countries. This work presents a new application of CRISPR diagnostics for highly sensitive and specific detection of

parasitic pathogens in remote areas and could have a significant impact on the elimination of neglected tropical diseases.

[Establishment and evaluation of a method for extracting exogenous short DNA fragments of Schistosoma japonicum from urine samples].

Zhang Q, Zhao S, Ye Y, Bi N, Wang X, Zhang J, Li W, Yang K.

09-03-2023

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36974010/>

Objective: To establish the method for extracting exogenous short DNA fragments of *Schistosoma japonicum* from urine samples, and to evaluate the efficiency of this method for extraction from urine samples treated with various methods. **Methods:** The *S. japonicum* *SjG28* gene fragment was selected as a target sequence, and the 81 bp short DNA fragment was amplified on the target sequence using PCR assay. Following characterization using sequencing, the short DNA fragment was added into the urine samples as an exogenous short DNA fragment. Primers and probes were designed with *SjG28* as a target gene, to establish the real-time fluorescent quantitative PCR (qPCR) assay. The sensitivity of this qPCR assay was evaluated with exogenous short DNA fragments that were diluted at a 1:10 dilution ratio as the DNA template, and the specificity of the qPCR assay was evaluated with the genomic DNA of *S. mansoni*, *S. haematobium*, *Babesia*, *Ancylostoma duodenale*, *Cionorchis sinensis*, and *Paragonimus westermani* as DNA templates. Exogenous short DNA fragments were added into artificial and healthy volunteers' urine samples, followed by pH adjustment, centrifugation and concentration, and the efficiency of extracting exogenous short DNA fragments from urine samples was compared with the QIAmp Viral RNA Mini Kit (Qiagen kit) and BIOG cfDNA easy kit (BIOG kit). **Results:** An 81 bp small DNA fragment of *S. japonicum* was successfully prepared, and the lowest detection limit of the established qPCR assay was 100 copies/μL of the 81 bp small DNA fragment of *S. japonicum*. If the genomic DNA of *S. japonicum*, *S. mansoni*, *S. haematobium*, *Babesia*, *A. duodenale*, *C. sinensis*, and *P. westermani* served as DNA templates, the qPCR assay only detected fluorescent signals with *S. japonicum* genomic DNA as the DNA template. If the pH values of artificial urine samples were adjusted to 5, 6, 7 and 8, the recovery rates were (49.12 ± 2.09)%, (84.52 ± 4.96)%, (89.38 ± 3.32)% and (87.82 ± 3.90)% for extracting the exogenous short DNA fragment of *S. japonicum* with the Qiagen kit, and were (2.30 ± 0.07)%, (8.11% ± 0.26)%, (13.35 ± 0.61)% and (20.82 ± 0.68)% with the BIOG kit, respectively ($t = 38.702$, 26.955, 39.042 and 29.571; all P values < 0.01). If the Qiagen kit was used for extracting the exogenous short DNA fragment from artificial urine samples, the lowest recovery rate was seen from urine samples with a pH value of 5 (all P values < 0.05), and there were no significant differences in the recovery rate from urine samples with pH values of 6, 7 and 8 (all P values > 0.05). Following centrifugation of artificial [(64.30 ± 1.00)% vs. (58.87 ± 0.26)%; $t = 12.033$, P

< 0.05] and healthy volunteers' urine samples [(31 165 ± 1 017) copies/μL vs. (28 471 ± 818) copies/μL; $t = 23.164$, $P < 0.05$]. In addition, concentration of artificial urine samples with the 10 kDa Centrifugal Filter and concentration of healthy volunteers' urine samples with the 100 kDa Centrifugal Filter were both effective to increase the recovery of the Qiagen kit for extracting the exogenous short DNA fragment of *S. japonicum* (both P values < 0.01). **Conclusions:** A method for extracting exogenous short DNA fragments of *S. japonicum* from urine samples has been successfully established, and the Qiagen kit has a high extraction efficiency. Adjustment of urine pH to 6 to 8 and concentration of healthy volunteers' urine samples with the 100 kDa Centrifugal Filter are both effective to increase the efficiency of extracting exogenous short DNA fragments of *S. japonicum*.

MALDI-TOF: A new tool for the identification of *Schistosoma cercariae* and detection of hybrids.

Huguenin A, Kincaid-Smith J, Depaquit J, Boissier J, Ferté H.

28-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36976804/>

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

High Diversity of *Giardia duodenalis* Assemblages and Sub-Assemblages in Asymptomatic School Children in Ibadan, Nigeria.

Tijani MK, Köster PC, Guadano-Procesi I, George IS, Abodunrin E, Adeola A, Dashti A, Bailo B, González-Barrio D, Carmena D.

28-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977153/>

Giardia duodenalis is a significant contributor to the burden of diarrheal disease in sub-Saharan Africa. This study assesses the occurrence and molecular diversity of *G. duodenalis* and other intestinal parasites in apparently healthy children ($n = 311$) in Ibadan, Nigeria. Microscopy was used as a screening method and PCR and Sanger sequencing as confirmatory and genotyping methods, respectively. Haplotype analyses were performed to examine associations between genetic variants and epidemiological variables. At microscopy examination, *G. duodenalis* was the most prevalent parasite found (29.3%, 91/311; 95% CI: 24.3-34.7), followed by *Entamoeba* spp. (18.7%, 58/311; 14.5-23.4), *Ascaris lumbricoides* (1.3%, 4/311; 0.4-3.3), and *Taenia* sp. (0.3%, 1/311; 0.01-1.8). qPCR confirmed the presence of *G. duodenalis* in 76.9% (70/91) of the microscopy-positive samples. Of them, 65.9% (60/91) were successfully genotyped. Assemblage B (68.3%, 41/60) was more prevalent than assemblage A

(28.3%, 17/60). Mixed A + B infections were identified in two samples (3.3%, 2/60). These facts, together with the absence of animal-adapted assemblages, suggest that human transmission of giardiasis was primarily anthroponotic. Efforts to control *G. duodenalis* (and other fecal-orally transmitted pathogens) should focus on providing safe drinking water and improving sanitation and personal hygiene practices.

Effects of Age, Gender and Soil-Transmitted Helminth Infection on Prevalence of Plasmodium Infection among Population Living in Bata District, Equatorial Guinea.

Meñe GR, Mpina MG, Lopelo A, Nyakarungu EL, Bijeri JR, Elo AME, Ondo FA, Garcia GA, Phiri WP, Ali AM, Agobé JCD, Adegnika AA, Abdulla SM.

27-03-2023

Trop Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36977150/>

Introduction: Malaria and soil-transmitted helminth (STH) co-infection is an important parasitic infection affecting populations in co-endemic countries including Equatorial Guinea. To date, the health impact of STH and malaria co-infection is inconclusive. The current study aimed to report the malaria and STH infection epidemiology in the continental region of Equatorial Guinea. **Methods:** We performed a cross-sectional study between October 2020 and January 2021 in the Bata district of Equatorial Guinea. Participants aged 1-9 years, 10-17 years and above 18 were recruited. Fresh venous blood was collected for malaria testing via mRDTs and light microscopy. Stool specimens were collected, and the Kato-Katz technique was used to detect the presence of *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm spp. and intestinal *Schistosoma* eggs. **Results:** A total of 402 participants were included in this study. An amount of 44.3% of them lived in urban areas, and only 51.9% of them reported having bed nets. Malaria infections were detected in 34.8% of the participants, while 50% of malaria infections were reported in children aged 10-17 years. Females had a lower prevalence of malaria (28.8%) compared with males (41.7%). Children of 1-9 years carried more gametocytes compared with other age groups. An amount of 49.3% of the participants infected with *T. trichiura* had malaria parasites compared with those infected with *A. lumbricoides* (39.6%) or both (46.8%). **Conclusions:** The overlapping problem of STH and malaria is neglected in Bata. The current study forces the government and other stakeholders involved in the fight against malaria and STH to consider a combined control program strategy for both parasitic infections in Equatorial Guinea.

Prevalence and Determinant Factors of Intestinal Parasitic Infections and Undernutrition among Primary School Children in North-Central Ethiopia: A School-Based Cross-Sectional Study.

Bisetegn H, Debash H, Ebrahim H, Erkihun Y, Tilahun M, Feleke DG.

15-03-2023

Modeling the effectiveness of One Health interventions against the zoonotic hookworm *Ancylostoma ceylanicum*.

Walker M, Lambert S, Neves MI, Worsley AD, Traub R, Colella V.

07-03-2023

Front Med (Lausanne).

<https://pubmed.ncbi.nlm.nih.gov/36960338/>

Hookworm disease is a major global public health concern, annually affecting 500-700 million of the world's poorest people. The World Health Organization is targeting the elimination of hookworm as a public health problem by 2030 using a strategy of mass drug administration (MDA) to at-risk human populations. However, in Southeast Asia and the Pacific the zoonotic hookworm species, *Ancylostoma ceylanicum*, is endemic in dogs and commonly infects people. This presents a potential impediment to the effectiveness of MDA that targets only humans. Here, we develop a novel multi-host (dog and human) transmission model of *A. ceylanicum* and compare the effectiveness of human-only and "One Health" (human plus dog) MDA strategies under a range of eco-epidemiological assumptions. We show that One Health interventions-targeting both dogs and humans-could suppress prevalence in humans to $\leq 1\%$ by the end of 2030, even with only modest coverage (25-50%) of the animal reservoir. With increasing coverage, One Health interventions may even interrupt transmission. We discuss key unresolved questions on the eco-epidemiology of *A. ceylanicum*, the challenges of delivering MDA to animal reservoirs, and the growing importance of One Health interventions to human public health.

Gale

A patient's experience of crusted scabies in the context of immunosuppression.

Duff E, Lyons D, Eustace K, Collins S.

30-03-2023

Clin Exp Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36994790/>

Deep learning for AI-based diagnosis of skin-related neglected tropical diseases: a pilot study.

Yotsu R, Ding Z, Hamm J, Blanton R.

15-03-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/36993502/>

Background: Deep learning, which is a part of a broader concept of artificial intelligence (AI) and/or machine learning has achieved remarkable success in vision tasks. While there is growing interest in the use of this technology in diagnostic support for skin-related neglected tropical diseases (skin NTDs), there have been limited studies in this area and fewer focused on dark skin. In this study, we aimed to develop deep learning based AI

models with clinical images we collected for five skin NTDs, namely, Buruli ulcer, leprosy, mycetoma, scabies, and yaws, to understand how diagnostic accuracy can or cannot be improved using different models and training patterns. **Methodology:** This study used photographs collected prospectively in Côte d'Ivoire and Ghana through our ongoing studies with use of digital health tools for clinical data documentation and for teledermatology. Our dataset included a total of 1,709 images from 506 patients. Two convolutional neural networks, ResNet-50 and VGG-16 models were adopted to examine the performance of different deep learning architectures and validate their feasibility in diagnosis of the targeted skin NTDs. **Principal findings:** The two models were able to correctly predict over 70% of the diagnoses, and there was a consistent performance improvement with more training samples. The ResNet-50 model performed better than the VGG-16 model. Model trained with PCR confirmed cases of Buruli ulcer yielded 1-3% increase in prediction accuracy over training sets including unconfirmed cases. **Conclusions:** Our approach was to have the deep learning model distinguish between multiple pathologies simultaneously - which is close to real-world practice. The more images used for training, the more accurate the diagnosis became. The percentages of correct diagnosis increased with PCR-positive cases of Buruli ulcer. This demonstrated that it may be better to input images from the more accurately diagnosed cases in the training models also for achieving better accuracy in the generated AI models. However, the increase was marginal which may be an indication that the accuracy of clinical diagnosis alone is reliable to an extent for Buruli ulcer. Diagnostic tests also have its flaws, and they are not always reliable. One hope for AI is that it will objectively resolve this gap between diagnostic tests and clinical diagnoses with addition of another tool. While there are still challenges to be overcome, there is a potential for AI to address the unmet needs where access to medical care is limited, like for those affected by skin NTDs. **Author summary:** The diagnosis of skin diseases depends in large part, though not exclusively on visual inspection. The diagnosis and management of these diseases is thus particularly amenable to teledermatology approaches. The widespread availability of cell phone technology and electronic information transfer provides new potential for access to health care in low-income countries, yet there are limited efforts targeting these neglected populations with dark skin and consequently limited availability of tools. In this study, we leveraged a collection of skin images gathered through a system of teledermatology in the West African countries of Côte d'Ivoire and Ghana, and applied deep learning, a form of artificial intelligence (AI) - to see if deep learning models can distinguish between different diseases and support their diagnosis. Skin-related neglected tropical diseases, or skin NTDs, prevail in these regions and were our target conditions: Buruli ulcer, leprosy, mycetoma, scabies, and yaws. The accuracy of prediction depended on the number of images that were fed into the model for training with marginal improvement using laboratory confirmed cases in training. Using more images and greater efforts in this area, it is possible that AI can help address the unmet needs where access to medical care is limited.

A Survey on Scabies Inpatients in South Korea Based on Health Insurance Claims Data from 2010 to 2019.

Kim HS, Bang JY, Cha KS.

13-03-2023

Healthcare (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36981498/>

Due to the growing aging population and the increased number of long-term patients staying in nursing facilities, the prevalence of scabies has recently been increasing, even in developed countries. This study aimed to identify the actual status of hospitalized patients with scabies in South Korea using the national health insurance claims data. From 2010 to 2019, 2586 patients were hospitalized with scabies (B86) as the primary diagnosis. There were more females than males ($\chi^2 = 31.960$, $p < 0.001$) and patients aged 80 years or older in long-term care hospitals ($\chi^2 = 431.410$, $p < 0.001$). Scabies patients were mainly hospitalized in internal medicine, family medicine, and dermatology for all provider types ($\chi^2 = 170.033$, $p < 0.001$). In long-term care hospitals, the rate of accompanying dementia was 31.9% ($\chi^2 = 193.418$, $p < 0.001$), cerebral infarction was 10.4% ($\chi^2 = 106.271$, $p < 0.001$), and cancer was 2.1% ($\chi^2 = 17.963$, $p < 0.001$), which was higher than other provider types. Additionally, 20.6% in general hospitals ($\chi^2 = 198.952$, $p < 0.001$) had an indwelling catheter, while 49.1% in hospitals and 41.1% in general hospitals were administered steroids ($\chi^2 = 214.440$, $p < 0.001$). The KOH smear test was performed in 11.3% of all inpatients with scabies. We suggest recognizing these characteristics of scabies patients and thoroughly checking the skin lesions during physical examination for early diagnosis and prevention of scabies infection.

One versus two doses of ivermectin-based mass drug administration for the control of scabies: A cluster randomised non-inferiority trial.

Lake SJ, Engelman D, Zinihite J, Sokana O, Boara D, Nasi T, Gorae C, Osti MH, Phelan S, Parnaby M, Grobler AC, Schuster T, Andrews R, Whitfeld MJ, Marks M, Romani L, Steer AC, Kaldor JM.

17-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36930667/>

Morsures de serpent

The genus Leucas: A review on phytochemistry and pharmacological activities.

Kumar S, Singh N, Mittal A, Kharkwal H, Jain SK, Goel B.

28-03-2023

Fitoterapia.

<https://pubmed.ncbi.nlm.nih.gov/36996945/>

Genus *Leucas* (family Lamiaceae) has been used as the traditional medicine for the treatment of a variety of disorders like skin diseases, diabetes, rheumatic pain, wounds, snake bites, etc. Several species of genus *Leucas*

have been explored for their pharmacological activities and found to possess diverse properties like antimicrobial, antioxidant, anti-inflammatory, cytotoxic and anticancer, antinociceptive, antidiabetic, antitussive, wound healing, phytotoxic, etc. Phytochemical investigations of the different plant parts of Genus *Leucas* have revealed the presence of phytochemicals including terpenoids, flavonoids, lignans, phenolic glycosides, sterols, and essential oils. Terpenoids have been obtained as the major components of the isolated compounds and could be used as the marker compounds for the genus *Leucas*. The traditional uses of *Leucas* spp. have been established scientifically and were shown due to the presence of different phytochemicals. Although the pharmacological activities of *Leucas* plants have been well-documented, further studies are needed to fully understand their mechanisms of action and clinical applications. In conclusion, the phytochemistry and pharmacological activity of genus *Leucas* make it a promising source of natural products for drug discovery and development. The present review aims to provide a comprehensive note on the phytochemistry and pharmacological properties of the genus *Leucas*.

Development of sandwich ELISA and lateral flow assay for the detection of Bungarus multicinctus venom.

Nong JF, Huang Z, Huang ZZ, Yang J, Li JC, Yang F, Huang DL, Wang F, Wang W.

30-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36996245/>

Clinical and epidemiological profile of snakebite cases - A study from an industrial teaching hospital at Jamshedpur, Jharkhand, India.

Satyanarayan B, Panda SK, Sunder A, Kumari S.

Dec-2022

J Family Med Prim Care.

<https://pubmed.ncbi.nlm.nih.gov/36994007/>

Introduction: India accounts for approximately half of the worldwide snakebite deaths. It is often a neglected public health problem and particularly in Jharkhand region where medical facilities are limited. Epidemiological and clinical profile-related studies are scarce. The present study aims to assess the epidemiological profile and clinical features of snakebites encountered in a tertiary-care teaching hospital at Jamshedpur, Jharkhand, India. **Aims and objective:** The aim of this study was to assess the clinical profile, outcome and epidemiological factors of snakebite cases, admitted to a tertiary care hospital in Jamshedpur. **Material and methods:** This was a retrospective study from 2014 to 2021 wherein a total of 427 snakebite patients were admitted and had received treatment for snakebite at a tertiary-care teaching hospital at Jamshedpur, Jharkhand. All patients who reported with a history of snakebite were included in this study. The demographic and clinical details of each case were obtained and analysed. **Result:** A total of 427 snakebite cases were admitted to the hospital during the study period. The

victims were predominantly males. Majority of the bite cases encountered were from rural areas and were in the second quarter of the year. The site of the bite was largely on the lower limb and the upper limb had fewer bites. The Glasgow Coma Scale was normal in those who presented early. Acute kidney injury, neutrophilic leucocytosis and deranged liver enzymes were associated with bad prognosis. Timely intervention with anti-snake venom offered good result. **Conclusion:** We had more male patients (69.55%), belonging to rural areas (67.91%), more bites in lower limbs and more cases in the second quarter of the year. Mortality rate was 0.7%.

Prolonged asymptomatic venom induced consumption coagulopathy: Caused by hemotoxic snake bite.

Rijal P, Singh AP, Panwar P, Pathania M, Kant R.

Nov-2022

J Family Med Prim Care.

<https://pubmed.ncbi.nlm.nih.gov/36993133/>

Role of steroid on management of limb swelling and local pain in haematotoxic snake bite.

Ghosh M, Acharyya A, Bhattacharya P, Chakraborty S.

Nov-2022

J Family Med Prim Care.

<https://pubmed.ncbi.nlm.nih.gov/36993125/>

A cross-sectional study of various clinical and laboratory parameters in snakebite and their association with mortality at a tertiary care centre in Jharkhand.

Kumar A, Dungdung A, Kumar A, Shashank, Kumar R, Pandey V, Priya S.

Nov-2022

J Family Med Prim Care.

<https://pubmed.ncbi.nlm.nih.gov/36993079/>

Compartment syndrome following snakebite in a boy: A case report and literature review.

Navaeifar MR, Zakariaei Z, Ghadiri A, Soleymani M, Zakariaei A.

24-03-2023

Int J Surg Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36989626/>

Introduction and importance: Snake bites represent a significant public health issue worldwide, as venomous snake bites can result in lethal consequences if not treated promptly, including both local and systemic effects. The local symptoms of a snake bite commonly include tissue necrosis, edema, and compartment syndrome (CS). While CS is a rare complication following a snake bite, it may be more pronounced in children who typically have lower total dilution volume. Currently, the administration of anti-snake venom and prompt fasciotomy are the only specific treatments available for CS. **Case presentation:** The present report details a case of CS of the right upper extremity in a three-year-old boy who suffered a snake

bite on his right hand and was brought to the emergency department of a hospital in northern Iran after a lapse of 14 h. **Clinical discussion:** Snakebites frequently occur in the extremities, with about two thirds of them happening in the upper extremities. The skin of the dorsum is extremely thin, there is essentially little subcutaneous fat tissue, and there are numerous superficial veins in this area, particularly the hand. **Conclusions:** Following snake bites, the use of proximal tourniquets should be avoided, and the public's awareness of this need should be encouraged through health education. The prognosis for recovery following fasciotomy and the significance of follow-up and rehabilitation should also be explained to patients.

Pentaclethra macroloba: A Review of the Biological, Pharmacological, Phytochemical, Cosmetic, Nutritional and Biofuel Potential of this Amazonian Plant.

Nobre Lamarão ML, Ferreira LMMC, Gyles Lynch D, Morais LRB, Silva-Júnior JOC, Ribeiro-Costa RM.

15-03-2023

Plants (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36987018/>

Exploring the Profile of Cell Populations and Soluble Immunological Mediators in Bothrops atrox Envenomations.

Coelho KF, Neves JCF, Ibiapina HNS, Magalhães-Gama F, Barbosa FBA, Silva FS, Wellmann IAM, Sachett JAG, Tarragô AM, Ferreira LCL, Malheiro A, Monteiro WM, Costa AG.

03-03-2023

Toxins (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36977086/>

Bothrops atrox envenomations are common in the Brazilian Amazon. The venom of *B. atrox* is highly inflammatory, which results in severe local complications, including the formation of blisters. Moreover, there is little information on the immune mechanisms associated with this condition. Thus, a longitudinal study was carried out to characterize the profile of the cell populations and soluble immunological mediators in the peripheral blood and blisters in *B. atrox* patients according to their clinical manifestations (mild and severe). A similar response in both *B. atrox* patient groups (MILD and SEV) was observed, with an increase in inflammatory monocytes, NKT, and T and B cells, as well as CCL2, CCL5, CXCL9, CXCL10, IL-1 β and IL-10, when compared with the group of healthy blood donors. After the administration of antivenom, the participation of patrolling monocytes and IL-10 in the MILD group was observed. In the SEV group, the participation of B cells was observed, with high levels of CCL2 and IL-6. In the blister exudate, a hyperinflammatory profile was observed. In conclusion, we revealed the involvement of cell populations and soluble mediators in the immune response to *B. atrox* envenomation at the local and peripheral level, which is related to the onset and extent of the inflammation/clinical manifestation.

"Two Cultures in Favor of a Dying Patient": Experiences of Health Care Professionals Providing Snakebite Care to Indigenous Peoples in the Brazilian Amazon.

Murta F, Strand E, de Farias AS, Rocha F, Santos AC, Rondon EAT, de Oliveira APS, da Gama HSS, Vieira Rocha Y, Rocha GDS, Ferreira M, Azevedo Machado V, Lacerda M, Pucca M, Cerni F, Nickenig Vissoci JR, Tupetz A, Gerardo CJ, Moura-da-Silva AM, Hui Wen F, Sachett J, Monteiro W.

03-03-2023

Toxins (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36977085/>

The Effectiveness of Antibiotics in Managing Bacterial Infections on Bite Sites following Snakebite Envenomation.

Senthilkumaran S, Salim A, Almeida JR, Williams J, Vijayakumar P, Thirunavukarasu A, Christopoulos MA, Williams HF, Thirumalaikolundusubramanian P, Patel K, Vaiyapuri S.

03-03-2023

Toxins (Basel).

<https://pubmed.ncbi.nlm.nih.gov/36977081/>

Snakebite envenomation (SBE) is a life-threatening medical emergency with a high mortality rate. Common secondary complications following SBE, such as wound infections, are significant due to their impact on worsening local tissue damage and causing systemic infection. Antivenoms are not effective to treat wound infections following SBE. Moreover, in several rural clinical settings, broad-spectrum antibiotics are often used without clear guidelines or based on limited laboratory data, resulting in undesirable side effects and exacerbated treatment costs. Therefore, robust antibiotic strategies should be developed to tackle this critical issue. Currently, there is limited information available on the bacterial profiles of SBE-induced infections and antibiotic susceptibility. Hence, it is essential to improve the knowledge of bacterial profiles and their antibiotic sensitivity in SBE victims to develop better treatment strategies. This study aimed to address this issue by examining the bacterial profiles of SBE victims with a specific focus on Russell's viper envenomation. The most frequently found bacteria in the bites of SBE victims were *Staphylococcus aureus*, *Klebsiella* sp., *Escherichia coli*, and *Pseudomonas aeruginosa*. Linezolid, clindamycin, colistin, meropenem, and amikacin were some of the most effective antibiotics for commonly grown bacteria in SBE victims. Similarly, ciprofloxacin, ampicillin, amoxiclave, cefixime, and tetracyclin were the least effective antibiotics for common bacteria found in the wound swabs of SBE victims. These data provide robust guidance for infection management following SBE and offer useful insights to aid in designing effective treatment protocols for SBE with serious wound infections in rural areas where laboratory facilities may not be readily available.

Alarmins and inflammatory aspects related to snakebite envenomation.

Zuliani JP.

Apr-2023

Toxicon.

<https://pubmed.ncbi.nlm.nih.gov/36924999/>

Building an explanatory model for snakebite envenoming care in the Brazilian Amazon from the indigenous caregivers' perspective.

de Farias AS, do Nascimento EF, Gomes Filho MR, Felix AC, da Costa Arévalo M, Adrião AAX, Wen FH, de Carvalho FG, Murta F, Machado VA, Sachett J, Monteiro WM.

10-03-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36897928/>

Background: In the Brazilian Amazon, snakebite envenomings (SBE) disproportionately affect indigenous peoples. Communication between indigenous and biomedical health sectors in regards to SBEs has never been explored in this region. This study aims to build an explanatory model (EM) of the indigenous healthcare domain for SBE patients from the perspective of the indigenous caregivers. **Methodology/principal findings:** This is a qualitative study involving in-depth interviews of eight indigenous caregivers who are representatives of the Tikuna, Kokama and Kambaba ethnic groups, in the Alto Solimões River, western Brazilian Amazon. Data analysis was carried out via deductive thematic analysis. A framework was built containing the explanations based on three explanatory model (EM) components: etiology, course of sickness, and treatment. To indigenous caregivers, snakes are enemies and present conscience and intention. Snakebites have a natural or a supernatural cause, the last being more difficult to prevent and treat. Use of ayahuasca tea is a strategy used by some caregivers to identify the underlying cause of the SBE. Severe or lethal SBEs are understood as having been triggered by sorcery. Treatment is characterized by four components: i) immediate self-care; ii) first care in the village, mostly including tobacco smoking, chants and prayers, combined with the intake of animal bile and emetic plants; iii) a stay in a hospital, to receive antivenom and other treatments; iv) care in the village after hospital discharge, which is a phase of re-establishment of well-being and reintroduction into social life, using tobacco smoking, massages and compresses to the affected limb, and teas of bitter plants. Dietary taboos and behavioral interdictions (avoiding contact with menstruating and pregnant women) prevent complications, relapses, and death, and must be performed up to three months after the snakebite. Caregivers are in favor of antivenom treatment in indigenous areas. **Conclusions/significance:** There is a potential for articulation between different healthcare sectors to improve the management of SBEs in the Amazon region, and the aim is to decentralize antivenom treatment so that it occurs in indigenous health centers with the active participation of the indigenous caregivers.

Local envenoming by the coinsnake or Asian racer, *Hemorrhois nummifer* and

mountain racer or leopard snake, Hemorrhoids ravigieri (Serpentes: Colubridae, Colubrinae) in Iran: A reminder of the importance of species identification in the medical management of snakebites.

Kazemi SM, Jahan-Mahin MH, Mohammadian-Kalat T, Hosseinzadeh MS, Weinstein SA.

Apr-2023

Toxicon.

<https://pubmed.ncbi.nlm.nih.gov/36868482/>

In Iran, there are approximately 4500-6500 snakebites per year, but fortunately only 3-9 of these are fatal. However, in some population centers such as Kashan city (Isfahan Province, central Iran), approximately 80% of snakebites are attributed to "non-venomous" snakes that are often comprised of several species of non-front-fanged snakes (NFFS). NFFS comprise a diverse group that constitute approximately 2900 species belonging to an estimated 15 families. We report here two cases of local envenoming from *H. ravigieri*, and one from *H. nummifer* that occurred in Iran. The clinical effects consisted of local erythema, mild pain, transient bleeding and edema. Two victims experienced progressive local edema that distressed the victims. The medical team's unfamiliarity with snakebites contributed to the incorrect clinical management of one victim including the contraindicated, ineffective provision of antivenom. These cases provide further documentation about local envenoming caused by these species, and also emphasize the need for regional medical personnel to receive increased training in order to improve familiarity with the local snake fauna and evidence-based snakebite management.

Artificial intelligence-based snakebite identification using snake images, snakebite wound images, and other modalities of information: A systematic review.

Zhang J, Chen X, Song A, Li X.

May-2023

Int J Med Inform.

<https://pubmed.ncbi.nlm.nih.gov/36848781/>

Venom-Induced Reversible Leukoencephalopathy: A Novel Cause of Toxic Acute Leukoencephalopathy With Restricted Diffusion.

Kamate M, Basavanagowda T, Hattiholi V.

Apr-2023

Pediatr Neurol.

<https://pubmed.ncbi.nlm.nih.gov/36774684/>

Fatal intracranial bleedings in a viper bite: A case report.

Naveen A, Sahu MR, Mohanty MK, Padhi KS, Patnaik A.

Mar-2023

Chin J Traumatol.

<https://pubmed.ncbi.nlm.nih.gov/36180309/>

Viper bite envenomation represents a significant occupational hazard among agricultural workers in India. The viper bite envenomation is usually suspected when a patient presents with predominant local symptoms at the bitten site, including pain, swelling, and necrosis. Further, systemic findings such as diffuse intravascular coagulation, hypotension, and shock may alert physicians of viper bite envenomation rather than a neurotoxic snake bite. However, cerebral complications are rare in viper bites but may potentially be fatal. Central nervous system involvement in a viper bite is either due to neurotoxins or hemorrhagins present in the venom, which may induce cerebral thrombosis, ischemia, infarction, and hemorrhage. Here we present a case of a previously healthy adult male who succumbed to extensive subarachnoid, intracerebral, and intraventricular hemorrhages involving bilateral cerebral hemispheres following viper snake bite envenomation. This report highlights the importance of anticipating cerebral complications in viper bite envenomation, a rare occurrence. It also emphasizes the need for early antivenom administration to prevent and control systemic envenomation and its complications.