



Veille scientifique

Maladies tropicales négligées

Semaine 30
24 au 30 juillet 2023

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Cysticercose

Confirmation by necropsy of a high prevalence of porcine cysticercosis in a rural district of Madagascar.

Mananjara DEA, Rakotoarinoro M, Rakotoarison VC, Raliniaina M, Razafindraibe NP, Ravonirina C, Randriamparany T, Rasamoelina-Andriamanivo H, Rakotozandrindrainy R, Cardinale E, Lightowlers MW, Donadeu M, Mwape KE.

07-07-2032

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/37496390/>

Geostatistical analysis of active human cysticercosis: Results of a large-scale study in 60 villages in Burkina Faso.

Dermauw V, Van De Vijver E, Dorny P, Giorgi E, Ganaba R, Millogo A, Tarnagda Z, Cissé AK, Carabin H.

26-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37494329/>

Cysticercosis is a neglected tropical disease caused by the larval stage of the zoonotic tapeworm (*Taenia solium*). While there is a clear spatial component in the occurrence of the parasite, no geostatistical analysis of active human cysticercosis has been conducted yet, nor has such an analysis been conducted for Sub-Saharan Africa, albeit relevant for guiding prevention and control strategies. The goal of this study was to conduct a geostatistical analysis of active human cysticercosis, using data from the baseline cross-sectional component of a large-scale study in 60 villages in Burkina Faso. The outcome was the prevalence of active human cysticercosis (hCC), determined using the B158/B60 Ag-ELISA, while various environmental variables linked with the transmission and spread of the disease were explored as potential explanatory variables for the spatial distribution of *T. solium*. A generalized linear geostatistical model (GLGM) was run, and prediction maps were generated. Analyses were conducted using data generated at two levels: individual participant data and grouped village data. The best model was selected using a backward variable selection procedure and models were compared using likelihood ratio testing. The best individual-level GLGM included precipitation (increasing values were associated with an increased odds of positive test result), distance to the nearest river (decreased odds) and night land temperature (decreased odds) as predictors for active hCC, whereas the village-level GLGM only retained precipitation and distance to the nearest river. The range of spatial correlation was estimated at 45.0 [95%CI: 34.3; 57.8] meters and 28.2 [95%CI: 14.0; 56.2] km for the individual- and village-level datasets, respectively. Individual- and village-level GLGM unravelled large areas with active hCC predicted prevalence estimates of at least 4% in the south-east, the extreme south, and north-west of the study area, while patches of prevalence estimates below 2% were seen in the north and west. More research designed to analyse the spatial characteristics of hCC is needed with sampling strategies ensuring appropriate characterisation of spatial variability,

and incorporating the uncertainty linked to the measurement of outcome and environmental variables in the geostatistical analysis.

Cysticercosis in free-ranging agoutis (*Dasyprocta leporina*) in the Eastern Brazilian Amazon.

Souza AJS, Malheiros AP, Chagas AACD, Alves MM, Bernal MKM, Carneiro LA, Gomes-Gouvêa MS, Nunes HM.

21-07-2023

Rev Bras Parasitol Vet.

<https://pubmed.ncbi.nlm.nih.gov/37493786/>

The study describes the occurrence of cysticercosis in liver of 22 wild agoutis (*Dasyprocta leporina*) in the Brazilian Amazon. The phylogenetic analysis and microscopic characteristics of metacestodes in liver tissue sections, associated with the geographic distribution of the intermediate hosts indicated that a possibly novel *Taenia* sp. metacestode caused the parasitism. Additionally, two cases of hepatic co-infection by *Taenia* sp., *Calodium* sp. and *Echinococcus oligarthra* were also observed among the analyzed animals. The results point to the need for a better understanding of hepatotropic parasites among wild rodents in the Brazilian Amazon.

Spinal cysticercosis: A case report.

Manh BH, Dat T, Hai VT, He DV, Ha DD, Que NV, Duc NM.

06-07-2023

Radiol Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37483373/>

Improved latrine coverage may reduce porcine cysticercosis: a comparative cross-sectional study, Busia County, Kenya 2021.

Chege B, Ndambuki G, Owiny M, Kiyong'a A, Fèvre EM, Cook EAJ.

05-07-2023

Front Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37476824/>

Introduction: Smallholder pig farming is an important economic activity for many poor, rural communities in developing countries. Porcine cysticercosis is a growing public health risk in countries where pig rearing is popular. A sanitation-based intervention to reduce the prevalence of open defecation was completed in Busia County, Kenya in 2016. We capitalized on this third party intervention to evaluate its impact on porcine cysticercosis prevalence. **Methods:** We conducted a comparative cross-sectional survey from August through to September 2021. Household selection was done using multistage sampling. Household questionnaire data on pig production, transmission, risk factors and awareness of porcine cysticercosis were collected from 251 households. Lingual palpation was used to test for cysticerci in 370 pigs while serum was tested for circulating antigen using Ag-ELISA. We compared results of our survey to an effective baseline, which was a near equivalent cross sectional survey conducted in 2012 before the third party sanitary

intervention was established. The difference in prevalence was measured using Chi-square tests. Multivariable logistic regression analysis was used to identify risk factors for lingual cysts in pigs. **Results:** The prevalence of palpable lingual cysts was estimated to be 3.8% (95% CI 2.3-6.3%) (14/370). This was 6% (95% CI 0.8-13.9%; p -value 0.0178) lower than the prevalence reported in the pre-implementation period of 9.7% (95% CI: 4.5-17.6%). Circulating antigen was detected in 2 samples (0.54%, 95% CI: 0.2-1.9). Latrine coverage was 86% (95% CI: 81-90%), which was 11% (95% CI: 4.8-16.8%; $p < 0.001$) higher than the pre-implementation period coverage of 75% (95% CI: 71-79%). There was reduced prevalence of lingual cysts in pigs from households that had a latrine (OR = 0.14; 95% CI: 0.05-0.43; $p < 0.001$) and where pigs were confined or tethered (OR = 0.27; 95% CI: 0.07-1.02; $p = 0.053$). **Conclusion:** There was a reduction in the prevalence of porcine cysticercosis in Busia County over the study period from 2012 to 2021. This was not a trial design so we are unable to directly link the decline to a specific cause, but the data are consistent with previous research indicating that improved sanitation reduces porcine cysticercosis. Programs for controlling porcine cysticercosis should include a focus on sanitation in addition to other integrated One Health approaches.

In Vitro and In Vivo Cysticidal Effects of *Carica Papaya* Cell Suspensions.

Guzmán C, Villalobos N, Ortiz Caltempa A, Hernández M, Núñez G, Salazar J, Bobes RJ, Fragoso G, Sciutto E, Villarreal ML.
18-07-2023

Infect Immun.

<https://pubmed.ncbi.nlm.nih.gov/37341599/>

Parasitic diseases are a major public health problem worldwide. Plant-derived products appear to be ideal candidates from a biotechnological perspective, being sustainable and environmentally friendly. The antiparasitic properties of *Carica papaya* have been attributed to some of its components, including papain and other compounds that are concentrated in the latex and seeds. This study demonstrated *in vitro* a high and insignificantly different cysticidal activity of soluble extract that was obtained after the disruption of nontransformed wild-type (WT) cells as well as transformed papaya calluses (PC-9, PC-12, and PC-23) and papaya cell suspensions (CS-9, CS-12, and CS-23). *In vivo*, cell suspensions of CS-WT and CS-23 that had been previously lyophilized were tested with respect to their cysticidal effects, compared with those of three commercial antiparasitic drugs. CS-WT and CS-23 together reduced the number of cysticerci, the number of buds, and the percentage of calcified cysticerci in a similar extent to albendazole and niclosamide, whereas ivermectin was less effective. Mice were then orally immunized with CS-23 that expressed the anti-cysticercal KETc7 antigen (10 µg/mouse), CS-WT (10 mg/mouse), or both together to evaluate their preventive properties. CS-23 and CS-WT significantly reduced the expected parasite and increased the percentage of calcified cysticerci as well as recovery, being more effective when employed together. The results reported in this study support the feasibility of the development of an anti-cysticercosis vaccine from cells of

C. papaya in *in vitro* cultures, as they are a source of an anthelmintic, natural, and reproducible product.

Adenovirus Meningoencephalitis and Neurocysticercosis Co-infection: First Case from India.

Dinkar A, Singh J, Bhavya J, Singh S, Kumar N, Kumar K.
2023

Infect Disord Drug Targets.

<https://pubmed.ncbi.nlm.nih.gov/36999426/>

Development and Laboratory Evaluation of a Simple, Field-Applicable Coproantigen Enzyme-Linked Immunosorbent Assay for Diagnosis of Taeniasis in Northern Peru.

Castillo Y, Wardle MT, Gamboa R, Elizalde M, Vilchez P, Rodríguez S, Gilman RH, Gonzalez AE, O'Neal SE, Garcia HH.

20-07-2023

J Clin Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37367233/>

Coproantigen detection by enzyme-linked immunosorbent assay (coAg ELISA) is a vital tool for detecting and treating cases of *Taenia solium* taeniasis. However, the assay's procedures require costly materials and sophisticated equipment, which are typically inaccessible in rural settings where the disease is endemic. To overcome these barriers, we developed and evaluated a field-applicable coAg ELISA. The field coAg ELISA was developed and evaluated across four phases using known positive and negative stool samples collected from northern Peru. Phase I focused on field assay development, phase II on a small-scale performance evaluation, phase III on a large-scale evaluation, and phase IV on the use and reliability of a colorimetric scale card. All samples were processed using the field and standard assay procedures and compared using signal-to-noise ratios, correlation tests, performance characteristics, and agreement statistics where appropriate. The field coAg ELISA using reagents stored at -20°C and commercially available water and milk powder, and relying on spontaneous separation of the supernatant, had performance comparable to the standard assay. The field coAg ELISA was strongly correlated with the standard in both the small- and large-scale laboratory evaluation ($r = 0.99$ and $r = 0.98$, respectively). Finally, the field assay had an almost perfect agreement between independent readers (kappa = 0.975) and between each reader and the spectrophotometer. The field coAg ELISA demonstrated performance comparable to the standard, providing a low-cost alternative to the standard assay for identifying cases of intestinal taeniasis in a low-resource setting.

Dengue, chikungunya et maladie à virus Zika

A Rare Combination: Dengue Fever Complicated With Guillain-Barre Syndrome.

Lim CS, Kaisbain N, Lim WJ.

25-07-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37503499/>

The association of neutralizing antibodies with protection against symptomatic dengue virus infection varies by serotype, prior immunity, and assay condition.

Bos S, Graber A, Cardona-Ospina JA, Duarte E, Zambrana JV, Ruíz Salinas JA, Mercado-Hernandez R, Singh T, Katzelnick L, de Silva A, Kuan G, Balmaseda A, Harris E.

20-07-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37502957/>

The four dengue virus serotypes (DENV1-4) are the most prevalent arboviruses in humans and a major public health concern worldwide. Identification of the immune mechanisms that modulate DENV infection outcome is critical for development of a safe and effective vaccine. Neutralizing antibodies (nAbs) are considered an essential component of the protective response, yet measurement of their potency is primarily performed using a single cellular substrate and partially mature virions. This approach does not capture the full breadth of neutralizing activity and may lead to biased estimations of nAb potency and repertoire. Here, we evaluated the nAb response associated with protection against dengue cases using samples collected after one or more DENV infections but prior to a subsequent symptomatic versus inapparent DENV1, DENV2 or DENV3 infection from a long-standing pediatric cohort study in Nicaragua. We compared nAb titers in pre-inapparent and pre-symptomatic infection samples in Vero cells with or without DC-SIGN expression, and with either mature or partially mature virions. This method allowed us to measure the magnitude and characteristics of the nAb response associated with outcome and revealed that correlation of nAb titers with protection from symptomatic infection is dependent on the individual's prior DENV immune status as well as the subsequent infecting DENV serotype. Further, the nAb potency and the protective NT₅₀ cutoff was greatly impacted by virion maturation state and cell substrate. These results have important implications for determination of antibody correlates of protection for vaccines and natural infections.

Peptide aptamer-based time-resolved fluoroimmunoassay for CHIKV diagnosis.

Liu T, Gao C, Wang J, Song J, Chen X, Chen H, Zhao X, Tang H, Gu D.

27-07-2023

Virology.

<https://pubmed.ncbi.nlm.nih.gov/37501131/>

Background: Chikungunya virus (CHIKV) and Dengue virus (DENV) have similar clinical symptoms, which often induce misdiagnoses. Therefore, an antigen detection diagnostic system that can clearly identify these two viruses is desirable. **Methods:** In this study, we developed a novel peptide with high affinity and specificity to CHIKV, and further constructed peptide aptamer-based TRFIA assay to efficiently detect CHIKV. Peptide aptamer B2 (ITPQSSTTEAEL) and B3 (DTQGSNWI) were obtained through computer-aided design and selected as CHIKV-specific peptide aptamers based on their high binding affinity, strong hydrogen bonding, and RMSD of molecular docking. Then, a sandwich-Time-Resolved Fluoroimmunoassay (TRFIA) was successfully constructed for the detection of the interaction between peptide aptamers and viruses. **Results:** When using B2 as the detection element, highly specific detection of CHIKV E2 was achieved with detection limits of 8.5 ng/ml in PBS solution. Variation coefficient between inter-assay showed the disturbances received from the detection of clinical fluid specimens (including serum and urine), were also within acceptable limits. The detection limits for 10-fold dilution serum and urine were 57.8 ng/mL and 147.3 ng/mL, respectively. The fluorescent signal intensity exhibited a good linear correlation with E2 protein concentration in the range of 0-1000 ng/mL, indicating the potential for quantitative detection of E2 protein. **Conclusions:** These results demonstrate that the construction of peptide aptamers with high affinity and specificity provides an excellent method for rapid diagnostic element screening, and the developed peptide aptamer B2 contributed to better detection of CHIKV viral particles compared to traditional antibodies.

Dengue is breaking records in the Americas - what's behind the surge?

Lenharo M.

27-07-2023

Nature.

<https://pubmed.ncbi.nlm.nih.gov/37500998/>

A spatial analysis of co-circulating dengue and chikungunya virus infections during an epidemic in a region of Northeastern Brazil.

de Mendonça MFS, Silva APSC, Lacerda HR.

Août-2023

Spat Spatiotemporal Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/37500226/>

Linear epitope identification of monoclonal antibodies against the duck Tembusu virus NS1.

Tan H, Zhang S, Tan W, Hu T, He Y, Wu Z, Wang M, Jia R, Zhu D, Liu M, Zhao X, Yang Q, Wu Y, Zhang S, Huang J, Ou X, Gao Q, Sun D, Cheng A, Chen S.

07-07-2023

Poult Sci.

<https://pubmed.ncbi.nlm.nih.gov/37499611/>

Genetic differentiation among *Aedes aegypti* populations from different eco-geographical zones of India.

Sumitha MK, Kalimuthu M, Kumar MS, Paramasivan R, Kumar NP, Sunish IP, Balaji T, Sarma DK, Kumar D, Suman DS, Srivastava H, Bhowmick IP, Vaishnav K, Singh OP, Patil PB, Tyagi S, Mohanty SS, Barik TK, Uragayala S, Kumar A, Gupta B.

27-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37498944/>

The present study explicitly evaluated the genetic structure of *Aedes aegypti* Linn, the vector of dengue, chikungunya, and Zika viruses, across different geo-climatic zones of India and also elucidated the impact of ecological and topographic factors. After data quality checks and removal of samples with excess null alleles, the final analysis was performed on 589 individual samples using 10 microsatellite markers. Overall findings of this study suggested that, *Ae. aegypti* populations are highly diverse with moderate genetic differentiation between them. Around half of the populations (13 out of 22) formed two genetic clusters roughly associated with geographical regions. The remaining nine populations shared genetic ancestries with either one or both of the clusters. A significant relationship between genetic and geographic distance was observed, indicating isolation by distance. However, spatial autocorrelation analysis predicted the signs of long-distance admixture. Post-hoc environmental association analysis showed that 52.7% of genetic variations were explained by a combination of climatic and topographic factors, with latitude and temperature being the best predictors. This study indicated that though overall genetic differentiation among *Ae. aegypti* populations across India is moderate ($F_{st} = 0.099$), the differences between the populations are developing due to the factors associated with geographic locations. This study improves the understanding of the *Ae. aegypti* population structure in India that may assist in predicting mosquito movements across the geo-climatic zones, enabling effective control strategies and assessing the risk of disease transmission.

A comprehensive protein interaction map and druggability investigation prioritized dengue virus NS1 protein as promising therapeutic candidate.

Farooq QUA, Aiman S, Ali Y, Shaukat Z, Ali Y, Khan A, Samad A, Wadood A, Li C.

27-07-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37498862/>

Travel-Associated Dengue Cases - United States, 2010-2021.

Wong JM, Rivera A, Volkman HR, Torres-Velasquez B, Rodriguez DM, Paz-Bailey G, Adams LE.

28-07-2023

MMWR Morb Mortal Wkly Rep.

<https://pubmed.ncbi.nlm.nih.gov/37498793/>

Assessing the role of Ndel1 oligopeptidase activity in congenital Zika syndrome: Potential predictor of congenital syndrome endophenotype and treatment response.

Christoff RR, Nani JV, Lessa G, Rabello T, Rossi AD, Krenn V, Higa LM, Tanuri A, Garcez PP, Hayashi MAF.

27-07-2023

J Neurochem.

<https://pubmed.ncbi.nlm.nih.gov/37497817/>

Maternal infections are among the main risk factors for cognitive impairments in the offspring. Zika virus (ZIKV) can be transmitted vertically, causing a set of heterogeneous birth defects, such as microcephaly, ventriculomegaly and corpus callosum dysgenesis. Nuclear distribution element like-1 (Ndel1) oligopeptidase controls crucial aspects of cerebral cortex development underlying cortical malformations. Here, we examine Ndel1 activity in an animal model for ZIKV infection, which was associated with deregulated corticogenesis. We observed here a reduction in Ndel1 activity in the forebrain associated with the congenital syndrome induced by ZIKV isolates, in an in utero and postnatal injections of different inoculum doses in mice models. In addition, we observed a strong correlation between Ndel1 activity and brain size of animals infected by ZIKV, suggesting the potential of this measure as a biomarker for microcephaly. More importantly, the increase of interferon (IFN)-beta signaling, which was used to rescue the ZIKV infection outcomes, also recovered Ndel1 activity to levels similar to those of uninfected healthy control mice, but with no influence on Ndel1 activity in uninfected healthy control animals. Taken together, we demonstrate for the first time here an association of corticogenesis impairments determined by ZIKV infection and the modulation of Ndel1 activity. Although further studies are still necessary to clarify the possible role(s) of Ndel1 activity in the molecular mechanism(s) underlying the congenital syndrome induced by ZIKV, we suggest here the potential of monitoring the Ndel1 activity to predict this pathological condition at early stages of embryos or offspring development, during while the currently employed methods are unable to detect impaired corticogenesis leading to microcephaly. Ndel1 activity may also be possibly used to follow up the positive response to the treatment, such as that employing the IFN-beta that is able to rescue the ZIKV-induced brain injury.

Mapping *Aedes aegypti* indoor resting behavior reveals a preference vulnerable to householder-led vector control.

Facchinelli L, Alsharif B, Jones JD, Matope A, Barbosa RMR, Ayres CFJ, McCall PJ.

25-07-2023

PNAS Nexus.

<https://pubmed.ncbi.nlm.nih.gov/37497049/>

Many mosquito vectors rest inside human habitations, a behavioral trait that is exploited for vector control by indoor residual spraying (IRS) of interior walls with

insecticide. Although IRS and its refined version targeted IRS are very effective against *Aedes aegypti*, they are expensive and logistically challenging to deliver in densely populated urban areas where outbreaks of dengue and other arboviruses are the greatest challenge. In experiments in Recife, Brazil, we set out to quantify the indoor resting behavior of *Ae. aegypti* at a level beyond that previously reported. We found that significantly more *Ae. aegypti* males, unfed and fed females visited the base of walls (height 0-20 cm, corresponding to 12.3% of the total wall surface) more frequently than upper wall areas, with the difference more pronounced at higher temperatures. When the lowest 20 cm of the walls was treated with an appropriate insecticide and colored black, we recorded up to 85% cumulative mortality after 24-h exposure in the experimental room. The findings are significant because feasibly, householders could treat this small and accessible target zone manually, without the need for visits by costly IRS teams or equipment, reducing insecticide use and enabling communities to actively protect their own indoor environment.

Neonatal Zika virus infection causes transient perineuronal net degradation.

Engel K, Lee HN, Tewari BP, Lewkowicz AP, Ireland DDC, Manangeeswaran M, Verthelyi D.
11-07-2023

Front Cell Neurosci.

<https://pubmed.ncbi.nlm.nih.gov/37496706/>

Perineuronal nets (PNNs) form a specialized extracellular matrix that predominantly surrounds parvalbumin (PV)-expressing GABAergic inhibitory interneurons and help regulate neuronal activity. Their formation early in the postnatal period is regulated by neuronal signaling and glial activation raising concerns that part of the long-term effects ascribed to perinatal viral infections could be mediated by altered PNN formation. Previously, we developed a model of neonatal Zika virus (ZIKV) infection where mice have lifelong neurological sequelae that includes motor dysfunction and reduced anxiety coupled with a persistent low-grade expression in proinflammatory markers despite resolving the acute infection. Here, we demonstrate that ZIKV infection to P1 neonatal mice results in a reduction of PNN formation during the acute disease with significant reduction in Wisteria floribunda agglutinin (WFA) staining at the peak of infection [15 days post infection (dpi)] that persisted after the symptoms resolved (30 dpi). At 60 dpi, when there is residual inflammation in the CNS, the number of WFA⁺ cells and the level of WFA staining as well as levels of aggrecan and brevican in the brains of convalescent mice were not different from those in uninfected controls, however, there was increased frequency of PNNs with an immature phenotype. Over time the impact of the perinatal infection became less evident and there were no clear differences in PNN morphology between the groups at 1 year post infection. Of note, the reduction in PNNs during acute ZIKV infection was not associated with decreased mRNA levels of aggrecan or brevican, but increased levels of degraded aggrecan and brevican indicating increased PNN degradation. These changes were associated with increased expression of matrix metalloproteinase 12

(MMP12) and MMP19, but not MMP9, a disintegrin and metalloproteinase with thrombospondin motifs 4 (ADAMTS4) or ADAMTS5. Together our findings indicate that infection at the time of PNN development interferes with PNN formation, but the nets can reform once the infection and inflammation subside.

The interplay between lipid droplets and virus infection.

Qu Y, Wang W, Xiao MZX, Zheng Y, Liang Q.

Jul-2023

J Med Virol.

<https://pubmed.ncbi.nlm.nih.gov/37496184/>

Reinvestigation of the risk of stroke after dengue virus infection: A population-based cohort study.

Chien YW, Wang YP, Chi CY, Shih HI.

07-07-2023

J Infect Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37494777/>

Background: Dengue virus (DENV) infection is the most prevalent mosquito-borne viral disease. Stroke is a severe manifestation of dengue. However, few large-scale studies have investigated post-dengue risk of stroke. **Methods:** This population-based cohort study included 57,934 newly diagnosed, laboratory-confirmed dengue patients in Taiwan from 2002 to 2015; patients were matched to nondengue individuals by age, sex, and area of residence at a ratio of 1:4 (n = 231,736). We used subdistribution hazard regression to evaluate short-term (≤ 30 days), medium-term (31-365 days), and long-term (1-3 years) risk of stroke after DENV infection. The robustness of the results to unmeasured confounding was assessed with E-values. **Results:** DENV infection was associated with a significantly increased risk of overall stroke (aSHR 4.51; 95% CI: 3.23-6.32; $P < 0.0001$; E-value = 8.49), hemorrhagic stroke (aSHR 4.13; 95% CI: 2.20-7.76; $P < 0.0001$; E-value = 7.73), and ischemic stroke (aSHR 3.80; 95% CI: 2.37-6.11; $P < 0.0001$; E-value = 7.06) within 30 days. Stratified analysis by age showed that the aSHRs for overall stroke, hemorrhagic stroke, and ischemic stroke were larger among dengue patients aged ≥ 65 during the first 30 days. The 30-day risks of overall stroke, hemorrhagic stroke, and ischemic stroke among elderly dengue patients were 6.71, 1.29, and 3.49 per 1000, respectively. No increased risk was observed after 30 days. **Conclusion:** DENV infection was associated with a significant short-term increased risk of stroke. Clinical practitioners should remain alert to patients with stroke-associated symptoms during epidemic seasons, especially elderly patients.

Detection of acute dengue virus infection, with and without concurrent malaria infection, in a cohort of febrile children in Kenya, 2014-2019, by clinicians or machine learning algorithms.

Vu DM, Krystosik AR, Ndenga BA, Mutuku FM, Ripp K, Liu E, Bosire CM, Heath C, Chebii P, Maina PW, Jembe Z,

Malumbo SL, Amugongo JS, Ronga C, Okuta V, Mutai N, Makenzi NG, Litunda KA, Mukoko D, King CH, LaBeaud AD.

26-07-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37494331/>

Functional interferon-epsilon gene polymorphisms and sexually transmitted infections of the endometrium.

Taylor BD, Criscitiello MF, Bazer FW, Richardson LS, Noah A, Haggerty CL.

Août-2023

Am J Reprod Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37491918/>

First report of pediatric ehrlichiosis in Mexico.

Cisneros-Saldaña D, Osuna-Álvarez LE, Castillo-Bejarano JI, Santos AHML, Vaquera-Aparicio DN, Pérez-Cavazos S. 2023

Bol Med Hosp Infant Mex.

<https://pubmed.ncbi.nlm.nih.gov/37490688/>

Background: Ehrlichia chaffeensis is responsible for most cases of human ehrlichiosis, an acute febrile tick-borne disease. This clinical entity is more commonly reported in adults from the United States. Therefore, it is of special interest to characterize this disease in children, given that very few cases in children have been reported outside of this country. **Case report:** We describe the case of a 15-year-old female from northeastern Mexico with a five-day history of myalgias, arthralgias, fever, abdominal pain, rash, and somnolence. The possibility of tick-borne disease was suspected considering that she lived with three tick-infested dogs that had recently died and a neighbor with similar symptoms who deteriorated rapidly and died a week earlier. Ehrlichia spp. was detected in blood samples by polymerase chain reaction. The patient completed a seven-day course of doxycycline and was discharged with complete resolution of symptoms. **Conclusions:** This case is the first report of ehrlichiosis in a pediatric patient in Mexico, illustrating the importance of considering tick-borne diseases as a differential diagnosis in patients with rash, fever, and altered level of consciousness. This initial clinical presentation may be indistinct from other conditions such as dengue, meningococemia, and multisystem inflammatory syndrome in children (MIS-C), among others.

The Utilization and Development of Viral Vectors in Vaccines as a Prophylactic Treatment Against Ebola Virus as an Emerging and Zoonotic Infectious Disease.

Garcia A, Grundmann O.

25-07-2023

Mini Rev Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37489781/>

Alongside the prescription of commonly used antivirals, such as acyclovir, remdesivir, oseltamivir, and ciprofloxacin, the most efficient way to prevent or treat communicable diseases is by vaccination. Vaccines have been the most efficient way to prevent or treat highly transmissible infectious agents, such as Ebola, Anthrax, and Dengue Fever. Most epidemics of these highly transmissible infectious agents occur in places, such as South America, Central America, Tropical Asia, and Africa, where the availability of resources and access to adequate healthcare are limited. However, recent events in history have proven that even with access to resources and proper healthcare, those in first-world countries are not invincible when it comes to infectious diseases and epidemics. The Ebola virus outbreak in West Africa highlighted the gaps in therapeutic advancement and readiness and led to the rapid development of novel vaccine approaches. Viral vectors, in the case of the Ebola vaccine the vesicular stomatitis virus (VSV), can be safely used to activate or initiate the innate adaptive immune response to protect against viral infection. When developed properly and with extensive study, novel vaccine approaches allow physicians and health experts to control the rate at which viruses spread or prevent transmission. This review will discuss the advantages of viral vector vaccines, their chemistry and development, and the pathophysiology of the Ebola virus to develop advantageous and efficacious treatments.

Protective Effects of Caffeine on Chikungunya and Zika Virus Infections: An in-vitro and in-silico Study.

Medina YJL, Tamayo-Molina YS, Valdés-López JF, Urcuqui-Inchima S.

25-07-2023

Chem Biodivers.

<https://pubmed.ncbi.nlm.nih.gov/37489706/>

Clinicopathological Profile of Dengue Infection in a Tertiary Care Centre in Nepal.

Thapa B, Pandey A, Gautum S, Kc S, Chhetri PD, Pokhrel E, Poudel S, Shankar PR.

20-07-2023

J Nepal Health Res Counc.

<https://pubmed.ncbi.nlm.nih.gov/37489668/>

Rapid Epidemic Expansion of Chikungunya Virus East/Central/South African Lineage, Paraguay.

Giovanetti M, Vazquez C, Lima M, Castro E, Rojas A, Gomez de la Fuente A, Aquino C, Cantero C, Fleitas F, Torales J, Barrios J, Ortega MJ, Gamarra ML, Villalba S, Alfonso T, Xavier J, Adelino T, Fritsch H, Iani FCM, Pereira GC, de Oliveira C, Schuab G, Rodrigues ES, Kashima S, Leite J, Gresh L, Franco L, Tegally H, Van Voorhis WC, Lessels R, de Filippis AMB, Ojeda A, Sequera G, Montoya R, Holmes EC, de Oliveira T, Rico JM, Lourenço J, Fonseca V, Alcantara LCJ.

24-07-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37488810/>

The spread of Chikungunya virus is a major public health concern in the Americas. There were >120,000 cases and 51 deaths in 2023, of which 46 occurred in Paraguay. Using a suite of genomic, phylodynamic, and epidemiologic techniques, we characterized the ongoing large chikungunya epidemic in Paraguay.

Splenic macrophages escalate dengue disease.

Dunagan MM, Fox JM.

24-07-2023

Nat Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37488257/>

Effect of larval diets on the life table parameters of dengue mosquito, *Aedes aegypti* (L.) (Diptera: Culicidae) using age-stage two sex life table theory.

Salim M, Kamran M, Khan I, Saljoqi AUR, Ahmad S, Almutairi MH, Sayed AA, Aleya L, Abdel-Daim MM, Shah M.

24-07-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37488190/>

Galidesivir Triphosphate Promotes Stalling of Dengue-2 Virus Polymerase Immediately Prior to Incorporation.

Deshpande S, Huo W, Shrestha R, Sparrow K, Wood JM, Evans GB, Harris LD, Kingston RL, Bulloch EMM.

24-07-2023

ACS Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37488090/>

Millions of people are infected by the dengue and Zika viruses each year, resulting in significant morbidity and mortality. Galidesivir is an adenosine nucleoside analog that can attenuate flavivirus replication in cell-based assays and animal models of infection. Galidesivir is converted to the triphosphorylated form by host kinases and subsequently incorporated into viral RNA by viral RNA polymerases. This has been proposed to lead to the delayed termination of RNA synthesis. Here, we report direct in vitro testing of the effects of Galidesivir triphosphate on dengue-2 and Zika virus polymerase activity. Galidesivir triphosphate was chemically synthesized, and inhibition of RNA synthesis followed using a dinucleotide-primed assay with a homopolymeric poly(U) template. Galidesivir triphosphate was equipotent against dengue-2 and Zika polymerases, with IC_{50} values of $42 \pm 12 \mu M$ and $47 \pm 5 \mu M$, respectively, at an ATP concentration of $20 \mu M$. RNA primer extension assays show that the dengue-2 polymerase stalls while attempting to add a Galidesivir nucleotide to the nascent RNA chain, evidenced by the accumulation of RNA products truncated immediately upstream of Galidesivir incorporation sites. Nevertheless, Galidesivir is incorporated at isolated sites with low efficiency, leading to the subsequent synthesis of full-length RNA with no evidence of delayed chain termination. The incorporation

of Galidesivir at consecutive sites is strongly disfavored, highlighting the potential for modulation of inhibitory effects of nucleoside analogs by the template sequence. Our results suggest that attenuation of dengue replication by Galidesivir may not derive from the early termination of RNA synthesis following Galidesivir incorporation.

Mechanical transmission of dengue virus by *Aedes aegypti* may influence disease transmission dynamics during outbreaks.

Li HH, Su MP, Wu SC, Tsou HH, Chang MC, Cheng YC, Tsai KN, Wang HW, Chen GH, Tang CK, Chung PJ, Tsai WT, Huang LR, Yueh YA, Chen HW, Pan CY, Akbari OS, Chang HH, Yu GY, Marshall JM, Chen CH.

22-07-2023

EBioMedicine.

<https://pubmed.ncbi.nlm.nih.gov/37487418/>

High-resolution mapping reveals the mechanism and contribution of genome insertions and deletions to RNA virus evolution.

Aguilar Rangel M, Dolan PT, Taguwa S, Xiao Y, Andino R, Frydman J.

Aug-2023

Proc Natl Acad Sci U S A.

<https://pubmed.ncbi.nlm.nih.gov/37487061/>

RNA viruses rapidly adapt to selective conditions due to the high intrinsic mutation rates of their RNA-dependent RNA polymerases (RdRps). Insertions and deletions (indels) in viral genomes are major contributors to both deleterious mutational load and evolutionary novelty, but remain understudied. To characterize the mechanistic details of their formation and evolutionary dynamics during infection, we developed a hybrid experimental-bioinformatic approach. This approach, called MultiMatch, extracts insertions and deletions from ultradeep sequencing experiments, including those occurring at extremely low frequencies, allowing us to map their genomic distribution and quantify the rates at which they occur. Mapping indel mutations in adapting poliovirus and dengue virus populations, we determine the rates of indel generation and identify mechanistic and functional constraints shaping indel diversity. Using poliovirus RdRp variants of distinct fidelity and genome recombination rates, we demonstrate tradeoffs between fidelity and indel generation. Additionally, we show that maintaining translation frame and viral RNA structures constrain the indel landscape and that, due to these significant fitness effects, indels exert a significant deleterious load on adapting viral populations. Conversely, we uncover positively selected indels that modulate RNA structure, generate protein variants, and produce defective interfering genomes in viral populations. Together, our analyses establish the kinetic and mechanistic tradeoffs between misincorporation, recombination, and indel rates and reveal functional principles defining the central role of indels in virus evolution, emergence, and the regulation of viral infection.

Experimental infection of *Artibeus lituratus* bats and no detection of Zika virus in neotropical bats from French Guiana, Peru, and Costa Rica suggests a limited role of bats in Zika transmission.

Aguilar-Setién A, Salas-Rojas M, Gálvez-Romero G, Almazán-Marín C, Moreira-Soto A, Alfonso-Toledo J, Obregón-Morales C, García-Flores M, García-Baltazar A, Serra-Cobo J, López-Roig M, Reyes-Puma N, Piche-Ovares M, Romero-Vega M, Barrantes Murillo DF, Soto-Garita C, Alfaro-Alarcón A, Corrales-Aguilar E, López-Díaz O, Pontier D, Filippi-Codaccioni O, Pons JB, Duhayer J, Drexler JF.

24-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37486923/>

Bats are important natural reservoir hosts of a diverse range of viruses that can be transmitted to humans and have been suggested to play an important role in the Zika virus (ZIKV) transmission cycle. However, the exact role of these animals as reservoirs for flaviviruses is still controversial. To further expand our understanding of the role of bats in the ZIKV transmission cycle in Latin America, we carried out an experimental infection in wild-caught *Artibeus lituratus* bats and sampled several free-living neotropical bats across three countries of the region. Experimental ZIKV infection was performed in wild-caught adult bats (4 females and 5 males). The most relevant findings were hemorrhages in the bladder, stomach and patagium. Significant histological findings included inflammatory infiltrate consisting of a predominance of neutrophils and lymphocytes, in addition to degeneration in the reproductive tract of males and females. This suggests that bat reproduction might be at some level affected by ZIKV. Leukopenia was also observed in some inoculated animals. Hemorrhages, genital alterations, and leukopenia are suggested to be caused by ZIKV; however, since these were wild-caught bats, we cannot exclude other agents. Detection of ZIKV by qPCR was observed at low concentrations in only two urine samples in two inoculated animals. All other animals and tissues tested were negative. Finally, no virus-neutralizing antibodies were found in any animal. To determine ZIKV infection in nature, the blood of a total of 2056 bats was sampled for ZIKV detection by qPCR. Most of the sampled individuals belonged to the genus *Pteronotus* sp. (23%), followed by the species *Carollia* sp. (17%), *Anoura* sp. (14%), and *Molossus* sp. (13.7%). No sample of any tested species was positive for ZIKV by qPCR. These results together suggest that bats are not efficient amplifiers or reservoirs of ZIKV and may not have an important role in ZIKV transmission dynamics.

Alignment of multiple metabolomics LC-MS datasets from disparate diseases to reveal fever-associated metabolites.

Năstase AM, Barrett MP, Cárdenas WB, Cordeiro FB, Zambrano M, Andrade J, Chang J, Regato M, Carrillo E, Botana L, Moreno J, Regnault C, Milne K, Spence PJ, Rowe JA, Rogers S.

24-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37486920/>

Acute febrile illnesses are still a major cause of mortality and morbidity globally, particularly in low to middle income countries. The aim of this study was to determine any possible metabolic commonalities of patients infected with disparate pathogens that cause fever. Three liquid chromatography-mass spectrometry (LC-MS) datasets investigating the metabolic effects of malaria, leishmaniasis and Zika virus infection were used. The retention time (RT) drift between the datasets was determined using landmarks obtained from the internal standards generally used in the quality control of the LC-MS experiments. Fitted Gaussian Process models (GPs) were used to perform a high level correction of the RT drift between the experiments, which was followed by standard peakset alignment between the samples with corrected RTs of the three LC-MS datasets. Statistical analysis, annotation and pathway analysis of the integrated peaksets were subsequently performed. Metabolic dysregulation patterns common across the datasets were identified, with kynurenine pathway being the most affected pathway between all three fever-associated datasets.

Enhancement of VGG16 model with multi-view and spatial dropout for classification of mosquito vectors.

Pora W, Kasamsumran N, Tharawatcharasart K, Ampol R, Siriyasatien P, Jariyapan N.

24-07-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37486913/>

Advanced Age and Increased Risk for Severe Outcomes of Dengue Infection, Taiwan, 2014-2015.

Huang N, Shen YJ, Chou YJ, Tsai TF, Lien CE.

Aug-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37486786/>

Dengue, a mosquito-borne flavivirus infection, is increasingly a disease of older adults who are more likely to have chronic diseases that confer risk for severe outcomes of dengue infection. In a population-based study in Taiwan, adjusted risks for dengue-related hospitalization, intensive care unit admission, and death increased progressively with age.

Immunoinformatics-Based Identification of the Conserved Immunogenic Peptides Targeting of Zika Virus Precursor Membrane Protein.

Gupta Y, Baranwal M, Chudasama B.

24-07-2023

Viral Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37486711/>

Temporal trends of dengue cases and deaths from 2007 to 2020 in Belo Horizonte, Brazil.

da Consolação Magalhães Cunha M, Conrad Bohm B, Morais MHF, Dias Campos NB, Schultes OL, Pereira Campos Bruhn N, Pascoti Bruhn FR, Caiaffa WT.

24-06-2023

Int J Environ Health Res.

<https://pubmed.ncbi.nlm.nih.gov/37485862/>

Uncovering the Hidden Threat: A Case Report of Suspected Dengue Fever in Armenia.

Hashmi MF, Khan F, Matevosyan G, Asoyan V, Hovhannisyan A.

21-06-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37485179/>

Dengue is a viral infection transmitted by mosquitoes that causes fever, headache, joint pain, nausea, vomiting, and pain behind the eyes. In severe cases, it can progress to dengue hemorrhagic fever and dengue shock syndrome, which can be life-threatening. Armenia has not reported a single case of dengue to date and is non-endemic for this disease. However, it has been found that the vector of the disease, *Aedes albopictus*, is present in Armenia since 2016. The aim of this report is to present the imported case of suspected dengue hemorrhagic fever. A 23-year-old female who was admitted to the University Hospital experienced symptoms of general weakness, fever, joint pain, and chills after her return from Bali and had a three-day febrile period. A thorough examination revealed mosquito bites on her skin. On the fourth day of hospitalization, the patient's condition deteriorated. She started experiencing vaginal bleeding. On the same day, the patient noted a small petechiae rash sized 1-2 mm in diameter in the upper and lower extremities. The patient deteriorated, with progressive leukopenia and thrombocytopenia, and hypertransaminasemia. Screening tests for HIV and hepatitis A, B, C, and E were performed, and the results showed that the anti-hepatitis C antibody was positive, while the hepatitis C virus polymerase chain reaction was negative. The case was reported to the National Center for Disease Control and Prevention as an imported case of hemorrhagic fever. Unfortunately, no lab test was available there for confirmation of the diagnosis. The patient received IV infusion and symptomatic treatment. Her condition improved, and upon discharge, she was in a state of recovery. This case report highlights the importance of early diagnosis and appropriate treatment for hemorrhagic fevers, particularly dengue fever. The unavailability of diagnostic kits for dengue in Armenia highlights the need to invest in improving their availability. It also emphasizes the importance of maintaining dengue surveillance in non-endemic nations and carefully evaluating and monitoring febrile patients who have returned from dengue-endemic countries.

Scrub Typhus and Dengue Co-infection in an Adolescent Girl: A Diagnostic Challenge.

Kannabiran RK, Banerjee A, Jyothi L, Reddy M, Narang R. 22-06-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37485123/>

Scrub typhus and dengue fever are common infectious diseases in tropical regions, and both have overlapping clinico-epidemiological and laboratory features, which often pose a diagnostic challenge. This case report discusses a 15-year-old girl from the Indian subcontinent who presented with acute undifferentiated febrile illness (AUFI) without typical features of any of the common tropical infections. She was diagnosed with co-infection of scrub typhus and dengue fever using laboratory tests with good diagnostic accuracy. The patient was managed on an ambulatory basis, treated with oral doxycycline, and showed symptomatic improvement within 48 hours. Co-infections in endemic areas present a significant diagnostic and therapeutic challenge. This case report highlights the importance of considering co-infections in the differential diagnosis of AUFI, especially during the post-monsoon period, and the use of highly sensitive and specific tests for the diagnosis of co-infections.

Efficacy of household Aedes larval control practices in a peri-urban township, Yangon, Myanmar: Implication for entomological surveillance.

Aung SH, Mon Kyaw AM, Jittamala P, Lawpoolsri S, Soonthornworasiri N, Sriwichai P, Phuanukoonnon S.

07-07-2023

Heliyon.

<https://pubmed.ncbi.nlm.nih.gov/37483793/>

Proximal myopathy: causes and associated conditions.

Rao A, Nawaz I, Arbi FM, Ishtiaq R.

31-12-2022

Discoveries (Craiova).

<https://pubmed.ncbi.nlm.nih.gov/37483534/>

Proximal myopathy presents as generalized muscle weakness commonly involving the muscles of upper and/or lower limbs. Toxins, long-term use of statins, corticosteroids, alcohol, SGLT2 inhibitors, COVID-19 vaccination, and antimalarials have been attributed to its development. In endocrine and metabolic disorders, adrenal dysfunction including both overproduction and insufficiency of the adrenal gland hormones has been reported to cause myopathy. Moreover, parathyroid and thyroid disorders along with pituitary gland disorders can also directly or indirectly contribute to this condition. In idiopathic inflammatory myopathies including polymyositis, dermatomyositis, inclusion body myositis (IBM), and Systemic Lupus Erythematosus (SLE), Sjögren's Syndrome, and overlap syndromes, moderate to severe muscle weakness has been observed. IBM has been reported to be the most prevalent acquired myopathy above the age of 50. Hereditary or congenital myopathies include limb girdle muscular dystrophies, facioscapulohumeral muscular dystrophy, Duchenne and Becker muscular dystrophy, and proximal myotonic

myopathy. In addition to these, glycogen storage diseases such as the McArdle disease can also cause fast exhaustion, myalgia, and cramping in working muscles. It is pertinent to mention here that a class of hereditary metabolic myopathies, referred to as "lipid deposition myopathy" causes lipids to accumulate in skeletal muscle fibers, leading to lesions and degeneration. Among viral causes, HIV, dengue virus, influenza virus, hepatitis B virus, hepatitis C virus, SARS-CoV2 are also associated with muscle weakness. Sarcoidosis, an inflammatory disease, can also manifest as muscle weakness and myalgia. Owing to this complicated pathophysiology of proximal myopathy, this review aims to summarize the existing literature on conditions associated with this phenomenon and other recent developments that have been made regarding events leading to development of generalized muscle weakness. To the authors' knowledge this is the first narrative review that discusses causes and conditions associated with proximal myopathy in thorough detail.

In Vitro Reconstitution and Analysis of SARS-CoV-2/Host Protein-Protein Interactions.

Moradi SV, Wu Y, Walden P, Cui Z, Johnston WA, Petrov D, Alexandrov K.

06-07-2023

ACS Omega.

<https://pubmed.ncbi.nlm.nih.gov/37483225/>

Disease burden of congenital Zika virus syndrome in Brazil and its association with socioeconomic data.

de Amorin Vilharba BL, Yamamura M, de Azevedo MV, Fernandes WS, Santos-Pinto CDB, de Oliveira EF.

23-07-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37482558/>

Smartphone-integrated colorimetric and microfluidic paper-based analytical devices for the trace-level detection of permethrin.

Rasheed S, Ul Haq MA, Ahmad N, Sirajuddin, Hussain D.

17-07-2023

Food Chem.

<https://pubmed.ncbi.nlm.nih.gov/37480777/>

Permethrin is a pyrethroid pesticide and insect repellent that prevents mosquito-borne infections like dengue and malaria in tropical areas. This work describes a new colorimetric sensor based on metronidazole-stabilized silver nanoparticles (MTZ-AgNPs) for the first rapid, sensitive, and selective permethrin detection. The MTZ-AgNPs-based colorimetric sensor has a limit of detection (LOD) of 0.0104 μM and a limit of quantification (LOQ) of 0.0348 μM , respectively. The sensor is further integrated with smartphone and microfluidic fabrication of paper-based analytical devices (μPADs) for real-time and on-site detection of permethrin. Under optimal settings, no potential environmental contaminants interfere with permethrin detection, confirming its high selectivity. Finally, the practical applicability of sensors is confirmed in

real tomato and apple extract samples. The US environmental protection agency's recommended UPLC method validated the detection efficiency of the proposed colorimetric sensor. The % recoveries from UPLC and MTZ-AgNPs suggest that the present sensor can quantitatively analyze permethrin in real samples.

Potential role of lncRNA in impairing cellular properties of human neural progenitor cells following exposure to Zika virus E protein.

Arora H, Prajapati B, Seth P.

20-07-2023

Exp Neurol.

<https://pubmed.ncbi.nlm.nih.gov/37479020/>

Zika virus (ZIKV) infection during the first trimester of the pregnancy may lead to Congenital zika syndrome in the neonates. The viral infection hampers foetal brain development and causes microcephaly. Human neural progenitor cells (hNPCs) play an important role in brain development, however they are highly susceptible to ZIKV infection. In this study, we elucidated the molecular mechanisms that lead to cellular alterations in hNPCs due to ZIKV E-protein. We investigated proliferation, differentiation, migration and inflammation in hNPCs, which may lead to microcephaly. In our study, we found that ZIKV E-protein causes cell cycle arrest, decrease in proliferation and increase in mitotic length of the dividing hNPCs. We observed CyclinD1 and upstream molecules (p21 and p53) of the pathway are dysregulated, and intracellular calcium at basal level as well as upon ATP stimulation were reduced following over expression of ZIKV E-protein. ZIKV E-protein transfected hNPCs exhibited pre-mature differentiation with pro-neural genes upregulated. Furthermore, ZIKV E-protein disrupted migrational properties of hNPCs and caused elevated levels of inflammatory chemokines and cytokines. To gain insights into molecular mechanisms of these effects on hNPCs, we explored the possible involvement of long non coding RNAs in ZIKV neuropathogenesis. We have shortlisted lncRNAs associated with differentially expressed genes from publicly available transcriptomic data and found some of those lncRNAs are differentially expressed upon E-protein transfection of hNPCs. Gene ontology analysis suggest these lncRNAs play an important role in regulation of viral life cycle, host's defence response and cell proliferation.

Acetylation of the NS3 helicase by KAT5y is essential for flavivirus replication.

Serman T, Chiang C, Liu G, Sayyad Z, Pandey S, Volcic M, Lee H, Muppala S, Acharya D, Goins C, Stauffer SR, Sparrer KMJ, Gack MU.

14-07-2023

Cell Host Microbe.

<https://pubmed.ncbi.nlm.nih.gov/37478852/>

Direct targeting of essential viral enzymes such as proteases, polymerases, and helicases has long been the major focus of antiviral drug design. Although successful for some viral enzymes, targeting viral helicases is notoriously difficult to achieve, demanding alternative

strategies. Here, we show that the NS3 helicase of Zika virus (ZIKV) undergoes acetylation in its RNA-binding tunnel. Regulation of the acetylated state of K389 in ZIKV NS3 modulates RNA binding and unwinding and is required for efficient viral replication. NS3 acetylation is mediated by a specific isoform of the host acetyltransferase KAT5 (KAT5γ), which translocates from the nucleus to viral replication complexes upon infection. NS3 acetylation by KAT5γ and its proviral role are also conserved in West Nile virus (WNV), dengue virus (DENV), and yellow fever virus (YFV). Our study provides molecular insight into how a cellular acetyltransferase regulates viral helicase functions, unveiling a previously unknown target for antiviral drug development.

Structures of dengue virus RNA replicase complexes.

Osawa T, Aoki M, Ehara H, Sekine SI.

12-07-2023

Mol Cell.

<https://pubmed.ncbi.nlm.nih.gov/37478848/>

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

Rainey SM, Geoghegan V, Lefteri DA, Ant TH, Martinez J, McNamara CJ, Kamel W, de Laurent ZR, Castello A, Sinkins SP.

20-07-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37474590/>

Some strains of the inherited bacterium Wolbachia have been shown to be effective at reducing the transmission of dengue virus (DENV) and other RNA viruses by *Aedes aegypti* in both laboratory and field settings and are being deployed for DENV control. The degree of virus inhibition varies between Wolbachia strains. Density and tissue tropism can contribute to these differences but there are also indications that this is not the only factor involved: for example, strains wAu and wAlbA are maintained at similar intracellular densities but only wAu produces strong DENV inhibition. We previously reported perturbations in lipid transport dynamics, including sequestration of cholesterol in lipid droplets, with strains wMel/wMelPop in *Ae. aegypti*. To further investigate the cellular basis underlying these differences, proteomic analysis of midguts was carried out on *Ae. aegypti* lines carrying strains wAu and wAlbA: with the hypothesis that differences in perturbations may underlie Wolbachia-mediated antiviral activity. Surprisingly, wAu-carrying midguts not only showed distinct proteome perturbations when compared to non-Wolbachia carrying and wAlbA-carrying midguts but also wMel-carrying midguts. There are changes in RNA processing pathways and upregulation of a specific set of RNA-binding proteins in the wAu-carrying line, including genes with known antiviral activity. Lipid transport and metabolism proteome changes also differ between strains, and we show that strain wAu does not produce the same cholesterol sequestration phenotype as wMel. Moreover, in contrast to wMel, wAu antiviral

activity was not rescued by cyclodextrin treatment. Together these results suggest that wAu could show unique features in its inhibition of arboviruses compared to previously characterized Wolbachia strains.

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

Roth NM, Delgado-López C, Wiggins LD, Muñoz NN, Mulkey SB, Nieves-Ferrer L, Woodworth KR, Rosario GM, Huertas MM, Moore CA, Tong VT, Gilboa SM, Valencia-Prado M.

21-07-2023

MMWR Morb Mortal Wkly Rep.

<https://pubmed.ncbi.nlm.nih.gov/37471268/>

From dengue outbreaks to endemicity: Reunion Island, France, 2018 to 2021.

Vincent M, Paty MC, Gerardin P, Balleydier E, Etienne A, Daoudi J, Thouillot F, Jaffar-Bandjee MC; Clinical Investigation Team; Laboratory Network; study collaborators Réseau de médecins sentinelles de la Réunion; Menudier L.

Juil-2023

Euro Surveill.

<https://pubmed.ncbi.nlm.nih.gov/37470738/>

Knowledge, attitude, and practice of healthcare workers regarding dengue fever in Mazandaran Province, northern Iran.

Nikookar SH, Moosazadeh M, Fazeli-Dinan M, Zaim M, Sedaghat MM, Enayati A.

04-07-2023

Front Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37469697/>

Background: Dengue fever is a rapidly emerging infection worldwide with a high public health burden. Adequate training of healthcare workers is essential to warrant the timely provision of health services to improve the outcome of dengue management. **Methods:** This is an analytical cross-sectional study, conducted to assess the knowledge, attitudes and practice (KAP) of healthcare workers regarding dengue from April 2021 to March 2022 in Mazandaran Province, northern Iran. Data was collected using a researcher-made structured questionnaire, prepared as Google Forms, and sent to target groups through social media and email. Data analysis was performed by SPSS 22 software using descriptive and inferential statistics (Chi-square) at a significant level of 5%. **Results:** Most of the respondents had heard about dengue (83.8%); media (32.7%) and academic education (25%) were the main sources of information. Respondents had less knowledge associated with dengue symptoms (52%) than prevention and control (69%), transmission (72.2%) and clinical management (81%). Based on the 70% cut-off point, the majority of the participants had a good attitude (81%) and practice (73%). However, only 49.6% of the respondents showed good practice regarding dengue local transmission. A significant difference was observed

between participants knowledge on clinical management with occupation; attitude with gender and occupation; and practice with gender ($p < 0.05$). **Conclusion:** The results of this study revealed gaps in some dimensions of KAP in healthcare workers, therefore, a greater focus should be placed on future training programs to raise knowledge and attitude leading to sound practice and behavior for adequate management of dengue.

Attenuated Dengue virus PV001-DV induces oncolytic tumor cell death and potent immune responses.

Goldufsky JW, Daniels P, Williams MD, Gupta K, Lyday B, Chen T, Singh G, Kaufman HL, Zloza A, Marzo AL.

19-07-2023

J Transl Med.

<https://pubmed.ncbi.nlm.nih.gov/37468934/>

Background: Viral therapies developed for cancer treatment have classically prioritized direct oncolytic effects over their immune activating properties. However, recent clinical insights have challenged this longstanding prioritization and have shifted the focus to more immune-based mechanisms. Through the potential utilization of novel, inherently immune-stimulating, oncotropic viruses there is a therapeutic opportunity to improve anti-tumor outcomes through virus-mediated immune activation. PV001-DV is an attenuated strain of Dengue virus (DEN-1 #45A25) with a favorable clinical safety profile that also maintains the potent immune stimulatory properties characteristic of Dengue virus infection. **Methods:** In this study, we utilized in vitro tumor killing and immune multiplex assays to examine the anti-tumor effects of PV001-DV as a potential novel cancer immunotherapy. **Results:** In vitro assays demonstrated that PV001-DV possesses the ability to directly kill human melanoma cells lines as well as patient melanoma tissue ex vivo. Importantly, further work demonstrated that, when patient peripheral blood mononuclear cells (PBMCs) were exposed to PV001-DV, a substantial induction in the production of apoptotic factors and immunostimulatory cytokines was detected. When tumor cells were cultured with the resulting soluble mediators from these PBMCs, rapid cell death of melanoma and breast cancer cell lines was observed. These soluble mediators also increased dengue virus binding ligands and immune checkpoint receptor, PD-L1 expression. **Conclusions:** The direct in vitro tumor-killing and immune-mediated tumor cytotoxicity facilitated by PV001-DV contributes support of its upcoming clinical evaluation in patients with advanced melanoma who have failed prior therapy.

A management perspective on resilience in healthcare: a framework and avenues for future research.

Agostini L, Onofrio R, Piccolo C, Stefanini A.

9-07-2023

BMC Health Serv Res.

<https://pubmed.ncbi.nlm.nih.gov/37468875/>

Recent major health shocks, such as the 2014-16 Ebola, the Zika outbreak, and, last but not least, the COVID-19 pandemic, have strongly contributed to drawing attention

to the issue of resilience in the healthcare domain. Nevertheless, the scientific literature appears fragmented, creating difficulties in developing incremental research in this relevant managerial field. To fill this gap, this systematic literature review aims to provide a clear state of the art of the literature dealing with resilience in healthcare. Specifically, from the analysis of the theoretical articles and reviews, the key dimensions of resilience are identified, and a novel classification framework is proposed. The classification framework is then used to systematize extant empirical contributions. Two main dimensions of resilience are identified: the approach to resilience (reactive vs. proactive) and the type of crisis to deal with (acute shocks vs. chronic stressors). Four main streams of research are thus identified: (i) proactive approaches to acute shocks; (ii) proactive approaches to chronic stressors; (iii) reactive approaches to acute shocks; and (iv) reactive approaches to chronic stressors. These are scrutinised considering three additional dimensions: the level of analysis, the resources to nurture resilience, and the country context. The classification framework and the associated mapping contribute to systematising the fragmented literature on resilience in healthcare, providing a clear picture of the state of the art in this field and drawing a research agenda that opens interesting paths for future research.

[Relevance of social networks in social mobilization to deal with arboviruses in the municipality of Betim, in the State of Minas Gerais, Brazil].

Coelho P, Batista JV, Profeta Z.

17-07-2023

Cad Saude Publica.

<https://pubmed.ncbi.nlm.nih.gov/37466557/>

Spatio-temporal dengue risk modelling in the south of Thailand: a Bayesian approach to dengue vulnerability.

Abdulsalam FI, Antúnez P, Jawjit W.

14-07-2023

PeerJ.

<https://pubmed.ncbi.nlm.nih.gov/37465156/>

Background: More than half of the global population is predicted to be living in areas susceptible to dengue transmission with the vast majority in Asia. Dengue fever is of public health concern, particularly in the southern region of Thailand due to favourable environmental factors for its spread. The risk of dengue infection at the population level varies in time and space among sub-populations thus, it is important to study the risk of infection considering spatio-temporal variation. **Methods:** This study presents a joint spatio-temporal epidemiological model in a Bayesian setting using Markov chain Monte Carlo (MCMC) simulation with the CARBayesST package of R software. For this purpose, monthly dengue records by district from 2002 to 2018 from the southern region of Thailand provided by the Ministry of Public Health of Thailand and eight environmental variables were used. **Results:** Results show that an increasing level of temperature, number of rainy

days and sea level pressure are associated with a higher occurrence of dengue fever and consequently higher incidence risk, while an increasing level of wind speed seems to suggest a protective factor. Likewise, we found that the elevated risks of dengue in the immediate future are in the districts of Phipun, Phrom Kili, Lan Saka, Phra Phrom and Chaloeam Phakiat. The resulting estimates provide insights into the effects of covariate risk factors, spatio-temporal trends and dengue-related health inequalities at the district level in southern Thailand. **Conclusion:** Possible implications are discussed considering some anthropogenic factors that could inhibit or enhance dengue occurrence. Risk maps indicated which districts are above and below baseline risk, allowing for the identification of local anomalies and high-risk boundaries. In the event of near future, the threat of elevated disease risk needs to be prevented and controlled considering the factors underlying the spread of mosquitoes in the Southeast Asian region.

Dengue Fever among Patients Visiting the Outpatient Department of Dermatology in a Tertiary Care Centre: A Descriptive Cross-sectional Study.

Aryal E, Bista R, Shrestha PR, Regmi G.

01-06-2023

JNMA J Nepal Med Assoc.

<https://pubmed.ncbi.nlm.nih.gov/37464860/>

Introduction: Dengue is in an increasing trend in our part of the world mostly due to global warming. It can present with various manifestations including cutaneous manifestations. The main objective of our study was to find out the prevalence of dengue fever among patients visiting the Outpatient Department of Dermatology in a tertiary care centre. **Methods:** A descriptive cross-sectional study was conducted among patients visiting the Outpatient Department of Dermatology in a tertiary care centre after taking ethical approval from the Institutional Review Committee (Reference number: 09092022\04). Data from 1 June 2022 to 8 September 2022 were collected between 1 December 2022 to 20 February 2023 from the hospital records. The laboratory data of individuals were analyzed to find out the prevalence of dengue fever. A Visual Analogue Scale was used to assess the severity of pruritus. Convenience sampling method was used. Point estimate and 95% Confidence Interval were calculated. **Results:** Among 7442 patients, dengue fever was found to be in 202 (2.71%) (2.34-3.08, 95% Confidence Interval) patients. The mean duration of fever was 3.02±2.960 days. The mean duration of onset of rash after having a fever was 2.56±2.032 days. The most common cutaneous manifestation was maculopapular rash 70 (34.65%). **Conclusions:** The prevalence of dengue fever was found to be lower than in the studies done in similar settings.

[Chikungunya Virus replicates in the human testis and transiently decreases testosterone production in infected men].

Ciesielski V, Cartron M, Houzet L, Kuassivi NO, Abiven H, Guillou YM, Roques P, Cabié A, Plotton I, Mahé-Poiron D, Dejuicq-Rainsford N.

01-06-2023

Virologie (Montrouge).

<https://pubmed.ncbi.nlm.nih.gov/37462940/>

Dengue Outbreak Response during COVID-19 Pandemic, Key Largo, Florida, USA, 2020.

Rowe D, McDermott C, Veliz Y, Kerr A, Whiteside M, Coss M, Huff C, Leal A, Kopp E, LaCrue A, Heberlein LA, Adams LE, Santiago GA, Munoz-Jordan JL, Paz-Bailey G, Morrison AM; Florida Department of Health Dengue Investigation Team1.

01-06-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37385262/>

We report a dengue outbreak in Key Largo, Florida, USA, from February through August 2020, during the COVID-19 pandemic. Successful community engagement resulted in 61% of case-patients self-reporting. We also describe COVID-19 pandemic effects on the dengue outbreak investigation and the need to increase clinician awareness of dengue testing recommendations.

Increased interregional virus exchange and nucleotide diversity outline the expansion of chikungunya virus in Brazil.

Xavier J, Alcantara LCJ, Fonseca V, Lima M, Castro E, Fritsch H, Oliveira C, Guimarães N, Adelino T, Evaristo M, Rodrigues ES, Santos EV, de La-Roque D, de Moraes L, Tosta S, Neto A, Rosewell A, Mendonça AF, Leite A, Vasconcelos A, Silva de Mello AL, Vasconcelos B, Montalbano CA, Zanluca C, Freitas C, de Albuquerque CFC, Duarte Dos Santos CN, Santos CS, Dos Santos CA, Gonçalves CCM, Teixeira D, Neto DFL, Cabral D, de Oliveira EC, Noia Maciel EL, Pereira FM, Iani F, de Carvalho FP, Andrade G, Bezerra G, de Castro Lichs GG, Pereira GC, Barroso H, Franz HCF, Ferreira H, Gomes I, Riediger IN, Rodrigues I, de Siqueira IC, Silva J, Rico JM, Lima J, Abrantes J, do Nascimento JPM, Wasserheit JN, Pastor J, de Magalhães JJF, Luz KG, Lima Neto LG, Frutuoso LCV, da Silva LB, Sena L, de Sousa LAF, Pereira LA, Demarchi L, Câmara MCB, Astete MG, Almiron M, Lima M, Umaki Zardin MCS, Presibella MM, Falcão MB, Gale M Jr, Freire N, Marques N, de Moura NFO, Almeida Da Silva PE, Rabinowitz P, da Cunha RV, Trinta KS, do Carmo Said RF, Kato R, Stabeli R, de Jesus R, Hans Santos R, Kashima S, Slavov SN, Andrade T, Rocha T, Carneiro T, Nardy V, da Silva V, Carvalho WG, Van Voorhis WC, Araujo WN, de Filippis AMB, Giovanetti M.

21-07-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37479700/>

Posterior Reversible Leucoencephalopathy Syndrome: Case Series, Comments, and Diagnostic Dilemma.

Chaudhuri J, Basu S, Roy MK, Chakravarty A.

Aug-2023

Curr Neurol Neurosci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37378723/>

Purpose of review: To report a series of patients with clinical and radiological features suggestive of posterior reversible encephalopathy syndrome (PRES) related to diverse etiologies emphasizing its pathophysiological basis. **Recent findings:** Posterior reversible encephalopathy syndrome (PRES) may present with a broad range of clinical symptoms from headache and visual disturbances to seizure and altered mentation. Typical imaging findings include posterior-circulation predominant vasogenic edema. Although there are many well-documented diseases associated with PRES, the exact pathophysiologic mechanism has yet to be fully elucidated. Generally accepted theories revolve around disruption of the blood-brain barrier secondary to elevated intracranial pressures or endothelial injury induced by ischemia from a vasoconstrictive response to rising blood pressure or toxins/cytokines. While clinical and radiographic reversibility is common, long-standing morbidity and mortality can occur in severe forms. In patients with malignant forms of PRES, aggressive care has markedly reduced mortality and improved functional outcomes. Various factors that have been associated with poor outcome include altered sensorium, hypertensive etiology, hyperglycemia, longer time to control the causative factor, elevated C reactive protein, coagulopathy, extensive cerebral edema, and hemorrhage on imaging. Reversible cerebral vasoconstriction syndromes (RCVS) and primary angiitis of the central nervous system (PACNS) are invariably considered in the differential diagnosis of new cerebral arteriopathies. Recurrent thunderclap headache (TCH), and single TCH combined with either normal neuroimaging, border zone infarcts, or vasogenic edema, have 100% positive predictive value for diagnosing RCVS or RCVS-spectrum disorders. Diagnosis of PRES in some circumstances can be challenging and structural imaging may not be sufficient to distinguish it from other differential diagnostic considerations like ADEM. Advanced imaging techniques, such as MR spectroscopy or positron emission tomography (PET) can provide additional information to determine the diagnosis. Such techniques are more useful to understand the underlying vasculopathic changes in PRES and may answer some of the unresolved controversies in pathophysiology of this complex disease. Eight patients with PRES resulting from different etiologies varying from pre-eclampsia/eclampsia, post-partum headache with seizures, neuropsychiatric systemic lupus erythematosus, snake bite, Dengue fever with encephalopathy, alcoholic liver cirrhosis with hepatic encephalopathy, and lastly reversible cerebral vasoconstriction syndrome (RCVS). Additionally, a diagnostic dilemma between PRES and acute disseminated encephalomyelitis (ADEM) was notable in one patient. Some of these patients did not have or only very transiently had arterial hypertension. PRES may underlie the clinical conundrum of headache, confusion, altered sensorium, seizures, and visual impairment. PRES need not necessarily be always associated with high blood pressure. Imaging findings may also be variable. Both

clinicians and radiologists need to familiarize themselves with such variabilities.

Metformin restrains ZIKV replication and alleviates virus-induced inflammatory responses in microglia.

Wang X, Wang H, Yi P, Baker C, Casey G, Xie X, Luo H, Cai J, Fan X, Soong L, Hu H, Shi PY, Liang Y, Sun J.

Aug-2023

Int Immunopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37343373/>

Employing oxford nanopore technologies (ONT) for understanding the ecology and transmission dynamics of flaviviruses in mosquitoes (Diptera: Culicidae) from Eastern Colombia.

Martínez D, Gómez M, De Las Salas JL, Hernández C, Flórez AZ, Muñoz M, Ramírez JD.

Sept-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37331645/>

Neurotoxic properties of the Zika virus envelope protein.

Steiner JP, Bachani M, Malik N, Li W, Tyagi R, Sampson K, Abrams RPM, Kousa Y, Solis J, Johnson TP, Nath A.

Sept-2023

Exp Neurol.

<https://pubmed.ncbi.nlm.nih.gov/37327963/>

Prenatal Zika virus (ZIKV) infection is a serious global concern as it can lead to brain injury and many serious birth defects, collectively known as congenital Zika syndrome. Brain injury likely results from viral mediated toxicity in neural progenitor cells. Additionally, postnatal ZIKV infections have been linked to neurological complications, yet the mechanisms driving these manifestations are not well understood. Existing data suggest that the ZIKV envelope protein can persist in the central nervous system for extended periods of time, but it is unknown if this protein can independently contribute to neuronal toxicity. Here we find that the ZIKV envelope protein is neurotoxic, leading to overexpression of poly adenosine diphosphate-ribose polymerase 1, which can induce parthanatos. Together, these data suggest that neuronal toxicity resulting from the envelope protein may contribute to the pathogenesis of post-natal ZIKV-related neurologic complications.

Dual pattern recognition receptor ligands CL401, CL413, and CL429 as adjuvants for inactivated chikungunya virus.

Gosavi M, Kulkarni-Munje A, Patil HP.

Aug-2023

Virology.

<https://pubmed.ncbi.nlm.nih.gov/37321145/>

Chikungunya virus (CHIKV) is responsible for incapacitating joint pains and is a significant health hazard in many

countries. Though a definite need for a CHIKV vaccine is felt, long disappearance of CHIKV from circulation in humans has been a concern for vaccine development. Use of two separate pattern recognition receptor ligands has been shown to enhance immune response to the administered antigen. In addition, intradermal delivery of vaccine tends to mimic the natural mode of CHIKV infection. Therefore, in this study, we explored whether intradermal and intramuscular immunization with inactivated CHIKV (I-CHIKV) supplemented with dual pattern-recognition receptor ligands, CL401, CL413, and CL429, is an effective approach to enhancing antibody response to CHIKV. Our in vivo data show that I-CHIKV supplemented with these chimeric PRR ligands induces enhanced neutralizing antibody response after intradermal delivery, but is less efficient after intramuscular immunization. These results suggest that intradermal delivery of I-CHIKV with chimeric adjuvants is a possible way to elicit a better antibody response.

Spatial and temporal analyses of the influences of meteorological and environmental factors on *Aedes albopictus* (Diptera: Culicidae) population dynamics during the peak abundance period at a city scale.

Wang F, Zhu Y, Zhang H, Fan J, Leng P, Zhou J, Yao S, Yang D, Liu Y, Wang J, Yao J, Zhou Y, Zhao T.

Sept-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37307888/>

Highly Attenuated Poxvirus-Based Vaccines Against Emerging Viral Diseases.

Perdiguerio B, Pérez P, Marcos-Villar L, Albericio G, Astorgano D, Álvarez E, Sin L, Gómez CE, García-Arriaza J, Esteban M.

01-08-2023

J Mol Biol.

<https://pubmed.ncbi.nlm.nih.gov/37301278/>

Although one member of the poxvirus family, variola virus, has caused one of the most devastating human infections worldwide, smallpox, the knowledge gained over the last 30 years on the molecular, virological and immunological mechanisms of these viruses has allowed the use of members of this family as vectors for the generation of recombinant vaccines against numerous pathogens. In this review, we cover different aspects of the history and biology of poxviruses with emphasis on their application as vaccines, from first- to fourth-generation, against smallpox, monkeypox, emerging viral diseases highlighted by the World Health Organization (COVID-19, Crimean-Congo haemorrhagic fever, Ebola and Marburg virus diseases, Lassa fever, Middle East respiratory syndrome and severe acute respiratory syndrome, Nipah and other henipaviral diseases, Rift Valley fever and Zika), as well as against one of the most concerning prevalent virus, the Human Immunodeficiency Virus, the causative agent of Acquired Immunodeficiency Syndrome. We discuss the implications in human health of the 2022 monkeypox

epidemic affecting many countries, and the rapid prophylactic and therapeutic measures adopted to control virus dissemination within the human population. We also describe the preclinical and clinical evaluation of the Modified Vaccinia virus Ankara and New York vaccinia virus poxviral strains expressing heterologous antigens from the viral diseases listed above. Finally, we report different approaches to improve the immunogenicity and efficacy of poxvirus-based vaccine candidates, such as deletion of immunomodulatory genes, insertion of host-range genes and enhanced transcription of foreign genes through modified viral promoters. Some future prospects are also highlighted.

Innate immune response in patients with acute Chikungunya disease.

Bezerra WP, Moizéis RNC, Salmeron ACA, Pereira HWB, de Araújo JMG, Guedes PMM, Fernandes JV, Nascimento MSL.

Août-2023

Med Microbiol Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37285099/>

Holobiont perspectives on tripartite interactions among microbiota, mosquitoes, and pathogens.

Zheng R, Wang Q, Wu R, Paradkar PN, Hoffmann AA, Wang GH.

Août-2023

ISME J.

<https://pubmed.ncbi.nlm.nih.gov/37231184/>

Mosquito-borne diseases like dengue and malaria cause a significant global health burden. Unfortunately, current insecticides and environmental control strategies aimed at the vectors of these diseases are only moderately effective in decreasing disease burden. Understanding and manipulating the interaction between the mosquito holobiont (i.e., mosquitoes and their resident microbiota) and the pathogens transmitted by these mosquitoes to humans and animals could help in developing new disease control strategies. Different microorganisms found in the mosquito's microbiota affect traits related to mosquito survival, development, and reproduction. Here, we review the physiological effects of essential microbes on their mosquito hosts; the interactions between the mosquito holobiont and mosquito-borne pathogen (MBP) infections, including microbiota-induced host immune activation and Wolbachia-mediated pathogen blocking (PB); and the effects of environmental factors and host regulation on the composition of the microbiota. Finally, we briefly overview future directions in holobiont studies, and how these may lead to new effective control strategies against mosquitoes and their transmitted diseases.

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.

Juil-2023

Nat Biomed Eng.

<https://pubmed.ncbi.nlm.nih.gov/36959404/>

The threat of new viral outbreaks has heightened the need for ready-to-use vaccines that are safe and effective. Here we show that a subcutaneous vaccine consisting of live Zika virus electrostatically entrapped in a self-adjuvanting hydrogel recruited immune cells at the injection site and provided mice with effective protection against a lethal viral challenge. The hydrogel prevented the escape of the viral particles and upregulated pattern recognition receptors that activated innate antiviral immunity. The local inflammatory niche facilitated the engulfment of the virus by immune cells infiltrating the hydrogel, the processing and cross-presentation of antigens and the expansion of germinal centre B cells and induced robust antigen-specific adaptive responses and immune memory. Inflammatory immune niches entrapping live viruses may facilitate the rapid development of safe and efficacious vaccines.

Preschool neurodevelopment in Zika virus-exposed children without congenital Zika syndrome.

Mulkey SB, Peyton C, Anusinha E, Corn E, Arroyave-Wessel M, Zhang A, Biddle C, Gutierrez C, Sorkar A, Cure A, Cure D, du Plessis AJ, DeBiasi RL, Msall ME, Cure C.

Jul-2023

Pediatr Res.

<https://pubmed.ncbi.nlm.nih.gov/36446920/>

Background: Children with in utero Zika virus (ZIKV) exposure without congenital Zika syndrome (CZS) are at risk for abnormal neurodevelopment. Preschool-age outcomes for children with antenatal ZIKV exposure have not yet been established. **Methods:** Children with in utero ZIKV exposure and non-exposed controls had neurodevelopmental evaluations at age 3-5 years in Sabanalarga, Colombia. Cases did not have CZS and were previously evaluated prenatally through age 18 months. Controls were born before ZIKV arrival to Colombia. Neurodevelopmental assessments included Pediatric Evaluation of Disability Inventory (PEDI-CAT), Behavior Rating Inventory of Executive Function (BRIEF-P), Bracken School Readiness Assessment (BSRA), and Movement Assessment Battery for Children (MABC). Family demographics and child medical history were recorded. **Results:** Fifty-five ZIKV-exposed children were evaluated at mean age 3.6 years and 70 controls were evaluated at 5.2 years. Family demographics were similar between groups. BRIEF-P t-scores were higher for cases than controls in shift and flexibility domains. Cases had lower PEDI-CAT mobility t-scores compared to controls. There was no difference in MABC between groups. In 11% of cases and 1% of controls, parents reported child mood problems. **Conclusions:** Children with in utero ZIKV exposure without CZS may demonstrate emerging differences in executive function, mood, and adaptive mobility that require continued evaluation. **Impact:** Preschool neurodevelopmental outcome in children with in utero Zika virus exposure is not yet known, since the Zika virus epidemic occurred in 2015-2017 and these children are only now entering school age. This study finds that Colombian children with in utero Zika virus exposure

without congenital Zika syndrome are overall developing well but may have emerging differences in executive function, behavior and mood, and adaptive mobility compared to children without in utero Zika virus exposure. Children with in utero Zika virus exposure require continued multi-domain longitudinal neurodevelopmental evaluation through school age.

Is dengue the new rising global health problem? The outbreak of 2019 in Pakistan.

Baloch M, Baig AM, Ochani RK.

Aug-2023

Minerva Med.

<https://pubmed.ncbi.nlm.nih.gov/32486614/>

Echinococcosis

A rare case of recurrent hydatid cyst of the spleen: A case report.

Hassan A, Azhar A, Mazhar S, Yadav S, Tahir MB, Basnet R, Bhattarai P.

22-07-2023

Radiol Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/37502480/>

Cystic echinococcosis (CE), or hydatid disease, is a parasitic infection caused by *Echinococcus granulosus* endemic to areas with considerable pastoral farming and animal husbandry. Typical presentations include hydatid cyst formation in the liver, lungs, brain, kidneys, or bones. An isolated splenic hydatid cyst is an extremely rare occurrence, accounting for only 0.5%-4% worldwide incidence rates, and recurrent cases are even more infrequent. Globalization, cross-border travel, and altered immigration patterns over time have shifted some of the burden of CE from the developing to the developed world, making the diagnosis challenging for these nonendemic areas. Judicious use of imaging modalities for prompt diagnosis and effective intervention is necessary to treat the initial disease and prevent a recurrence. Herein, we present the case of a 13-year-old male with recurrent isolated splenic hydatid cyst. The patient presented with chronic and nonradiating pain in his left hypochondrium. Physical examination revealed splenomegaly. Ultrasonography showed multiple cysts. Computerized tomography (CT) scan showed cystic lesions in splenic parenchyma with numerous internal enhancing septae. Surgical evacuation was performed for the management of disease.

Cysticercosis in free-ranging agoutis (*Dasyprocta leporina*) in the Eastern Brazilian Amazon.

Souza AJS, Malheiros AP, Chagas AACD, Alves MM, Bernal MKM, Carneiro LA, Gomes-Gouvêa MS, Nunes HM.

21-07-2023

Rev Bras Parasitol Vet.

<https://pubmed.ncbi.nlm.nih.gov/37493786/>

Cryptic species *Hydatigera kamiyai* and other taeniid metacestodes in the populations of small mammals in Serbia.

Miljević M, Rajčić M, Umhang G, Bajić B, Bjelić Čabrilo O, Budinski I, Blagojević J.

25-07-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37491284/>

mmu-miRNA-342-3p promotes hepatic stellate cell activation and hepatic fibrosis induced by *Echinococcus multilocularis* infection via targeting *Zbtb7a*.

Cao S, Wang D, Wu Y, Zhang J, Pu L, Luo X, Zhang X, Sun X, Zheng Y, Wang S, Guo X.

25-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37490505/>

Liver fibrosis is one of the histopathological characters during *Echinococcus multilocularis* infection. The activation of hepatic stellate cells (HSCs) is a key event in the development of liver fibrosis. However, the molecular mechanism of HSC activation in the *E. multilocularis* infection-induced liver fibrosis remains largely unclear. Here, we reported that mmu-miR-342-3p was most dominantly expressed in HSCs and was upregulated in the HSCs in response to *E. multilocularis* infection. We further showed that mmu-miR-342-3p was able to bind to the 3' UTR of the *Zbtb7a* gene and regulated its expression. Moreover, mmu-miR-342-3p expression was negatively correlated with its target gene *Zbtb7a* in HSCs during *E. multilocularis* infection. Knockdown of mmu-miR-342-3p promoted the expression of *Gfap* in the activated HSCs in vitro. In the *E. multilocularis*-infected mice, knockdown of mmu-miR-342-3p suppressed the expression of α -Sma, *Col1 α 1*, and TGF- β but promoted the expression of *Gfap*. Therefore, mmu-miR-342-3p is a key regulator for activation of HSCs, and inhibiting mmu-miR-342-3p to suppressed *Zbtb7a*-mediated TGF- β signaling in activated HSCs could be a novel strategy to treat liver fibrosis induced by *E. multilocularis*.

Genetic Characterization of *Echinococcus granulosus sensu stricto* Isolated from Human Cysts from Sardinia, Italy.

Santuoccu C, Bonelli P, Peruzzu A, Fancellu A, Farà A, Mastrandrea S, Drocchi G, Cossu A, Profili S, Porcu A, Masala G.

27-07-2023

Diseases.

<https://pubmed.ncbi.nlm.nih.gov/37489443/>

This study involved 20 patients affected by cystic echinococcosis (CE) who were referred to different hospitals of Sardinia (Italy) from 2017 to 2022. By means of a multidisciplinary approach, diagnosis was confirmed for CE in 18 patients and for different aetiologies in two subjects. Moreover, serology was positive for 15 subjects. Since multiple CE cysts were found in five patients, a total

of 27 lesions were collected; however, only one for each patient was investigated for genetic characterization of *E. granulosus* s.s. DNA isolates. Our results included 15 fertile cysts that underwent DNA extraction and amplification by three different PCRs targeting nuclear (*calreticulin*) and mitochondrial genes (*cox1* and *nad5*). DNA was sequenced, and by neighbour-joining phylogenetic trees we determined 10 G1 and five G3 genotypes previously reported in Sardinia. These sequences were used to construct a network, along with those circulating in Mediterranean areas. The haplotype network calculated on *cox1* evidenced seven different haplotypes of the 15 isolates, with SAR2 the most represented, carried by seven cysts, and SAR17 never described in the Mediterranean area. Meanwhile, the *nad5* sequences showed the most common haplotype as nd5SAR7, as well as two new haplotypes not previously described, nd5SAR13, isolated from a Sardinian patient, and nd5SAR14, isolated from a Romanian patient.

Environmental Influence on the Occurrence of Multi-Organ Cystic Echinococcosis Infection in a Patient from Sardinia, Italy.

Santuoccu C, Ferrari PA, Grimaldi G, Murenu A, Nemolato S, Bonelli P, Masala G, Porcu GS, Cherchi R.

27-07-2023

Diseases.

<https://pubmed.ncbi.nlm.nih.gov/37489442/>

Large right ventricular hydatid cyst in a child: a case report.

Vahidshahi K, Tahouri T, Farahmandi F, Hekmat M.

22-07-2023

Egypt Heart J.

<https://pubmed.ncbi.nlm.nih.gov/37480492/>

Background: Cystic Hydatid disease is a parasitic infection with a worldwide distribution. It is caused by the larval stages of a species of tapeworms known as *Echinococcus granulosus*. Even in endemic areas; Cardiac involvement by hydatidiosis is very rare and has atypical presentations as well as localization which make it undiagnosed in about 10% of cases. The left ventricle is the most Common chamber involved by the hydatid cyst and isolated involvement of the right ventricle is very rare, especially in children. The aim of the present study was to describe hydatid cardiac cyst of the right ventricle of a child. **Case presentation:** We present a rare case of an 8 year-old boy, living in a rural area, who was diagnosed with a cardiac hydatid cyst in the right ventricle. He also had multiple pulmonary hydatid cysts and presented with dyspnea, cough and atypical chest pain. The patient underwent surgery for the resection of pulmonary cysts and, subsequently, cardiac hydatid cyst. The outcome was favorable seven weeks after surgery and there was no clinical and echocardiographic recurrence. **Conclusion:** Cardiac Echinococcosis must be suspected in endemic areas, diagnosed with appropriate imaging techniques, and treated appropriately.

Establishment of a secondary infection laboratory model of *Echinococcus shiquicus* metacestode using BALB/c mice and Mongolian jirds (*Meriones unguiculatus*).

Wu Y, Li L, Xu F, Yan H, Ohiolei JA, Shumuye NA, Nian X, Li W, Zhang N, Fu B, Jia W.

03-07-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/37475454/>

Dogs as a source for the spreading of enteric parasites including zoonotic ones in Giza Province, Egypt.

Khalifa MM, Fouad EA, Kamel NO, Auda HM, El-Bahy MM, Ramadan RM.

Août-2023

Res Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37379694/>

Effects of Dihydroartemisinin against Cystic Echinococcosis In Vitro and In Vivo.

Wen L, Zhang J, Zhao J, Gong Y, Zhang H, Yang J, Wang J.

18-07-2023

Infect Immun.

<https://pubmed.ncbi.nlm.nih.gov/37310215/>

Cystic echinococcosis (CE) is a disease caused by the infection of *Echinococcus granulosus*. We sought to investigate the effects of dihydroartemisinin (DHA) against CE under *in vitro* and *in vivo* conditions. Protoscoleces (PSCs) from *E. granulosus* were divided into control, DMSO, ABZ, DHA-L, DHA-M, and DHA-H groups. PSC viability after DHA treatment was determined based on the eosin dye exclusion test, alkaline phosphatase content detection, and ultrastructure observation. DNA oxidative damage inducer hydrogen peroxide (H₂O₂), reactive oxygen species (ROS) scavenger mannitol, and the DNA damage repair inhibitor velparib were used to explore the anti-CE mechanism of DHA. The anti-CE effects and CE-induced liver injury and oxidative stress of DHA at different doses (50, 100, and 200 mg/kg) were assessed in CE mice. DHA showed antiparasitic effects on CE in both *in vivo* and *in vitro* experiments. DHA could elevate the ROS level and induce oxidative DNA damage in PSCs, thereby destroying hydatid cysts. DHA could inhibit the growth of cysts in a dose-dependent manner and reduce the content of biochemical parameters associated with liver injury in CE mice. It also significantly reversed oxidative stress in CE mice, which was characterized as the decreased tumor necrosis factor alpha and H₂O₂ content, as well as the increase of the ratio of glutathione/oxidized glutathione and total superoxide dismutase content. DHA showed antiparasitic effects. DNA damages induced by oxidative stress played important roles in this process.

First isolation of *Echinococcus granulosus sensu lato* genotype 7 in the archipelago of Cape Verde.

Gonçalves Baptista L, Laurimäe T, Muchaamba G, Cathomas L, Barros Olende AL, Mata Dos Santos I, Lobo de Pina Â, Deplazes P.

Juillet-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/37194602/>

Filariose lymphatique

Identification and molecular characterization of *Culex flavivirus* in *Culex quinquefasciatus* (Diptera: Culicidae): first report from India.

Anakha A, Shah HK, Fathima PA, Aiswarya RS, Ajithlal PM, Kumar NP, Kumar A, Saini P.

27-07-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37497735/>

Spatial predictive risk mapping of lymphatic filariasis residual hotspots in American Samoa using demographic and environmental factors.

Cadavid Restrepo AM, Martin BM, Fuimaono S, Clements ACA, Graves PM, Lau CL.

24-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37486947/>

Background: American Samoa successfully completed seven rounds of mass drug administration (MDA) for lymphatic filariasis (LF) from 2000-2006. The territory passed the school-based transmission assessment surveys in 2011 and 2015 but failed in 2016. One of the key challenges after the implementation of MDA is the identification of any residual hotspots of transmission.

Method: Based on data collected in a 2016 community survey in persons aged ≥8 years, Bayesian geostatistical models were developed for LF antigen (Ag), and Wb123, Bm14, Bm33 antibodies (Abs) to predict spatial variation in infection markers using demographic and environmental factors (including land cover, elevation, rainfall, distance to the coastline and distance to streams).

Results: In the Ag model, females had a 26.8% (95% CrI: 11.0-39.8%) lower risk of being Ag-positive than males. There was a 2.4% (95% CrI: 1.8-3.0%) increase in the odds of Ag positivity for every year of age. Also, the odds of Ag-positivity increased by 0.4% (95% CrI: 0.1-0.7%) for each 1% increase in tree cover. The models for Wb123, Bm14 and Bm33 Abs showed similar significant associations as the Ag model for sex, age and tree coverage. After accounting for the effect of covariates, the radii of the clusters were larger for Bm14 and Bm33 Abs compared to Ag and Wb123 Ab. The predictive maps showed that Ab-positivity was more widespread across the territory, while Ag-positivity was more confined to villages in the north-west of the main island. **Conclusion:** The findings may facilitate more specific targeting of post-MDA surveillance activities by prioritising those areas at higher risk of ongoing transmission.

Vitellogenin genes are transcribed in *Culex quinquefasciatus* ovary.

Moura AS, Costa-da-Silva AL, Peixoto PS, Maciel C, Cardoso AF.

17-07-2023

Mem Inst Oswaldo Cruz.

<https://pubmed.ncbi.nlm.nih.gov/37466532/>

Background: *Culex quinquefasciatus*, a cosmopolitan, domestic, and highly anthropophilic mosquito, is a vector of pathogenic arboviruses such as West Nile virus and Rift Valley virus, as well as lymphatic filariasis. The current knowledge on its reproductive physiology regarding vitellogenin expression in different tissues is still limited.

Objectives: In this study, we analysed the transcriptional profiles of vitellogenin genes in the fat body and ovaries of *C. quinquefasciatus* females during the first gonotrophic cycle. **Methods:** *C. quinquefasciatus* ovaries and/or fat bodies were dissected in different times during the first gonotrophic cycle and total RNA was extracted and used for reverse transcription polymerase chain reaction, quantitative real time-PCR, and in situ hybridisation.

Findings: We confirmed the classical descriptions of the vitellogenic process in mosquitoes by verifying that vitellogenin genes are transcribed in the fat bodies of *C. quinquefasciatus* females. Using RNA in situ hybridisation approach, we showed that vitellogenin genes are also transcribed in developing ovaries, specifically by the follicle cells. **Main conclusions:** This is the first time that vitellogenin transcripts are observed in mosquito ovaries. Studies to determine if Vg transcripts are translated into proteins and their contribution to the reproductive success of the mosquito need to be further investigated.

Ivermectin and doxycycline treatments against Onchocerciasis: Adaptations and impact among semi-nomadic population in Massangam Health District, Cameroon.

Nditanchou R, Dixon R, Atekem K, Biholong B, Wilhelm A, Selby R, Oye J, Kamgno J, Boakye D, Schmidt E, Senyonjo L.

12-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37437096/>

A Phase-I pharmacokinetic, safety and food-effect study on flubentylisin, a novel analog of Tylosin-A having potent anti-Wolbachia and antifilarial activity.

Alami N, Carter DC, Kwatra NV, Zhao W, Snodgrass L, Porcalla AR, Klein CE, Cohen DE, Gallenberg L, Neenan M, Carr RA, Marsh KC, Kempf DJ.

10-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37428804/>

Assessment of wing geometric morphometrics of urban *Culex quinquefasciatus* (Diptera: Culicidae) populations.

Oliveira-Christe R, de Carvalho GC, Wilke ABB, Marrelli MT.

Sept-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37331646/>

Culex quinquefasciatus is a cosmopolitan species distributed throughout tropical and subtropical areas of the world. The species is of great epidemiological importance as it is responsible for vectoring the causative agent of lymphatic filariasis and several arboviruses, including West Nile virus. Wing geometric morphometrics has been widely used to assess phenotypic variations in mosquito species. Here, we hypothesize that *Cx. quinquefasciatus* populations in urban parks in the city of São Paulo, Brazil, have been subjected to anthropogenic selective pressures that are responsible for driving their ecology and behavior. Mosquitoes were collected by CDC traps in five municipal parks in the city of São Paulo. Eighteen anatomical landmark coordinates on each female right wing were digitized. Canonical variate analysis, wireframe graphs, cross-validated reclassification tests and the neighbor-joining method were used to assess phenotypical dissimilarity in wing shape between populations. Centroid size was calculated to assess differences in wing size between populations, which can result from different environmental conditions during immature mosquito development. Moderately heterogeneous wing shape and wing size patterns were found in the populations analyzed, indicating that selective pressures in the urban environment are affecting the wing patterns of *Cx. quinquefasciatus* populations in the city of São Paulo, Brazil.

Gale

Therapie der Skabies.

Sunderkötter C.

Août-2023

Dermatologie (Heidelb).

<https://pubmed.ncbi.nlm.nih.gov/37417978/>

Skin diseases in a 19th century English workhouse: analysis of the admission book for the Wakefield Workhouse Infirmary, 1826-1857.

Labbouz S, Manley AL, Gawkrödger DJ.

21-07-2023

Clin Exp Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/37070391/>

Use of Complementary and Alternative Medicine in Children with Scabies.

Akca G, Sen NO, Akca U.

2023

Complement Med Res.

<https://pubmed.ncbi.nlm.nih.gov/36731431/>

Introduction: Scabies is a highly contagious infestation that is becoming increasingly resistant to treatment. The use of complementary and alternative medicine (CAM) has gradually increased for numerous diseases, and the aim of

this study is to investigate the parental use of CAM in the treatment of scabies. **Methods:** The study was planned as a cross-sectional study involving children who came to the departments of child health and diseases and dermatology departments for any reason and were diagnosed with scabies. Questionnaires were given to parents by physicians during face-to-face interviews, and responses were recorded. **Results:** 75.9% of the 162 parents participating in the study were mothers, and 40% of the parents reported that their income was below expenses. The mean number of people living in the household was 4 (min 3-max 13), and the proportion of extended family was 34%. The mean duration of symptoms in patients with scabies was 4.8 ± 3.92 weeks (min. 1-max. 27), and scabies was diagnosed on average at the second visit to the doctor. CAM was used by 80.9% of parents for children with scabies. They most commonly used tea tree oil for itching and ice for the rash. Parents working in education and health care were less likely to use CAM ($p < 0.001$), while more than 90% of housewives used at least one CAM method on their children. Analysis showed that 61.7% of female users had benefited from CAM. Significant differences between parents who used CAM and those who did not were found in education ($p = 0.003$), monthly income ($p = 0.023$), number of children ($p = 0.022$), and living in large families ($p = 0.001$). The use of CAM was six times higher in parents in large families (OR: 6.143, 95% CI 0.776-21.252). **Conclusions:** With regard to the treatment of scabies, it is important to strengthen the education of health professionals at all levels, put the treatment of patients on a regular basis, explain the conditions that require special attention, and monitor patients closely. New treatment protocols must also be developed for refractory scabies, including alternative therapies.

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

Investigating Environmental Determinants of Soil-Transmitted Helminths Transmission using GPS Tracking and Metagenomics Technologies.

Sumboh JG, Agyenkwa-Mawuli K, Schwinger E, Donkor IO, Akorli JEB, Dwomoh D, Ashong Y, Osabutey D, Ababio FO, Koram KA, Humphries D, Cappello M, Kwofie SK, Wilson MD.

23-07-2023

medRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37503260/>

Background: The Global Health community aims to eliminate soil-transmitted helminth (STH) infections by 2030. Current preventive methods such as Mass Drug Administration, WASH practices, and health education needs to be complimented to halt transmission. We tracked the movement of hookworm-infected and non-infected persons and investigated soil factors in the places

they frequented within an endemic community to further understand the role of human movement and sources of infections. **Methods:** 59 positive and negative participants wore GPS tracking devices for 10 consecutive days and their movement data captured in real time. The data was overlaid on the community map to determine where each group differentially spent most of their time. Soil samples were collected from these identified sites and other communal places. Physical and chemical properties were determined for each sample using standard methods and helminth eggs cultured into larvae using the Baermann technique. Bivariate and multivariate analyses were used to determine associations between larvae counts and soil factors. Helminth species were identified with metagenomic sequencing and their distributions mapped to sampling sites in the community. **Results:** The study found that there was no significant difference in the average larvae counts in soil between sites assessed by infected and non-infected participants ($P = 0.59$). However, soil factors, such as pH, carbon and sandy-loamy texture were associated with high larvae counts ($P < 0.001$) while nitrogen and clay content were associated with low counts ($P < 0.001$). The dominant helminth species identified were *Panagrolaimus superbus* (an anhydrobiotic helminth), *Parastrongyloides trichosuri* (a parasite of small mammals), *Trichuris trichiura* (whipworm), and *Ancylostoma caninum* (dog hookworm). Notably, no *Necator americanus* was identified in any soil sample. **Conclusion:** This study provides important insights into the association between soil factors and soil-transmitted helminths. These findings contribute to our understanding of STH epidemiology and support evidence-based decision-making for elimination strategies. **Author summary:** Soil-transmitted helminth (STH) infections has been set to be eliminated 2030. To better understand how infections spread to achieve this, we tracked the movement of people positive and negative for infections. We enrolled 59 participants and equipped them with GPS tracking devices for 10 days continuously monitoring their movements in real time. We identified areas where each group spent the most time. Soil samples were collected from these locations and other communal areas. The physical and chemical properties of the soils were analysed using standard methods and helminth eggs cultured into larvae. Bivariate and multivariate analyses were used to study the relationship between larvae counts and soil factors. Metagenomic sequencing identified the types of helminths present in the soil samples. The study revealed that soil factors such as pH, carbon content, and sandy-loamy texture were associated with high larvae counts, while nitrogen and clay content were associated with lower counts. The dominant helminth species identified were *Panagrolaimus superbus*, *Parastrongyloides trichosuri*, *Trichuris trichiura* (whipworm), and *Ancylostoma caninum* (dog hookworm). Interestingly, no samples contained *Necator americanus*. This study provides important insights into the connection between soil factors and STHs infections enhancing our understanding of STH epidemiology to inform evidence-based strategies for eliminating.

Intestinal parasitic infections and risk analysis among urban refugees in the Klang Valley, Malaysia.

Mohd Hanapi IR, Behnke JM, Sahimin N, Saifulazmi NF, Golam Mohammad Khan ASJ, Abdul Mutalib RNS, Lau YL, Mohd Zain SN.

27-07-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37497742/>

Effect of experimental hookworm infection on insulin resistance in people at risk of type 2 diabetes.

Pierce DR, McDonald M, Merone L, Becker L, Thompson F, Lewis C, Ryan RYM, Hii SF, Zendejas-Heredia PA, Traub RJ, Field MA, Rahman T, Croese J, Loukas A, McDermott R, Giacomini PR.

26-07-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37495576/>

The reduced prevalence of insulin resistance and type 2 diabetes in countries with endemic parasitic worm infections suggests a protective role for worms against metabolic disorders, however clinical evidence has been non-existent. This 2-year randomised, double-blinded clinical trial in Australia of hookworm infection in 40 male and female adults at risk of type 2 diabetes assessed the safety and potential metabolic benefits of treatment with either 20 (n = 14) or 40 (n = 13) *Necator americanus* larvae (L3) or Placebo (n = 13) (Registration ACTRN12617000818336). Primary outcome was safety defined by adverse events and completion rate. Homeostatic model assessment of insulin resistance, fasting blood glucose and body mass were key secondary outcomes. Adverse events were more frequent in hookworm-treated participants, where 44% experienced expected gastrointestinal symptoms, but completion rates were comparable to Placebo. Fasting glucose and insulin resistance were lowered in both hookworm-treated groups at 1 year, and body mass was reduced after L3-20 treatment at 2 years. This study suggests hookworm infection is safe in people at risk of type 2 diabetes and associated with improved insulin resistance, warranting further exploration of the benefits of hookworms on metabolic health.

Burden and factors associated with ongoing transmission of soil-transmitted helminths infections among the adult population: A community-based cross-sectional survey in Muleba district, Tanzania.

Zacharia F, Silvestri V, Mushi V, Ogwen G, Makene T, Mhamilawa LE.

26-07-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37494358/>

Background: In Tanzania, school-based Mass Drug Administration (MDA) campaigns have been the main strategy for the prevention and control of Soil Transmitted

Helminths (STH) infection. Adults are not part of the program and could remain as the reservoir of infection, favoring continuity in transmission. Water, Sanitation, and Hygiene (WaSH) issues and slow progress in community awareness promotion campaigns contribute to the persistence of STH as public health issue among target populations notwithstanding the achievements of the control interventions. **Objective:** This study aimed to determine the current prevalence and the risk factors associated with ongoing transmission of STH infection among adults in Muleba District, Tanzania. **Methodology:** A household-based quantitative cross-sectional study was carried out among 552 adults in Muleba district. Through a quantitative interviewer-administered questionnaire, information was registered related to socio-demographic characteristics, level of knowledge on the disease, and WaSH factors. The prevalence of STH and estimation of its intensity were assessed by analyzing stool samples through formol-ether concentration and the Kato-Katz technique. Descriptive statistics was used to summarise data; logistic regression to determine the association between STH infection and socio-demographic and WaSH factors. A p-value < 0.05 was considered statistically significant. **Results:** A total of 552 adults were included in the study; 50.7% (280/552) were female. The median age was of 30 years, ranging from 18 to 73 years. A prevalence of 9.1% (50/552) for STH infection was reported; the prevalence of Hookworm Spp., *Ascaris lumbricoides*, and *Trichuris trichiura* was 7.43%, 0.91%, and 0.72%, respectively. The factors significantly associated with STH infection were farming (aOR = 3.34, 95% CI: 1.45-7.70), the habit of not wearing shoes in general (aOR = 5.11, 95% CI: 1.55-16.87), and during garden activities (aOR = 4.89, 95% CI: 1.47-16.28). **Conclusions and recommendations:** We observed an aggregated prevalence of STH infections (*Ancylostoma duodenale*, *Trichuris trichiura*, and *Ascaris lumbricoides*) of 9.1% among the adult population, indicating a decreasing prevalence but ongoing transmission. Integrated management is needed to address practices contributing to ongoing transmission.

First molecular data on the human roundworm *Ascaris lumbricoides* species complex from the Bronze and Iron Age in Hallstatt, Austria.

Barsch E, Kowarik K, Rodler K, Hörweg C, Reschreiter H, Sattmann H, Walochnik J.

25-07-2023

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37491505/>

Dogs as a source for the spreading of enteric parasites including zoonotic ones in Giza Province, Egypt.

Khalifa MM, Fouad EA, Kamel NO, Auda HM, El-Bahy MM, Ramadan RM.

August-2023

Res Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37379694/>

The Relationship of Parasite Allergens to Allergic Diseases.

Caraballo L, Llinás-Caballero K.

Jul-2023

Curr Allergy Asthma Rep.

<https://pubmed.ncbi.nlm.nih.gov/37269427/>

Purpose of review: Helminth infections modify the natural history of allergic diseases, by either decreasing or increasing their symptoms. Several helminth components are involved in the increasing of the allergic response and symptoms, overcoming the concomitant immunosuppression of helminthiasis. However, the role of individual IgE-binding molecules in this process remains to be defined. **Recent findings:** We updated the list of helminth allergens and IgE-binding molecules, their effects on asthma presentation, and their impact on allergy diagnosis. Data from genetic and epigenetic studies of ascariasis are analyzed. A new species-specific *A. lumbricoides* allergen has been discovered, with potential use in molecular diagnosis. Most helminth IgE-binding components are not officially classified as allergens in the WHO/IUIS database, although there is evidence of their influence increasing allergic manifestations. Further immunological characterization of these components is needed to better understand their mechanisms of action and evaluate the ways in which they can influence the diagnosis of allergy.

Multiple anthelmintic drug resistant *Ancylostoma caninum* in foxhounds.

Balk JD, Mitchell ND, Hughes J, Soto Nauto P, Rossi J, Ramirez-Barrios R.

20-07-2023

Int J Parasitol Drugs Drug Resist.

<https://pubmed.ncbi.nlm.nih.gov/37481894/>

Ancylostoma caninum is the most common and important gastrointestinal nematode of dogs in the United States. Despite recent reports of *A. caninum* isolates resistant to all classes of anthelmintics, little is known about the frequency and extent of this anthelmintic resistance. The study aim was to evaluate the efficacy of three commercial anthelmintic products in the treatment of foxhound dogs with a history of persistent *A. caninum* infections. In the first phase of this study, 35 foxhounds were randomly divided into three treatment groups: moxidectin/imidacloprid (MI), pyrantel pamoate/febantel/praziquantel (PFP), and emodepside/praziquantel (EP). Fecal samples were collected on day 0, 11, and 33 post-treatment (PT), and hookworm eggs were quantified using the mini-FLOTAC technique with a multiplication factor of 5 eggs per gram (EPG). The fecal egg count reduction (FECR) on day 11 PT was 65% (95% CI: 62%-68%) for MI, 69% (95% CI: 66%-72%) for PFP, and 96% (95% CI: 94%-97%) for EP. On day 33 PT, the FEC in the MI and PFP groups returned to almost the same values as on day 0, while in the EP group, the FEC remained low. Since MI and PFP proved ineffective, 32 animals were randomly divided into two groups in the second phase. They were treated either with a combination of MI/PFP or EP. The FECR at day 13 PT for the combination MI/PFP was 89% (95% CI: 87%-91%) and

99% (95% CI: 98%-99%) for EP. These results suggest that this *A. caninum* population is resistant to multiple anthelmintics. Although the combination of MI/PFP improved the anthelmintic efficacy, the FECR remained below 90%. Future studies are indicated to evaluate further the epidemiology of persistent hookworm infections in dogs in the US and to identify more effective treatment protocols as they pose a significant health risk to canine and human health.

Leishmaniose

Field-Deployable Treatments For Leishmaniasis: Intrinsic Challenges, Recent Developments and Next Steps.

Pacheco-Fernandez T, Markle H, Verma C, Huston R, Gannavaram S, Nakhasi HL, Satoskar AR.

20-07-2032

Res Rep Trop Med.

<https://pubmed.ncbi.nlm.nih.gov/37492219/>

Structure-based drug designing against *Leishmania donovani* using docking and molecular dynamics simulation studies: exploring glutathione synthetase as a drug target.

Sarma M, Borkotoky S, Dubey VK.

25-07-2023

J Biomol Struct Dyn.

<https://pubmed.ncbi.nlm.nih.gov/37491862/>

Disposable electrochemical platform based on solid-binding peptides and carbon nanomaterials: an alternative device for leishmaniasis detection.

Braz BA, Hospinal-Santiani M, Martins G, Beirão BCB, Bergamini MF, Marcolino-Junior LH, Soccol CR, Thomaz-Soccol V.

25-07-2023

Mikrochim Acta.

<https://pubmed.ncbi.nlm.nih.gov/37491620/>

Neglected tropical diseases are those caused by infectious agents or parasites and are considered endemic in low-income populations. These diseases also have unacceptable indicators and low investment in research, drug production, and control. Tropical diseases such as leishmaniasis are some of the main causes of morbidity and mortality around the globe. Electrochemical immunosensors are promising tools for diagnostics against these diseases. One such benefit is the possibility of assisting diagnosis in isolated regions, where laboratory infrastructure is lacking. In this work, different peptides were investigated to detect antibodies against *Leishmania* in human and canine serum samples. The peptides evaluated (395-KKG and 395-G) have the same recognition site but differ on their solid-binding domains, which ensure affinity to spontaneously bind to either graphene oxide (GO) or graphene quantum dots (GQD). Cyclic voltammetry and differential pulse voltammetry were employed to investigate the electrochemical behavior of

each assembly step and the role of each solid-binding domain coupled to its anchoring material. The graphene affinity peptide (395-G) showed better reproducibility and selectivity when coupled to GQD. Under the optimized set of experimental conditions, negative and positive human serum samples responses were distinguished based on a cut-off value of 82.5% at a 95% confidence level. The immunosensor showed selective behavior to antibodies against *Mycobacterium leprae* and *Mycobacterium tuberculosis*, which are similar antibodies and potentially sources of false positive tests. Therefore, the use of the graphene affinity peptide as a recognition site achieved outstanding performance for the detection of *Leishmania* antibodies.

Evolution of RNA viruses in trypanosomatids: new insights from the analysis of *Sauroleishmania*.

Klocek D, Grybchuk D, Tichá L, Votýpka J, Volf P, Kostygov AY, Yurchenko V.

25-07-2023

Parasitol Res.

<https://pubmed.ncbi.nlm.nih.gov/37490143/>

Unilateral keratitis secondary to *Leishmania* spp. infection in a horse: Clinical signs and successful topical therapy.

Matas Riera M, Cardenas Nadal M, Martínez-Sogues L, Ferrer L.

25-07-2023

Vet Ophthalmol.

<https://pubmed.ncbi.nlm.nih.gov/37489904/>

Dermatological clinical signs have been seldom reported in the literature secondary to equine leishmaniasis. This case depicts the clinical signs, treatment, and outcome of a young horse with a pink, elevated lesion on the ventromedial quadrant of the cornea. A corneal cytology was performed and revealed the presence of *Leishmania* amastigotes reaching the diagnosis of keratitis secondary to leishmaniasis. Surgical resection was recommended but the owner declined the procedure, and the lesion was treated with a topical antimonial for 6 weeks. The lesion reduced remarkably during the first weeks of treatment. The patient had not shown recurrence of the lesion for 2 years since the treatment was started. *Leishmania* spp. can be responsible for ocular surface abnormalities such as keratitis. Corneal cytology is an inexpensive diagnostic method that should be considered when ocular surface abnormalities are identified in horses in endemic areas.

Case Report: Extensive Facial Cutaneous Leishmaniasis in a Neonate.

Itzhaki Gabay S, Valdman-Grinshpoun Y, Ling G, Ben-Shimol S, Test G, Kaplan O, Horev A.

24-07-2023

Am J Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37487561/>

Cutaneous leishmaniasis (CL) is a skin infection caused by various species of the *Leishmania* parasite and is spread by

the bite of an infected female sandfly. In southern Israel, CL caused by *Leishmania major* is endemic. Cutaneous leishmaniasis is considered a self-limiting disease, characterized by progressive, long-lasting nodulo-ulcerative skin lesions, which usually resolve in several months to years, and leads to scarring, cosmetic disfigurement, and future stigmatization. Although CL is a common disease among children, reports of CL in children younger than 1 year are rare. We present a case of extensive facial CL in an infant whose initial lesions appeared only 25 days after birth. The patient was treated with intravenous liposomal amphotericin B. Two months later, marked improvement was seen, with complete resolution of the inflammation and atrophic scar formation. To our knowledge, this is the earliest age of CL published to date.

A disfiguring neglected tropical disease sweeps war-torn Yemen: a community-based study of prevalence and risk factors of cutaneous leishmaniasis among rural communities in the western highlands.

Al-Ashwal MA, Atroosh WM, Al-Adhroey AH, Al-Subbary AA, Yee-Ling L, Al-Mekhlafi HM.

24-07-2023

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/37486252/>

Total serum N-glycans mark visceral leishmaniasis in human infections with *Leishmania infantum*.

Porcino GN, Bladergroen MR, Dotz V, Nicolardi S, Memarian E, Gardinassi LG, Nery Costa CH, Pacheco de Almeida R, Ferreira de Miranda Santos IK, Wuhrer M.

05-06-2023

iScience.

<https://pubmed.ncbi.nlm.nih.gov/37485378/>

Visceral leishmaniasis (VL) is a clinical form of leishmaniasis with high mortality rates when not treated. Diagnosis suffers from invasive techniques and sub-optimal sensitivities. The current (affordable) treatment with pentavalent antimony as advised by the WHO is possibly harmful to the patient. There is need for an improved diagnosis to prevent possibly unnecessary treatment. *N*-glycan analysis may aid in diagnosis. We evaluated the *N*-glycan profiles from active VL, asymptomatic infections (ASYMP) and controls from non-endemic (NC) and endemic (EC) areas. Active VL has a distinct *N*-glycome profile that associates with disease severity. Our study suggests that the observed glycan signatures could be a valuable additive to diagnosis and assist in identifying possible markers of disease and understanding the pathogenesis of VL. Further studies are warranted to assess a possible future role of blood glycome analysis in active VL diagnosis and should aim at disease specificity.

In Vitro Reconstitution and Analysis of SARS-CoV-2/Host Protein-Protein Interactions.

Moradi SV, Wu Y, Walden P, Cui Z, Johnston WA, Petrov D, Alexandrov K.

06-07-2023

ACS Omega.

<https://pubmed.ncbi.nlm.nih.gov/37483225/>

Development of chimeric protein as a multivalent vaccine for human Kinetoplastid infections: Chagas disease and leishmaniasis.

Clímaco MC, de Figueiredo LA, Lucas RC, Pinheiro GRG, Dias Magalhães LM, Oliveira ALG, Almeida RM, Barbosa FS, Castanheira Bartholomeu D, Bueno LL, Mendes TA, Zhan B, Jones KM, Hotez P, Bottazzi ME, Oliveira FMS, Fujiwara RT.

19-07-2023

Vaccine.

<https://pubmed.ncbi.nlm.nih.gov/37479612/>

Leishmania spp. and *Trypanosoma cruzi* are parasitic kinetoplastids of great medical and epidemiological importance since they are responsible for thousands of deaths and disability-adjusted life-years annually, especially in low- and middle-income countries. Despite efforts to minimize their impact, current prevention measures have failed to fully control their spread. There are still no vaccines available. Taking into account the genetic similarity within the Class Kinetoplastida, we selected CD8⁺ T cell epitopes preserved among *Leishmania* spp. and *T. cruzi* to construct a multivalent and broad-spectrum chimeric polyprotein vaccine. In addition to inducing specific IgG production, immunization with the vaccine was able to significantly reduce parasite burden in the colon, liver and skin lesions from *T. cruzi*, *L. infantum* and *L. mexicana* challenged mice, respectively. These findings were supported by histopathological analysis, which revealed decreased inflammation in the colon, a reduced number of degenerated hepatocytes and an increased proliferation of connective tissue in the skin lesions of the corresponding *T. cruzi*, *L. infantum* and *L. mexicana* vaccinated and challenged mice. Collectively, our results support the protective effect of a polyprotein vaccine approach and further studies will elucidate the immune profile associated with this protection. Noteworthy, our results act as conceptual proof that a single multi-kinetoplastida vaccine can be used effectively to control different infectious etiologies, which in turn can have a profound impact on the development of a new generation of vaccines.

Immunopathological investigation of a gerbil model of cutaneous leishmaniasis.

Mor B, Görmez A, Demirci B.

20-07-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37479161/>

Leishmaniasis, caused by *Leishmania* species (intracellular protozoans), is a chronic, systemic disease that causes skin (cutaneous) and internal organ infections (visceral). Its prevalence has increased in recent years. *Leishmania* species are considered important pathogens that affect public health. After infecting an individual, the pathogen

disrupts the immune system, but, there are not enough studies on which immune mechanisms are affected. The aim of this study was to establish a *Leishmania* major infection model (the causative agent of cutaneous leishmaniasis) in gerbils (*Meriones unguiculatus*) and to investigate the immune response in this model by examining the expression of important inflammatory genes (IL-1 β , IL-2, IL-6, IFN- γ and TNF- α). The presence of parasites was confirmed by microscopic examination of samples taken from the lesions and culture studies. The expression of inflammatory cytokine genes was significantly increased in infected gerbils. The changes indicated that both the Th1 and Th2 pathways are activated in cutaneous leishmaniasis infection. Hence, different immunopathological mechanisms should be evaluated in the pathogenesis of the disease.

Dogs with canine visceral leishmaniasis have a boost of extracellular vesicles and miR-21-5p up-expression.

da Cruz AB, Carneiro FM, Maia MM, Pereira IS, Taniwaki NN, Namiyama GM, Gava R, Hiramoto RM, Pereira-Chioccia VL.

20-07-2023

Parasite Immunol.

<https://pubmed.ncbi.nlm.nih.gov/37475490/>

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

Koh CC, Gollob KJ, Dutra WO.

20-07-2023

Cell Death Dis.

<https://pubmed.ncbi.nlm.nih.gov/37474501/>

Morphological and DNA-based description of *Trichophoromyia peixotoi* n. sp. (Diptera: Psychodidae), a new sand fly species from the Brazilian Amazon.

Rodrigues BL, de Souza Pinto I, Galati EAB.

19-07-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37468935/>

Background: Phlebotomine sand flies of the genus *Trichophoromyia* Barretto, 1962 are of great relevance to public health as vectors of *Leishmania* protozoans. A new phlebotomine species named *Trichophoromyia peixotoi* n. sp. is here described based on both male morphology and COI DNA barcodes. **Methods:** The sand fly specimens were collected in the Parque Nacional da Amazônia (PNA), situated in the municipality of Itaituba, state of Pará, Brazil. Morphological description was done based on 10 male specimens. Five specimens were DNA barcoded for the COI gene. **Results:** The morphological and molecular analyses allowed the delimitation of this new species from others of *Trichophoromyia*. *Trichophoromyia peixotoi* n. sp. is closely related to other species with aedeagal ducts > 4 times the length of the sperm pump, from which it may be distinguished by the gonocoxite bristles and paramere shape. **Conclusions:** The description of *T. peixotoi* n. sp.

brings the number of species of *Trichophoromyia* to 45, including 24 for Brazil. The integrative taxonomy effort through the analysis of COI barcodes proved to be effective in the species delimitation of some *Trichophoromyia* spp.

Snakes and Souks: Zoonotic pathogens associated to reptiles in the Marrakech markets, Morocco.

Mendoza-Roldan JA, Noll Louzada-Flores V, Lekouch N, Khouchfi I, Annoscia G, Zatelli A, Beugnet F, Walochnik J, Otranto D.

19-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37467211/>

Proteomic research on new urinary biomarkers of renal disease in canine leishmaniosis: Survival and monitoring response to treatment.

González MA, Barrera-Chacón R, Peña FJ, Belinchón-Lorenzo S, Robles NR, Pérez-Merino EM, Martín-Cano FE, Duque FJ.

Août-2023

Res Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/37419051/>

The objective of our study was to search for survival biomarkers (SB) and treatment response monitoring biomarkers (TRMB) in the urinary proteome of dogs with renal disease secondary to canine leishmaniosis (CanL), using UHPLC-MS/MS. The proteomic data are available via ProteomeXchange with identifier PXD042578. Initially, a group of 12 dogs was evaluated and divided into survivors (SG; n = 6) and nonsurvivors (NSG; n = 6). A total of 972 proteins were obtained from the evaluated samples. Then, bioinformatic analysis reduced them to 6 proteins like potential SB increased in the NSG, specifically, Haemoglobin subunit Alpha 1, Complement Factor I, Complement C5, Fibrinogen beta chain (fragment), Peptidase S1 domain-containing protein, and Fibrinogen gamma chain. Afterwards, SG was used to search for TRMB, studying their urine at 0, 30, and 90 days, and 9 proteins that decreased after treatment were obtained: Apolipoprotein E, Cathepsin B, Cystatin B, Cystatin-C-like, Lysozyme, Monocyte differentiation CD14, Pancreatitis-associated precursor protein, Profilin, and Protein FAM3C. Finally, enrichment analysis provided information about the biological mechanisms in which these proteins are involved. In conclusion, this study provides 15 new candidate urinary biomarkers and an improved understanding of the pathogenesis of kidney disease in CanL.

Smartphone-readable RPA-LFA for the high-sensitivity detection of *Leishmania* kDNA using nanophosphor reporters.

Danthanarayana AN, Nandy S, Kourentzi K, Vu B, Shelite TR, Travi BL, Brgoch J, Willson RC.

03-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37399214/>

Co-expression analysis of lncRNA and mRNA suggests a role for ncRNA-mediated regulation of host-parasite interactions in primary skin lesions of patients with American tegumentary leishmaniasis.

Almeida MC, Felix JS, Lopes MFDS, de Athayde FRF, Troiano JA, Scaramele NF, Furlan AO, Lopes FL.

Sept-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37302689/>

Leishmaniasis, caused by different *Leishmania* species, manifests as cutaneous or visceral forms. In the American continent, the cutaneous form is called American tegumentary leishmaniasis (ATL) and is primarily caused by *Leishmania (Viannia) braziliensis*. Mucosal leishmaniasis (ML), the most severe form of ATL, arises in approximately 20% of patients from a primary cutaneous lesion. Evidence indicates changes in overall expression patterns of mRNAs and lncRNAs of the host in response to *Leishmania* infection, with the parasite capable of modulating host immune response, which may contribute to disease progression. We evaluated whether the co-expression of lncRNAs and their putative target mRNAs in primary cutaneous lesions of patients with ATL could be associated with the development of ML. Previously available public RNA-Seq data from primary skin lesions of patients infected with *L. braziliensis* was employed. We identified 579 mRNAs and 46 lncRNAs differentially expressed in the primary lesion that subsequently progressed to mucosal disease. Co-expression analysis revealed 1324 significantly correlated lncRNA-mRNA pairs. Among these, we highlight the positive correlation and trans-action between lncRNA SNHG29 and mRNA S100A8, both upregulated in the ML group. S100A8 and its heterodimeric partner S100A9 form a pro-inflammatory complex expressed by immune cells and seems to participate in host innate immune response processes of infection. These findings expand the knowledge of the *Leishmania*-host interaction and indicate that the expression of lncRNAs in the primary cutaneous lesion could regulate mRNAs and play roles in disease progression.

Regiospecific Reduction of 4,6-Dinitrobenzimidazoles: Synthesis, Characterization, and Biological Evaluation.

Abouelhaoul EA, El Kihel A, Ahbala M, Sdassi H, Köhler LHF, Bauchat P, Roisnel T, Khan TA, Al Nasr IS, Koko WS, Schobert R, Biersack B.

Juil-2023

Chem Biodivers.

<https://pubmed.ncbi.nlm.nih.gov/37294393/>

The regiospecific reduction of 4,6-dinitrobenzimidazole derivatives leading to the corresponding 4-amino-6-nitrobenzimidazoles was studied. The identification of the formed product structures was accomplished by spectroscopic and X-ray diffraction data. The anticancer and antiparasitic activities of the synthesized compounds were examined, and promising activities against *Toxoplasma gondii* and *Leishmania* major parasites were

discovered for certain 4,6-dinitrobenzimidazoles in addition to moderate anticancer activities of the 4-amino-6-nitrobenzimidazole derivatives against *T. gondii* cells. However, the tumor cell experiments revealed a promising sensitivity of p53-negative colon cancer cells to these compounds.

Antiproliferative Activity and Ultrastructural Changes in Promastigote and Amastigote forms of *Leishmania amazonensis* Caused by Limonene-Acylthiosemicarbazide Hybrids.

Graça Contato A, Kaplum V, Botura Scariot D, Pelegrin Garcia F, Falzirolli H, Vandresen F, Ueda-Nakamura T, de Oliveira Silva S, Conceição da Silva C, Vataru Nakamura C.

Jul-2023

Chem Biodivers.

<https://pubmed.ncbi.nlm.nih.gov/37263974/>

Leishmaniasis is a tropical zoonotic disease. It is found in 98 countries, with an estimated 1.3 million people being affected annually. During the life cycle, the *Leishmania* parasite alternates between promastigote and amastigote forms. The first line treatment for leishmaniasis are the pentavalent antimonials, such as N-methylglucamine antimoniate (Glucantime®) and sodium stibogluconate (Pentostam®). These drugs are commonly related to be associated with dangerous side effects such as cardiotoxicity, nephrotoxicity, hepatotoxicity, and pancreatitis. Considering these aspects, this work aimed to obtain a new series of limonene-acylthiosemicarbazides hybrids as an alternative for the treatment of leishmaniasis. For this, promastigotes, axenic amastigotes, and intracellular amastigotes of *Leishmania amazonensis* were used in the antiproliferative assay; J774-A1 macrophages for the cytotoxicity assay; and electron microscopy techniques were performed to analyze the morphology and ultrastructure of parasites. ATZ-S-04 compound showed the best result in both tests. Its IC₅₀, in promastigotes, axenic amastigotes and intracellular amastigotes was 0.35±0.08 µM, 0.49±0.06 µM, and 15.90±2.88 µM, respectively. Cytotoxicity assay determined a CC₅₀ of 16.10±1.76 µM for the same compound. By electron microscopy, it was observed that ATZ-S-04 affected mainly the Golgi complex, in addition to morphological changes in promastigote forms of *L. amazonensis*.

Green Synthesis of Molecules for the Treatment of Neglected Diseases.

Anghinoni JM, Dilelio MC, Shiguemoto CYK, Schumacher RF, Baroni ACM, Lenardão EJ.

2023

Curr Top Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/37246323/>

An anti-leishmanial compound 4',7-dihydroxyflavone elicits ROS-mediated apoptosis-like death in *Leishmania* parasite.

Sasidharan S, Saudagar P.

Jul-2023

FEBS J.

<https://pubmed.ncbi.nlm.nih.gov/36871140/>

Lèpre

Recurrent Genital Herpes Triggering Ulcerative Pyoderma Gangrenosum.

Deoghare S, Gupta S, Pol D, Masare A, Kumar A.

25-06-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37503492/>

Pyoderma gangrenosum (PG) is a neutrophilic dermatosis that presents as painful, rapidly growing skin ulcers with undermined edges and a violaceous, ragged border at the periphery and is non-responsive to conventional treatments. The average onset age is in the fourth decade, with a female preponderance. Genital PG is uncommon and may present singly or coexist with common sexually transmitted genital ulcerative diseases, which causes delays in the diagnosis and treatment of genital PG, thereby adding to the morbidity. Here, we highlight a case of non-healing genital ulcers that did not respond to conventional antibiotic treatment and aggravated each month with menstruation. In this case, menstruation acted as a trigger factor for the development of a herpes genital infection. The latter acts as a pathergy for the monthly aggravation of genital PG. The patient responded to treatment with anti-viral medications and immunosuppressive medications.

A Clinicoepidemiological Study of Cutaneous and Systemic Comorbidities of Seborrheic Dermatitis in Adolescent and Adult Females.

T S R, Waikhom S, K SK, Reddy ME.

26-06-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37503468/>

Factors affecting treatment adherence among leprosy patients: Perceptions of healthcare providers.

Pepito VCF, Loreche AM, Samontina RED, Abdon SJA, Fuentes DNL, Saníel OP.

06-07-2023

Heliyon.

<https://pubmed.ncbi.nlm.nih.gov/37501956/>

Background: Treatment adherence is a vital aspect in the management of chronic diseases like leprosy; however, most studies on treatment adherence focus on patients. This study aims to examine the perceptions of healthcare providers on factors that can promote or prevent patients from adhering to treatment. **Methods:** We conducted three focus group discussions (FGDs) with healthcare providers who have at least one year experience in managing leprosy in three large leprosy case-holding hospitals in Metro Manila, Philippines. We audio-recorded, transcribed, translated the FGD proceedings,

and analyzed the transcripts thematically to identify patient-intrinsic and patient-extrinsic enablers and barriers to treatment adherence of leprosy patients.

Results: Patient-intrinsic motivators to complete treatment include innate desire to be cured, fear of infecting family and friends, fear of disability, good knowledge about the disease, need for medical clearance to be considered fit to work, and experiencing leprosy reactions. Patient-extrinsic motivators to complete treatment include free treatment, immediate and sufficient counselling, flexibility in treatment, follow-up and motivation of healthcare workers, and presence of Hansen's Club and support groups. Patient-intrinsic barriers to good treatment adherence include distance between residence and hospital, financial and opportunity costs, adverse drug reactions, misconceptions about being cured, disabilities and presence of leprosy reactions, stubbornness and/or laziness, and undergoing clinical depression. Patient-extrinsic barriers to good treatment adherence include poor availability of MDT, transfer to other leprosy treatment facilities without informing current facility, and stigma. **Conclusion:** Healthcare providers perceive that patient-intrinsic and patient-extrinsic factors influence the treatment adherence of leprosy patients through different mechanisms. We highlight the role of healthcare provider attitudes, stigma, and support groups in promoting treatment adherence.

Comparative Study of Combination of Oral Tranexamic Acid With Modified Kligman's Formula Versus Oral Tranexamic Acid With Azelaic Acid 15% in the Treatment of Melasma.

Singh R, Maheshwari P, Madke B, Singh A, Jawade S.

24-06-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37496546/>

Background Melasma is a persistent skin condition affecting individuals of Asian, African, and Hispanic backgrounds. It causes dark patches on sun-exposed areas of the face. The exact causes are unclear, but UV light and hormonal factors play a role. Melasma significantly impacts physical appearance and quality of life, causing emotional and social distress. Objective The objective was to compare the efficacy of a combination of oral tranexamic acid and modified Kligman's formula vs. oral tranexamic acid and 15% azelaic acid. Material and methods This two-year interventional study occurred at the Outpatient Department of Dermatology, Venereology, and Leprosy in Sawangi, Maharashtra. It included male and female patients aged 18-50 with melasma seeking treatment. Ethical approval was obtained, and data collection involved medical histories, skin examinations, and calculating the Melasma Area and Severity Index (MASI). Results The study found no significant association between age groups and subject distribution in Groups A and B. Significant differences were observed in MASI scores within each group over time. There was a significant difference in mean MASI scores between Group A and Group B at the eight-week mark. A burning sensation was significantly associated with the groups, while no significant association was found for erythema. Conclusion

This study concludes that combining oral tranexamic acid with a modified Kligman's formula is more effective in treating melasma than combining oral tranexamic acid with azelaic acid 15%.

Use of tofacitinib in baricitinib-refractory atopic dermatitis: An example of JAK inhibitor switching.

Dhir B, Meena SK, Sardana K, Sharath S.

26-07-2023

Pediatr Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/37495552/>

Leprosy in the Upper Midwest.

Bach K, Hinshaw MA, Shields BE.

Jul-2023

WMJ.

<https://pubmed.ncbi.nlm.nih.gov/37494653/>

Clinical standards for drug-susceptible TB in children and adolescents.

Chiang SS, Graham SM, Schaaf HS, Marais BJ, Sant'Anna CC, Sharma S, Starke JR, Triasih R, Achar J, Amanullah F, Armitage LY, Aurilio RB, Buck WC, Centis R, Chabala C, Cruz AT, Demers AM, du Preez K, Enimil A, Furin J, Garcia-Prats AJ, Gonzalez NE, Hoddinott G, Isaakidis P, Jaganath D, Kabra SK, Kampmann B, Kay A, Kitai I, Lopez-Varela E, Maleche-Obimbo E, Malaspina FM, Velásquez JN, Nuttall JJC, Oliwa JN, Andrade IO, Perez-Velez CM, Rabie H, Seddon JA, Sekadde MP, Shen A, Skrahina A, Soriano-Arandes A, Steenhoff AP, Tebruegge M, Tovar MA, Tsogt B, van der Zalm MM, Welch H, Migliori GB.

01-08-2023

Int J Tuberc Lung Dis.

<https://pubmed.ncbi.nlm.nih.gov/37491754/>

BACKGROUND: These clinical standards aim to provide guidance for diagnosis, treatment, and management of drug-susceptible TB in children and adolescents. **METHODS:** Fifty-two global experts in paediatric TB participated in a Delphi consensus process. After eight rounds of revisions, 51/52 (98%) participants endorsed the final document. **RESULTS:** Eight standards were identified: Standard 1, Age and developmental stage are critical considerations in the assessment and management of TB; Standard 2, Children and adolescents with symptoms and signs of TB disease should undergo prompt evaluation, and diagnosis and treatment initiation should not depend on microbiological confirmation; Standard 3, Treatment initiation is particularly urgent in children and adolescents with presumptive TB meningitis and disseminated (miliary) TB; Standard 4, Children and adolescents should be treated with an appropriate weight-based regimen; Standard 5, Treating TB infection (TBI) is important to prevent disease; Standard 6, Children and adolescents should receive home-based/community-based treatment support whenever possible; Standard 7, Children, adolescents, and their families should be provided age-appropriate support to optimise engagement in care and clinical outcomes; and Standard 8, Case reporting and contact tracing should be conducted for each child and adolescent. **CONCLUSION:** These

consensus-based clinical standards, which should be adapted to local contexts, will improve the care of children and adolescents affected by TB.

Use of stool swabs in molecular transport media increases access to Xpert Ultra testing for TB in children.

Chibolela M, de Haas P, Klinkenberg E, Kosloff B, Chunda-Liyoka C, Lungu P, Chabala C.

01-08-2023

Int J Tuberc Lung Dis.

<https://pubmed.ncbi.nlm.nih.gov/37491746/>

Leprosy misdiagnosed as chronic Urticaria in a migrant.

Magnaterra E, Scandagli I, Zuccaro B, Maio V, Simi S, Massi D, Fiallo P, Francalanci S, Difonzo E, Pisano L.

25-07-2023

J Travel Med.

<https://pubmed.ncbi.nlm.nih.gov/37490396/>

A Sri Lankan man presents with the suspicion of chronic idiopathic urticaria with angioedema, but facial swelling leads to an unexpected discovery. Thickened skin, nodules, and neurological symptoms reveal the true culprit. Leprosy challenges diagnosis in nonendemic regions. Vigilance and comprehensive assessment are crucial to unmask this great imitator.

Evaluation of 2 Artificial Intelligence Software for Chest X-Ray Screening and Pulmonary Tuberculosis Diagnosis: Protocol for a Retrospective Case-Control Study.

Mohd Hisham MF, Lodz NA, Muhammad EN, Asari FN, Mahmood MI, Abu Bakar Z.

25-07-2023

JMIR Res Protoc.

<https://pubmed.ncbi.nlm.nih.gov/37490330/>

Genodermatoses Picture: Difficulties Faced And Way Forward in Nepal.

Parajuli N, Baskota R, Jain R.

20-06-2023

J Nepal Health Res Counc.

<https://pubmed.ncbi.nlm.nih.gov/37489694/>

Genodermatoses are group of genetic disorders that present with cutaneous manifestations. The exact prevalence on many of these conditions are unknown due to its rarity, need of specialized tests for diagnosis and lack of proper reporting system. Most of the patients are faced with life-long disability and associated stigma. There is a need for specialized centers for proper diagnosis of these conditions and a very elaborated yet simple reporting system in Nepal. These rare conditions should be kept in priority by the government in align with the sustainable development goals to ensure healthy-lives and promote well-being for all. A wider engagement of patient-led support groups might be useful in providing necessary information on the disease to the general population and alleviate the stigma associated with these diseases.

Keywords: Epidermolysis bullosa; genodermatoses; rare diseases; Nepal.

The effect of an oral product containing Amla fruit (*Phyllanthus emblica* L.) on female androgenetic alopecia: A randomized controlled trial.

Akhbari M, Firooz A, Rahimi R, Shirzad M, Esmaealzadeh N, Shirbeigi L.

22-07-2023

J Ethnopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37487962/>

Ethnopharmacological relevance: Amla (*Phyllanthus emblica*) fruit has been emphasized as a hair tonic in Traditional Persian Medicine (TPM) and recommended for hair loss orally and topically. **Aim of the study:** This study aimed to investigate the effect of an oral product containing Amla fruit on Female Androgenetic Alopecia (FAGA). **Materials and methods:** This study was a triple-blind, randomized, controlled clinical trial. Sixty women with FAGA were randomly assigned into two groups of thirty. The intervention group received ten cc Amla syrup thrice a day for 12 weeks. The second group received a placebo with the same dose and duration. Hair growth parameters were analyzed using TrichoScan before and after 12 weeks of intervention. Physician and patient satisfaction were assessed using the CGI-I and PGI-I questionnaires, respectively. **Results:** Twenty-seven participants in the intervention group and 25 in the placebo group completed the trial. Based on our findings, the anagen-to-telogen ratio increased significantly in the intervention group compared with the group who received placebo ($F = 10.4$, $P = 0.002$). Physician and patient satisfaction increased in the amla group compared with placebo at 12th weeks of intervention ($P < 0.001$), ($P < 0.001$). The formula had no remarkable side effects. Only one case of mild constipation was reported in one of the participants after one month of consuming Amla syrup. **Conclusion:** The results of this study demonstrated that Amla syrup could help treat androgenic hair loss in women and increase the anagen phase. Further studies are needed to evaluate this potential treatment for FAGA.

Case Report of Leprosy in Central Florida, USA, 2022.

Bhukhan A, Dunn C, Nathoo R.

Aug-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37486691/>

Rituximab in Pemphigus Vulgaris: A Review of Monoclonal Antibody Therapy in Dermatology.

Khandelwal K, Jajoo V, Bajpai K, Madke B, Prasad R, Wanjari MB, Munjewar PK, Taksande AB.

21-07-2023

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/37485224/>

Catastrophic ocular complications in leprosy: a case report.

Ganjre SA, Jeria S, Madke B.

24-04-2023

Pan Afr Med J.

<https://pubmed.ncbi.nlm.nih.gov/37484589/>

Leprosy is a chronic, granulomatous infectious disease commonly affecting the skin, nerves, mucosa and eyes. The stigma associated with the disease frequently leads to delay in presentation to health professionals. Treated patients, though considered cured presumptively, many continue to live with physical disabilities and deformities. Intact visual acuity prevents humans from trauma and any reduction in visual acuity, especially in leprosy, increases the risk of getting injured by many folds. Here, we present a case of leprosy with complete loss of vision due to bilateral anterior staphyloma secondary to keratitis and his physical deformities preventing him to take care of his eyes. This paper aims to emphasize on the importance of a baseline ophthalmology consultation in all newly diagnosed leprosy patients and repeat examination at onset of any new symptoms of the eye.

Nonvascularized Double Metatarsal Transfer After Excision of Epithelioid Hemangioma of Hand: A Case Report.

Raj Pallapati SC, Joyson D R K, Kiran Sasi P, Thomas BP, Prabhu AJ.

21-07-2023

JBJS Case Connect.

<https://pubmed.ncbi.nlm.nih.gov/37478334/>

Single-cell sequencing analysis reveals development and differentiation trajectory of Schwann cells manipulated by *M. leprae*.

Ma S, Mi Z, Wang Z, Sun L, Liu T, Shi P, Wang C, Xue X, Chen W, Wang Z, Yu Y, Zhang Y, Bao F, Wang N, Wang H, Xia Q, Liu H, Sun Y, Zhang F.

21-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37478057/>

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

Xu CY, Peng W.

2-05-2023

Zhonghua Yi Shi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/37474336/>

The North of Jiangsu was a traditional area for leprosy in Chinese history. In the period of the Republic of China, one of the largest leprosy clinics in China was established in Ru Gao (Jugao) with the help of Chinese and foreign charitable organizations, the Chinese central government and some squires. It was the only large clinic for leprosy in the North of Jiangsu. It was officially opened in 1924, attached to the Presbyterian Church hospital, and was closed in 1927 after the breakout of the civil war. It reopened in May 1933, hosted by a leprologist, Lee S.

Huizenga. Ru Gao (Jugao) leprosy clinic treated around 1,000 lepers in the North of Jiangsu with medicines and language communication. The establishment of the leprosy clinic made a historical contribution in terms of preventing leprosy from spreading to Shanghai. It closed in the spring of 1938 because of the invasion of the Japanese military.

Predictors of mortality among drug-resistant tuberculosis patients in Kaduna State, Nigeria.

Oyefabi AM, Tobin West CI, Ameh S, Jiya EN, Sadiq A, Dauda H, Onoh M.

Juin-2023

Niger J Clin Pract.

<https://pubmed.ncbi.nlm.nih.gov/37470659/>

Background: Specific death due to DR-TB has significantly contributed to tuberculosis (TB) mortality and overall global deaths. **Aim:** This study examines the predictors of mortality among DR-TB patients in Kaduna State, Nigeria. **Subject and method:** This was a retrospective longitudinal study of DR-TB mortality carried out among 370 DR-TB patients from the 23 LGAs in Kaduna State. It involves a retrospective review of the MDR-TB records of the patients over a period of 10 years (2012-2021). Demographic and clinical data of all DR-TB patients enrolled in Kaduna State, Nigeria, between April 1, 2012, and March 31, 2021, were used. Survival analysis was performed with SPSS version 25, using Kaplan-Meier and Cox proportional hazard regression modeling, at 5% significance level. **Results:** The majority of the patients, 255 (68.9%), were below the age of 40 years, while 53 (14.3%) of the patients died within the study period. Most deaths 26 (49.1%) were associated with HIV co-infection and the disease severity. Results for the Cox proportional model show that there was a significantly lower risk of death when a patient had MDR-TB compared to pre-XDR-TB (adjusted hazard ratio, AHR = 0.34, 95% CI = 0.16-0.72, P = 0.04). Both models show that age, sex, residence, or year of treatment had no significant association with survival or death. **Conclusion:** HIV co-infection and DRTB with progression to more resistant and difficult-to-treat strains contributed to higher deaths. There is a need for concerted efforts from all DR-TB stakeholders to control the disease.

The elimination of trachoma as a public health problem in Togo: Successes and challenges.

Bakoubayi AW, Gadah DAY, Gnossike P, Zida-Compaore WIC, Bando PP, Alaglo K, Tchalim M, Patchali P, Bitty-Anderson A, Ekouevi DK.

18-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37463175/>

Background: As of May 2022, 15 countries have declared that they have reached their trachoma elimination targets, but only 13 of them, including Togo, have been validated by the World Health Organization as having eliminated the disease as a public health problem. The aim of this study was to describe the broad interventions that have

supported the elimination of trachoma as a public health problem in Togo from its inception in 2006 to the validation of its elimination in 2022. **Method:** A review and compilation of data and information contained in the country's submission to World Health Organization for validation of trachoma elimination as a public health problem was conducted. Data from national and local surveillance systems and reports on actions taken after achieving the elimination target were also included. **Results:** Togo has achieved the elimination of trachoma as a public health problem by 2022. The prevalence of follicular trachoma among children aged 1-9 years is <5% in all nationally defined administrative units suspected of having trachoma after stopping mass treatment for at least 2 years. The prevalence of trichiasis among persons aged 15 years and older is less than 0.2% in all administrative units previously endemic for trachoma and evidence of the ability to manage incident cases of emerging trichiasis in the community has been demonstrated. The key of the success in the elimination process was primarily the political commitment of the health authorities with financial and technical support from various international organizations. **Conclusion:** The elimination of trachoma as a public health problem in Togo is a real success story that can serve as an example for the elimination of other neglected tropical diseases in Africa. But regular monitoring and surveillance is essential to avoid the re-emergence of such disease in the country.

TLR7/8 stress response drives histiocytosis in SLC29A3 disorders.

Shibata T, Sato R, Taoka M, Saitoh SI, Komine M, Yamaguchi K, Goyama S, Motoi Y, Kitaura J, Izawa K, Yamauchi Y, Tsukamoto Y, Ichinohe T, Fujita E, Hiranuma R, Fukui R, Furukawa Y, Kitamura T, Takai T, Tojo A, Ohtsuki M, Ohto U, Shimizu T, Ozawa M, Yoshida N, Isobe T, Latz E, Mukai K, Taguchi T, Hemmi H, Akira S, Miyake K.

04-09-2023

J Exp Med.

<https://pubmed.ncbi.nlm.nih.gov/37462944/>

Skin Lesions, Foot Drop, and Hand Contractures.

Filley AR, Saad S, Altman K.

18-07-2032

JAMA.

<https://pubmed.ncbi.nlm.nih.gov/37389854/>

Tolerability and efficacy assessment of an oral collagen supplement for the improvement of biophysical and ultrasonographic parameters of skin in middle eastern consumers.

Samadi A, Movaffaghi M, Kazemi F, Yazdanparast T, Ahmad Nasrollahi S, Firooz A.

Août-2023

J Cosmet Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36912494/>

Background: Topical skin care products often do not reach the deeper layers of the skin, and oral hydrolyzed collagen

is one of the newest and most popular systemic supplementations for skin rejuvenation. However, there are limited information in case of Middle Eastern consumers **OBJECTIVE:** The purpose of this study was to evaluate the tolerability and efficacy of an oral collagen supplement for improvement of skin elasticity, hydration, and roughness in Middle Eastern consumers. **Methods and materials:** It was a 12-week, before-after clinical study, conducted on 20 participants (18 women and 2 men) aged 44.15 ± 5.36 years with skin type III-IV. Skin elasticity parameters (R0, R2, R5, and R7), skin hydration and friction, as well as the thickness and echo density of the dermis, were measured after six and 12 weeks daily intake of the study product, as well as 4 weeks after stopping its use (week 16). Participants' satisfaction was assessed on the basis of their answers to the standard questionnaire, and tolerability of the product was assessed by monitoring the adverse effects. **Results:** A significant improvement was detected in R2, R5, and skin friction at week 12 (p-values 0.041, 0.012 and <0.01, respectively). At week 16, the values remained at an increased level, which indicates the persistence of the results. The increase of dermis density in week 16 was also significant (p-value = 0.03). Moderate overall satisfaction was reported with the treatment, and a few gastrointestinal complications were reported. **Conclusion:** The study demonstrated that oral collagen peptides could significantly improve the skin elasticity, roughness, and dermis echo density, and they also proved to be safe and well-tolerated.

Altered levels of lymphocyte enhancer-binding factor-1 modulates the pigmentation in acral and non-acral lesions of non-segmental vitiligo patients: a follow-up-based study in North India.

Nayak D, Srivastava N, Dev A, Bishnoi A, Kumaran MS, Vinay K, Parsad D.

Sept-2023

Arch Dermatol Res.

<https://pubmed.ncbi.nlm.nih.gov/36877308/>

Morsures de serpent

Evaluation of Saxifraga stolonifera phenolic extracts as a potential antivenom against Deinagkistrodon acutus venom: In vitro and in vivo studies.

Liu ZT, Zhang Y, Fang R, Simmonds M, Zhang XJ, Zhang TT, Sun TT, Chen XQ.

24-07-2023

J Ethnopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37495028/>

Compartment Syndrome Secondary to Bothrops spp. Envenomation in Triângulo Mineiro, Region, Minas Gerais, Brazil.

Toffano LL, Silva LOD, Neves FF, Teixeira LAS, Silva-Vergara ML.

24-07-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/37493738/>

Background: Snakebite is a neglected global health problem with high morbidity. We describe compartment syndrome (CS) cases related to snakebites by Bothrops spp. **Methods:** The medical records of patients admitted with snakebites envenomation were reviewed. **Results:** Of 47 patients with Bothrops spp. envenomation (4 male; mean age: 42 years), 7 (15%) developed CS. The mean time to antivenom administration was 9.5 hours. The time to fasciotomy was variable. Seven patients developed infection and four had acute kidney injury. **Conclusions:** The incidence of CS is higher than that reported previously. This may be due to the clinical severity and long delay before administering antivenom.

Snake envenomation in three cats in South Korea.

Lee JM, Park MK, Lee GP, Song JH, Song KH.

21-07-2023

JFMS Open Rep.

<https://pubmed.ncbi.nlm.nih.gov/37492185/>

Case series summary: Three cats in South Korea were diagnosed with snake envenomation based on the appearance and location of bite wounds. Two cats were envenomed by the *Gloydus* species and one by an unidentified species. Clinical signs were detected, including local bite-site swelling, haemorrhagic discharge and necrosis. All three cats were given supportive treatment. An antivenom was administered to one cat, and the cat showed no adverse reactions. All cats survived, but skin necrosis remained a complication of the snake envenomation. This was observed during the 1-year follow-up period. **Relevance and novel information:** Cats with snake envenomation are extremely rare in South Korea, and information regarding clinical details are limited. This study is the first to describe the clinical details and prognosis of feline snake envenomation in South Korea.

Timber rattlesnake (*Crotalus horridus*): Biology, conservation, and envenomation in the Upper Mississippi River Valley (1982-2020).

Keyler DE.

30-06-2023

Toxicon X.

<https://pubmed.ncbi.nlm.nih.gov/37483845/>

Community members and healthcare workers' priorities for the control and prevention of snakebite envenoming in Ghana.

Aglanu LM, Amuasi JH, Prokesh E, Beyuo A, Dari CD, Ravensbergen SJ, Agbogbatey MK, Adobasom-Anane AG, Abass KM, Lalloo DG, Blessmann J, Kreuels B, Stienstra Y.

21-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37478151/>

Antivenom preclinical efficacy testing against Asian snakes and their availability in Asia: A systematic review.

Soopairin S, Patikorn C, Taychakhoonavudh S.

19-07-2023

PLoS One.

<https://pubmed.ncbi.nlm.nih.gov/37467278/>

Background: Cross-neutralizing strategy has been applied to improve access to antivenoms, a key to reducing mortality and disability of snakebite envenoming. However, preclinical studies have been conducted to identify antivenoms' cross-neutralizing ability when clinical studies may not be considered ethical. Therefore, this study aimed to identify and summarize scattered evidence regarding the preclinical efficacy of antivenoms against Asian snakes. **Methodology/principle findings:** In this systematic review, we searched for articles published until May 30, 2022, in PubMed, Scopus, Web of Science, and Embase. Preclinical studies that reported the available antivenoms' neutralizing ability against Asian snake lethality were included. Quality assessment was performed using the Systematic Review Centre for Laboratory animal Experimentation's risk of bias tool and the adapted the Animal Research Reporting In Vivo Experiments guidelines. The availability of effective antivenoms against Asian snakes was analyzed by comparing data from included studies with snakebite-information and data platforms developed by the World Health Organization. Fifty-two studies were included. Most studies assessed the antivenom efficacy against snakes from Southeast Asia (58%), followed by South Asia (35%) and East Asia (19%). Twenty-two (49%) medically important snakes had antivenom(s) with confirmed neutralizing ability. Situation analyses of the availability of effective antivenoms in Asia demonstrated that locally produced antivenoms did not cover all medically important snakes in each country. Among countries without local antivenom production, preclinical studies were conducted only in Bangladesh, Sri Lanka, and Malaysia. Risk of bias assessment was limited in some domains because of unreported data. **Conclusions/significance:** Cross-neutralizing of antivenoms against some medically important snakes in Asia was confirmed. This strategy may improve access to geographically effective antivenoms and bypass investment in novel antivenom development, especially in countries without local antivenom production. A database should be developed to aid the development of a snakebite-information system.

Snakebite envenomations and access to treatment in communities of two indigenous areas of the Western Brazilian Amazon: A cross-sectional study.

de Farias AS, Gomes Filho MR, da Costa Arévalo M, Cristino JS, Farias FR, Sachett A, Silva-Neto AV, de

Carvalho FG, Ambrosio SA, da Silva Carvalho E, Lacerda M, Murta F, Machado VA, Wen FH, Monteiro W, Sachett J.

13-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37440596/>

Background: The indigenous populations of Brazil present poor health indicators and a disproportionate prevalence and case-fatality rate of neglected tropical diseases, including snakebite envenomations (SBEs). This study aims to estimate access to medical care for SBEs and analyze the barriers that prevent victims from accessing healthcare in indigenous communities in two health districts located in the Western Brazilian Amazon.

Methodology/principal findings: This cross-sectional study used semi-structured interviews to collect data from individuals who experienced SBEs in the Upper Rio Solimões and Upper Rio Negro indigenous health districts. Of the 187 participants, 164 (87.7%) reported that they had access to healthcare and received assistance in a hospital in the urban area of the municipalities. Frequency was 95.4% in the Upper Rio Solimões SIHD, and 69.6% in the Upper Rio Negro SIHD ($P < 0.0001$). The study found that the availability of indigenous medicine as the only choice in the village was the main reason for not accessing healthcare (75%), followed by a lack of financial resources and means of transportation (28.1%). Four deaths were reported from SBEs, resulting in a case-fatality rate of 2.1%. **Conclusions/significance:** In the study areas, there are records of SBE patients who did not receive medical attention. Availability of pre-hospital emergency transport using motorboats, a greater number of hospitals and better navigability of the Solimões River and its tributaries would make access easier for indigenous people living in the region of the Upper Solimões River. The implementation of cross-cultural hospital care needs to be considered in order to reduce the resistance of indigenous populations in relation to seeking treatment for SBEs.

Posterior Reversible Leucoencephalopathy Syndrome: Case Series, Comments, and Diagnostic Dilemma.

Chaudhuri J, Basu S, Roy MK, Chakravarty A.

August-2023

Curr Neurol Neurosci Rep.

<https://pubmed.ncbi.nlm.nih.gov/37378723/>

Acute Demyelination Following Snake Bite - An Unusual Complication.

Kalpana S, Ravi S, Muthu T.

August-2023

Indian J Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/37249832/>

Mycétome

The critical state of children's health during the Sudan crisis.

Aborode AT, Fasawe AS, Agwuna FO, Badri R, Adewunmi RO.

August-2023

Lancet Child Adolesc Health.

<https://pubmed.ncbi.nlm.nih.gov/37331357/>

Pian

Rapid Serologic Test for Diagnosis of Yaws in Patients with Suspicious Skin Ulcers.

Suñer C, John LN, Houineï W, Ubals M, Ouchi D, Alemany A, Galván-Casas C, Marks M, Mitjà O, Vall-Mayans M, Beiras CG.

August-2023

Emerg Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37486318/>

The Chembio DPP (Dual Path Platform) Syphilis Screen & Confirm kit (<https://chembio.com>) is a rapid serologic test that can be used to diagnose yaws. We evaluated its capacity to detect patients with ulcers that tested PCR positive for *Treponema pallidum* subsp. *pertenue*. DPP detected 84% of ulcers that were positive by PCR.

Rage

Using One Health assessments to leverage endemic disease frameworks for emerging zoonotic disease threats in Libya.

Miller LN, Elmselati H, Fogarty AS, Farhat ME, Standley CJ, Abuabaid HM, Zorgani A, Elahmer O, Sorrell EM.

26-07-2023

PLOS Glob Public Health.

<https://pubmed.ncbi.nlm.nih.gov/37494334/>

Continued emergence, re-emergence and spread of zoonotic diseases demonstrates the imperative need for multisectoral communication and joint coordination of disease detection and response. While there are existing international frameworks underpinning One Health capacity building for pandemic prevention and response, often guidance does not account for challenges faced by countries undergoing long-term conflict and sociopolitical instability. The purpose of this research was to identify Libya's laboratory and surveillance networks and routes of inter- and multisectoral communication and coordination for priority zoonotic diseases. The One Health Systems Assessment for Priority Zoonoses (OH-SAPZ) tool is an established methodology that was adapted and applied to the Libyan context to support prioritization of zoonotic diseases, development of systems map schematics outlining networks of communication and coordination, and analysis of operations for targeted capacity building efforts. Five zoonotic diseases were selected to undergo assessment: highly pathogenic avian influenza, brucellosis, Rift Valley fever, leishmaniasis and rabies. Through decisive acknowledgement of Libya's unique health setting, we mapped how patient and sample information is both communicated within and between the human,

animal and environmental health sectors, spanning from local index case identification to international notification. Through our assessment we found strong communication within the public and animal health sectors, as well as existing multisectoral coordination on zoonotic disease response. However, local-level communication between the sectors is currently lacking. Due to the ongoing conflict, resources (financial and human) and access have been severely impacted, resulting in limited laboratory diagnostic capacity and discontinued disease prevention and control measures. We sought to identify opportunities to leverage existing operations for endemic diseases like brucellosis for emerging zoonotic threats, such as Rift Valley fever. Analysis of these operations and capabilities supports the development of targeted recommendations that address gaps and may be used as an implementation guide for future One Health capacity building efforts.

Characterization of a human-mouse chimeric monoclonal antibody targeting rabies virus glycoprotein.

Cai M, Hu Z, Yang Y, Mao T, Liu Y, Lu G, Yang F, Qi J, Huang W, Wang Y.

Jul-2023

J Med Virol.

<https://pubmed.ncbi.nlm.nih.gov/37493180/>

At present, the horse or human rabies immunoglobulin (RIG) used for postexposure prevention of human rabies (PEP) has high cost and limited availability. It is strongly encouraged to replace RIG with equivalent or more effective and safer products. Mouse and human monoclonal antibodies have been shown to protect rodents from lethal rabies virus (RABV) attacks. In this study, we reported a human-mouse chimeric monoclonal antibody, 12-2A12, which showed a strong neutralization potency and a wide breadth against multiple street viruses of RABV *in vitro*. The antibody binded the viral glycoprotein (G) with nanomolar affinity. The complex structure of 12-2A12 bound to RABV G revealed that the antibody recognizes an epitope that partially overlaps with the recognition region for the nicotinic acetylcholine receptor (nAChR). The antibody therefore would interfere with the nAChR/G interaction to block the viral receptor binding. In addition, comparison of our complex structure with the G structure in the acidic state reveals a clear steric clash, highlighting that the antibody would further prevent the conformational changes of the viral glycoprotein that are essential for membrane fusion. In light of these functional and structural data, we believe that 12-2A12 might be developed to be included in an antibody cocktail for potential use in human rabies PEP.

Active safety surveillance of rabies monoclonal antibody and rabies vaccine in patients with category III potential rabies exposure.

Kang G, Lakhkar A, Bhamare C, Dharmadhikari A, Narwadkar J, Kanujia A, Kapse D, Gunale B, Poonawalla CS, Kulkarni PS.

16-05-2023

Lancet Reg Health Southeast Asia.

<https://pubmed.ncbi.nlm.nih.gov/37492421/>

Cryptic species *Hydatigera kamiyai* and other taeniid metacestodes in the populations of small mammals in Serbia.

Miljević M, Rajičić M, Umhang G, Bajić B, Bjelić Čabrilo O, Budinski I, Blagojević J.

25-07-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37491284/>

Background: *Hydatigera* (Cestoda: Taeniidae) is a recently resurrected genus with the description of a new species, *Hydatigera kamiyai*, a cryptic entity within the *Hydatigera taeniaeformis* species complex. Rodents are intermediate hosts and correct taxonomic identification of *H. taeniaeformis sensu lato* (s.l.) species is difficult without the use of molecular methods. The aim of this study was to identify and explore the genetic diversity of *Hydatigera* and other taeniid species. **Methods:** Ten different small mammals species (856 individuals) (*Rattus rattus*, three *Apodemus*, three *Arvicolinae* and three *Soricidae* species) were examined from 2013 to 2023. Captured animals were visually examined for cysts and visible lesions. Two markers were used for amplification and sequencing: *cox1* and 12S rDNA. **Results:** Molecular analysis of cysts and visible lesions revealed four taeniid species: *Hydatigera kamiyai*, *H. taeniaeformis sensu stricto* (s.s.), *Taenia martis* and *T. crassiceps*. *Hydatigera kamiyai* was found in *Apodemus flavicollis*, *A. agrarius*, *Microtus arvalis* and *Crocidura leucodon*, while *H. taeniaeformis s.s.* is registered in *R. rattus*. *Hydatigera kamiyai cox1* sequences clustered with European populations and showed at least 25 nucleotide differences compared to Asian, African, Australian and one of our isolates of *H. taeniaeformis s.s.* acquired from a rat, followed by large sequence distances (9.4% to 12.9%), indicating clear molecular distinction of two species. **Conclusions:** This is one of the few mitochondrial gene-based studies performed after the description of cryptic entities within the *Hydatigera taeniaeformis* s.l. complex and represents a valuable contribution to understanding of genetic diversity, host suitability and geographic distribution of these tapeworm species. Also, our study provides an important basis of molecular data from this part of Europe for further studies. We emphasize the importance of additional studies of intermediate hosts, especially rats from Europe and *Apodemus* spp. and voles from Asia and Africa.

[Progress and prospect of clinical application of anti-rabies virus monoclonal antibody preparation].

Lyu XJ, Dong GM, Liu XQ, Liu S, Liu C, Chen QJ, Yin WW, Wang CL.

20-07-2023

Zhonghua Yi Xue Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/37491162/>

Pattern recognition receptor agonists in pathogen vaccines mediate antitumor T-cell cross-priming.

Aleynick M, Svensson-Arvelund J, Pantsulaia G, Kim K, Rose SA, Upadhyay R, Yellin M, Marsh H, Oreper D, Jhunjunwala S, Moussion CC, Merad M, Brown BD, Brody JD.

Jul-2023

J Immunother Cancer.

<https://pubmed.ncbi.nlm.nih.gov/37487664/>

RABIES VIRUS SEROSURVEY OF THE SMALL INDIAN MONGOOSE (URVA AUROPUNCTATA) ACROSS MULTIPLE HABITATS IN PUERTO RICO, 2014-21.

Berentsen AR, Rivera-Rodriguez MJ, Torres-Toledo FB, Davis AJ, Chipman RB, Gilbert AT.

24-07-2023

J Wildl Dis.

<https://pubmed.ncbi.nlm.nih.gov/37486871/>

The small Indian mongoose (*Urva auropunctata*) is a rabies reservoir in Puerto Rico and accounts for over 70% of reported animal rabies cases annually. The presence of rabies virus-neutralizing antibodies (RVNA) is often used as a tool to measure exposure to rabies virus in wildlife populations. We conducted a serosurvey of mongooses at 11 sites representing six habitat types across Puerto Rico. We collected a serum sample from 464 individual mongooses during 2014-21. Overall, 80/464 (17.0%; 95% confidence interval, 14.1-20.9%; 55 male, 23 female, and two sexes not recorded) of individual mongooses sampled across all habitats were RVNA positive. The geometric mean (SD) RVNA titer for 80 unique seropositive animals was 0.58 (2.92) IU/mL. Our models indicated that the probability of mongooses being RVNA seropositive mostly varied by habitat, with some influence of sex in the individual-level analyses. Population-level RVNA seroprevalence is dynamic in mongoose populations, but these data may shed light on rabies virus transmission across regions to help inform rabies management activities in Puerto Rico.

Transneuronal Circuit Analysis with Pseudorabies Viruses.

Engel EA, Card JP, Enquist LW.

Jul-2023

Curr Protoc.

<https://pubmed.ncbi.nlm.nih.gov/37486157/>

Our ability to understand the function of the nervous system is dependent upon defining the connections of its constituent neurons. Development of methods to define connections within neural networks has always been a growth industry in the neurosciences. Transneuronal spread of neurotropic viruses currently represents the best means of defining synaptic connections within neural networks. The method exploits the ability of viruses to invade neurons, replicate, and spread through the intimate synaptic connections that enable communication among neurons. Since the method was first introduced in the 1970s, it has benefited from an increased understanding of the virus life cycle, the function of viral genomes, and the ability to manipulate the viral genome in support of directional spread of virus and the expression of transgenes. In this article, we review these advances in

viral tracing technology and the ways in which they may be applied for functional dissection of neural networks. © 2023 The Authors. Current Protocols published by Wiley Periodicals LLC. Basic Protocol 1: Retrograde infection of CNS circuits by peripheral injection of virus Basic Protocol 2: Transneuronal analysis by intracerebral injection Alternate Protocol 1: Transneuronal analysis with multiple recombinant strains Alternate Protocol 2: Conditional replication and spread of PRV Alternate Protocol 3: Conditional reporters of PRV infection and spread Alternate Protocol 4: Reporters of neural activity in polysynaptic circuits Support Protocol 1: Growing and titrating a PRV viral stock Support Protocol 2: Immunohistochemical processing and detection Support Protocol 3: Dual-immunofluorescence localization.

Analysis of qualification for post-exposure prophylaxis against rabies in children in Poland.

Ostrowska A, Susło A, Zabłocka K, Bieńkowski C, Pokorska-Śpiewak M.

23-07-2023

Paediatr Int Child Health.

<https://pubmed.ncbi.nlm.nih.gov/37482764/>

Background: Rabies is a fatal disease caused by the rabies virus, usually transmitted by a bite by an infected animal. Because there is no effective treatment, prophylaxis is crucial. The aim of the study was to analyse the circumstances of exposure, characterise the animals that were a potential source of infection and evaluate the frequency of post-exposure prophylaxis in children.

Methods: This was a retrospective analysis of the medical records of 494 children who had been bitten, scratched or salivated on by an animal and were seen consecutively between 2015 and 2019 in the Department of Paediatric Infectious Diseases, Medical University of Warsaw.

Results: The study group was children aged 10 months to 17 years 11 months. The animals most commonly involved were dogs (347/494, 70.24%), cats (81/494 (16.40%) and squirrels (10/494, 2.02%). The contact was mainly with tame but unfamiliar animals (359/494, 72.67%, $p < 0.001$). The most common type of exposure was a bite (457/494, 92.51%). Surgical wound care was required most often after exposure in a town (64/90, 71.11%). A total of 412 children (80.83%) received post-exposure vaccination, including 333/412 using the Essen regimen. In 13/412 cases, the vaccination schedule (3.16%) was not completed because of an absence of signs of disease during veterinary observation of the animal. Anti-rabies immunoglobulin was administered to 13/412 (3.16%).

Conclusion: Most children who are referred after being bitten by an animal require post-exposure prophylaxis. Children are usually bitten by tame dogs with which they are unfamiliar, mostly on the hand. Surgical wound care is needed more often for urban patients than others.

The Rabies Free Burkina Faso initiative: an example of how one health-oriented civil society organizations can contribute towards the achievement of the rabies zero by 30 goal.

Savado M, Dahourou LD, Ilboudo AK, Ilboudo SG, Zangré H, Tarnagda G, Souli Z, Combari AHB, Diarra R, Bidima M, Traoré MGB, Mandé CD, Sondo KA, de Balogh K.

21-07-2023

One Health Outlook.

<https://pubmed.ncbi.nlm.nih.gov/37480134/>

On a mission to eliminate rabies.

Jarvis S.

22-07-2023

Vet Rec.

<https://pubmed.ncbi.nlm.nih.gov/37477307/>

Schistosomiasis

Advances in new target molecules against schistosomiasis: A comprehensive discussion of physiological structure and nutrient intake.

Zhu P, Wu K, Zhang C, Batool SS, Li A, Yu Z, Huang J.

27-07-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37498810/>

Schistosomiasis, a severe parasitic disease, is primarily caused by *Schistosoma mansoni*, *Schistosoma japonicum*, or *Schistosoma haematobium*. Currently, praziquantel is the only recommended drug for human schistosome infection. However, the lack of efficacy of praziquantel against juvenile worms and concerns about the emergence of drug resistance are driving forces behind the research for an alternative medication. Schistosomes are obligatory parasites that survive on nutrients obtained from their host. The ability of nutrient uptake depends on their physiological structure. In short, the formation and maintenance of the structure and nutrient supply are mutually reinforcing and interdependent. In this review, we focus on the structural features of the tegument, esophagus, and intestine of schistosomes and their roles in nutrient acquisition. Moreover, we introduce the significance and modes of glucose, lipids, proteins, and amino acids intake in schistosomes. We linked the schistosome structure and nutrient supply, introduced the currently emerging targets, and analyzed the current bottlenecks in the research and development of drugs and vaccines, in the hope of providing new strategies for the prevention and control of schistosomiasis.

The prevailing infection of *Schistosoma japonicum* and other zoonotic parasites in bubaline reservoir hosts in the ricefield of lake ecosystem: the case of Lake Mainit, Philippines.

Estaño LA, Jumawan JC.

27-07-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/37496395/>

The human blood fluke, *Schistosoma mansoni*, harbours bacteria throughout the parasite's life cycle.

Formenti F, Cortés A, Deiana M, Salter S, Parkhill J, Berriman M, Rinaldi G, Cantacessi C.

24-07-2023

J Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37487539/>

Development of CRISPR/Cas13a-based assays for the diagnosis of Schistosomiasis.

MacGregor SR, McManus DP, Sivakumaran H, Egwang TG, Adriko M, Cai P, Gordon CA, Duke MG, French JD, Collinson N, Olveda RM, Hartel G, Graeff-Teixeira C, Jones MK, You H.

22-07-2023

EBioMedicine.

<https://pubmed.ncbi.nlm.nih.gov/37487416/>

Microwave-assisted hydrothermal fabrication of hierarchical-stacked mesoporous decavanadate-intercalated ZnAl nanolayered double hydroxide to exterminate different developmental stages of *Trichinella spiralis* and *Schistosoma mansoni* in-vitro.

Darwish AS, Mahmoud SS, Bayaoumy FEA.

08-07-2023

Heliyon.

<https://pubmed.ncbi.nlm.nih.gov/37483817/>

Hierarchically stacked mesoporous zinc-aluminium nanolayered-double-hydroxide intercalated with decavanadate (ZnAl-LDH- $V_{10}O_{28}$) is constructed using anion-exchange process via microwave-hydrothermal treatment. Physicochemical properties of ZnAl-LDH- $V_{10}O_{28}$ are characterized in detail. Decavanadate anions are intimately interacted with ZnAl-LDH nanosheets, generating highly ordered architecture of well-dimensioned stacking blocks of brucite-like nanolayers (~8 nm). Such hierarchy improves surface-porosity and electrical-impedivity of ZnAl-LDH- $V_{10}O_{28}$ with declining its zeta-potential (ζ_{av} = 8.8 mV). *In-vitro* treatment of various developmental-stages of *Trichinella spiralis* and *Schistosoma mansoni* by ZnAl-LDH- $V_{10}O_{28}$ is recognized using parasitological and morphological (SEM/TEM) analyses. ZnAl-LDH- $V_{10}O_{28}$ exterminates muscle-larvae and adult-worms of *Trichinella spiralis*, and juvenile and adult *Schistosoma mansoni*, yielding near 100% mortality with rates achieving 5%/h within about 17 h of incubation. This parasitocidal behavior results from the symphony of biological activity gathering decavanadate and LDH-nanosheets. Indeed, ZnAl-LDH- $V_{10}O_{28}$ nanohybrid sample, as a promissory biocide for killing food-borne/waterborne parasites, becomes a futuristic research hotspot for studying its *in-vivo* bioactivity and impact-effectiveness on parasite molecular biology.

Amino acid usage and protein expression levels in the flatworm *Schistosoma mansoni*.

Lamolle G, Iriarte A, Simón D, Musto H.

19-07-2023

Mol Biochem Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/37478919/>

Schistosoma mansoni is a parasitic flatworm that causes a human disease called schistosomiasis, or bilharzia. At the genomic level, *S. mansoni* is AT-rich, but has some compositional heterogeneity. Indeed, some regions of its genome are GC-rich, mainly in the regions located near the extreme ends of the chromosomes. Recently, we showed that, despite the strong bias towards A/T ending codons, highly expressed genes tend to use GC-rich codons. Here, we address the following question: are highly expressed sequences biased in their amino acid frequencies? Our analyses show that these sequences in *S. mansoni*, as in species ranging from bacteria to human, are strongly biased in nucleotide composition. Highly expressed genes tend to use GC-rich codons (in the first and second codon positions), which code the energetically cheapest amino acids. Therefore, we conclude that amino acid usage, at least in highly expressed genes, is strongly shaped by natural selection to avoid energetically expensive residues. Whether this is an adaptation to the parasitic way of life of *S. mansoni*, is unclear since the same pattern occurs in free-living species.

A planetary health innovation for disease, food and water challenges in Africa.

Rohr JR, Sack A, Bakhoun S, Barrett CB, Lopez-Carr D, Chamberlin AJ, Civitello DJ, Diatta C, Doruska MJ, De Leo GA, Haggerty CJE, Jones IJ, Jouanard N, Lund AJ, Ly AT, Ndione RA, Remais JV, Riveau G, Schacht AM, Seck M, Senghor S, Sokolow SH, Wolfe C.

Jul-2023

Nature.

<https://pubmed.ncbi.nlm.nih.gov/37438520/>

Many communities in low- and middle-income countries globally lack sustainable, cost-effective and mutually beneficial solutions for infectious disease, food, water and poverty challenges, despite their inherent interdependence¹⁻⁷. Here we provide support for the hypothesis that agricultural development and fertilizer use in West Africa increase the burden of the parasitic disease schistosomiasis by fuelling the growth of submerged aquatic vegetation that chokes out water access points and serves as habitat for freshwater snails that transmit *Schistosoma* parasites to more than 200 million people globally⁸⁻¹⁰. In a cluster randomized controlled trial (ClinicalTrials.gov: [NCT03187366](https://clinicaltrials.gov/ct2/show/study?term=NCT03187366)) in which we removed invasive submerged vegetation from water points at 8 of 16 villages (that is, clusters), control sites had 1.46 times higher intestinal *Schistosoma* infection rates in schoolchildren and lower open water access than removal sites. Vegetation removal did not have any detectable long-term adverse effects on local water quality or freshwater biodiversity. In feeding trials, the removed vegetation was as effective as traditional livestock feed but

41 to 179 times cheaper and converting the vegetation to compost provided private crop production and total (public health plus crop production benefits) benefit-to-cost ratios as high as 4.0 and 8.8, respectively. Thus, the approach yielded an economic incentive-with important public health co-benefits-to maintain cleared waterways and return nutrients captured in aquatic plants back to agriculture with promise of breaking poverty-disease traps. To facilitate targeting and scaling of the intervention, we lay the foundation for using remote sensing technology to detect snail habitats. By offering a rare, profitable, win-win approach to addressing food and water access, poverty alleviation, infectious disease control and environmental sustainability, we hope to inspire the interdisciplinary search for planetary health solutions¹¹ to the many and formidable, co-dependent global grand challenges of the twenty-first century.

Development and evaluation of an indirect ELISA using a multiepitope antigen for the diagnosis of intestinal schistosomiasis.

Lopes KF, Freire ML, Souza Lima DC, Enk MJ, Oliveira E, Geiger SM.

Jul-2023

Parasitology.

<https://pubmed.ncbi.nlm.nih.gov/37092694/>

Trachome

Impact of personal protective equipment on the clarity of vision among trachoma survey graders and trichiasis surgeons in the context of COVID-19.

Ul Hassan E, Apadinuwe SC, Bisanzio D, Dejene M, Downs P, Harding-Esch EM, Jimenez C, Kabona G, Kebede BN, Kelly M, Kivumbi P, Millar T, Mosher AW, Mpyet C, Mkocha H, Ngondi JM, Olobio N, Palmer S, Teyil WM, Courtright P.

Jun-2023

BMJ Open Ophthalmol.

<https://pubmed.ncbi.nlm.nih.gov/37493675/>

Background/aims: The COVID-19 pandemic necessitated the use of personal protective equipment for those involved in trachoma survey grading and trichiasis surgery. We sought to determine which configuration of a face shield would be less likely to impact grading accuracy and ability to conduct trichiasis surgery. The research also included assessment of comfort, ease of cleaning and robustness. **Methods:** There were three research phases. In phase 1, assessment of four potential face shield configurations was undertaken with principal trachoma graders and trichiasis surgeon trainers to decide which two options should undergo further testing. In phase 2, clarity of vision and comfort (in a classroom environment) of the two configurations were assessed compared with no face shield (control), while grading trachomatous inflammation-follicular (TF). The second phase also included the assessment of impact of the configurations while performing trichiasis surgery using a training model. In phase 3, face shield ease of use was evaluated during

routine surgical programmes. **Results:** In phase 2, 124 trachoma graders and 28 trichiasis surgeons evaluated the 2 face shield configurations selected in phase 1. TF agreement was high ($\kappa=0.83$ and 0.82) for both configurations compared with not wearing a face shield. Comfort was reported as good by 51% and 32% of graders using the two configurations. Trichiasis skill scores were similar for both configurations. **Conclusion:** The face shield configuration that includes a cut-out for mounting the 2.5× magnifying loupes does not appear to impact the ability or comfort of trachoma graders or trichiasis surgeons to carry out their work.

Addressing neglected tropical diseases in Africa: a health equity perspective.

George NS, David SC, Nabiryo M, Sunday BA, Olanrewaju OF, Yangaza Y, Shomuyiwa DO.

25-07-2023

Glob Health Res Policy.

<https://pubmed.ncbi.nlm.nih.gov/37491338/>

The Association Between the Severity of Trichomatous Scarring and Trichomatous Trichiasis Severity in Surgical Patients in Tanzania.

Wolle MA, Misra N, Naufal F, Saheb Kashaf M, Munoz BE, Mkocha H, Funga N, West SK.

21-07-2023

Ophthalmic Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/37476930/>

Purpose: To determine the association between the severity of trichomatous conjunctival scarring (TS) of the upper eyelid conjunctiva and trichomatous trichiasis (TT) severity in TT surgical patients. **Methods:** A cross-sectional study was conducted amongst adults with TT who were referred to surgical camps in Bahi District, Tanzania, for TT surgery. Participants underwent ocular examination. The presence and severity of TS was evaluated in photographs of the everted upper eyelid. TT severity was assessed at the time of the ocular exam based on the number of lashes touching the globe and/or evidence and extent of epilation. Ordinal logistic models were used to examine the association between the severity of TS and TT severity. **Results:** A total of 627 eyes of 388 participants were included. Mean age was 65 years (ranging from 21-98), 81% were females, and 62% had bilateral TT. 93% of eyes with any TT had at least moderate TS; 62% of eyes had severe TS. An increase in TS severity was associated with an increase in the severity of TT. Using as a reference eyes with none to mild TS, in eyes with moderate TS the odds of increased severity of TT was 1.30 (95% CI 0.67-2.51), in eyes with severe TS the odds was 4.20 (95% CI 2.23-7.92). **Conclusion:** In cases of trichomatous trichiasis presenting for surgery, the severity of TT was significantly associated with the severity of TS with almost all cases of TT having moderate or severe scarring.

The elimination of trachoma as a public health problem in Togo: Successes and challenges.

Bakoubayi AW, Gadah DAY, Gnosike P, Zida-Compaore WIC, Bando PP, Alaglo K, Tchalim M, Patchali P, Bitty-Anderson A, Ekouevi DK.

18-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37463175/>

Background: As of May 2022, 15 countries have declared that they have reached their trachoma elimination targets, but only 13 of them, including Togo, have been validated by the World Health Organization as having eliminated the disease as a public health problem. The aim of this study was to describe the broad interventions that have supported the elimination of trachoma as a public health problem in Togo from its inception in 2006 to the validation of its elimination in 2022. **Method:** A review and compilation of data and information contained in the country's submission to World Health Organization for validation of trachoma elimination as a public health problem was conducted. Data from national and local surveillance systems and reports on actions taken after achieving the elimination target were also included. **Results:** Togo has achieved the elimination of trachoma as a public health problem by 2022. The prevalence of follicular trachoma among children aged 1-9 years is <5% in all nationally defined administrative units suspected of having trachoma after stopping mass treatment for at least 2 years. The prevalence of trichiasis among persons aged 15 years and older is less than 0.2% in all administrative units previously endemic for trachoma and evidence of the ability to manage incident cases of emerging trichiasis in the community has been demonstrated. The key of the success in the elimination process was primarily the political commitment of the health authorities with financial and technical support from various international organizations. **Conclusion:** The elimination of trachoma as a public health problem in Togo is a real success story that can serve as an example for the elimination of other neglected tropical diseases in Africa. But regular monitoring and surveillance is essential to avoid the re-emergence of such disease in the country.

Changes in trachoma indicators in Kiribati with two rounds of azithromycin mass drug administration, measured in serial population-based surveys.

Goodhew EB, Taoaba R, Harding-Esch EM, Gwyn SE, Bakhtiari A, Butcher R, Cama A, Guagliardo SAJ, Jimenez C, Mpyet CD, Tun K, Wickens K, Solomon AW, Martin DL, Tekeraoi R.

07-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37418501/>

Responding to Africa's burden of disease: accelerating progress.

Impouma B, Kalu AA, Makubalo L, Gasasira A, Cabore J, Moeti M.

20-07-2023

Epidemiol Infect.

<https://pubmed.ncbi.nlm.nih.gov/37337304/>

Although Africa is home to about 14% of the global population (1.14 billion people), it is growing three times faster than the global average [1]. The continent carries a high burden of disease, but there has been real progress in eradication, elimination, and control since 2015. Examples are the eradication of wild polio in 2020 [2] and the eradication or elimination of neglected tropical diseases, such as dracunculiasis in Kenya in 2018; Human African trypanosomiasis in Togo in 2022; and trachoma in Togo, Gambia, Ghana, and Malawi in 2022 [3]. New HIV infections reduced by 44% in 2021 compared to 2010 [4], and in 2021 the African region passed the 2020 milestone of the End TB Strategy, with a 22% reduction in new infections compared with 2015 [5].

Global Trends in Blindness and Vision Impairment Resulting from Corneal Opacity 1984-2020: A Meta-analysis.

Wang EY, Kong X, Wolle M, Gasquet N, Ssekasanvu J, Mariotti SP, Bourne R, Taylor H, Resnikoff S, West S.
Août-2023
Ophthalmology.
<https://pubmed.ncbi.nlm.nih.gov/36963570/>

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

The prevailing infection of *Schistosoma japonicum* and other zoonotic parasites in bubaline reservoir hosts in the ricefield of lake ecosystem: the case of Lake Mainit, Philippines.

Estañó LA, Jumawan JC.
27-07-2032
Parasitology.
<https://pubmed.ncbi.nlm.nih.gov/37496395/>

Bovines are important reservoir hosts of schistosomiasis, placing humans and animals in rice fields areas at risk of infection. This study reported the prevailing infection of zoonotic parasites from bovine feces in the rice fields adjacent to Lake Mainit, Philippines. Formalin Ethyl Acetate Sedimentation was performed on 124 bovine fecal samples from rice fields and documented eggs and cysts from seven parasites: *Schistosoma japonicum*, *Fasciola gigantica*, *Ascaris* sp., *Strongyloides* sp., *Balantidium coli*, coccidian oocyst and a hookworm species. Among these parasites, *F. gigantica* harboured the highest infection with a 100% prevalence rate, followed by hookworms (51.61%), *B. coli* (30.64%) and *S. japonicum* (12.09%), respectively. The intensity of infection of *S. japonicum* eggs per gram (MPEG = 4.19) among bovines is categorized as 'light.' Bovine contamination index (BCI) calculations revealed that, on

average, infected bovines in rice fields excrete 104 750 *S. japonicum* eggs daily. However, across all ricefield stations, bovines were heavily infected with fascioliasis with BCI at 162 700 *F. gigantica* eggs per day. The study reports that apart from the persistent cases of schistosomiasis in the area, bovines in these rice fields are also heavily infected with fascioliasis. The study confirms the critical role of bovines as a reservoir host for continued infection of schistosomiasis, fascioliasis and other diseases in the rice fields of Lake Mainit. Immediate intervention to manage the spread of these diseases in bovines is recommended.

Rapid, sensitive and visual detection of *Clonorchis sinensis* with an RPA-CRISPR/Cas12a-based dual readout portable platform.

Huang T, Li L, Li J, Li X, Li S, Wang X, Zhang N, Yu Y, Zhang X, Zhao Z, Guo Y, Cao L, Gong P.
24-07-2023
Int J Biol Macromol.
<https://pubmed.ncbi.nlm.nih.gov/37494991/>

Clonorchis sinensis is a food-borne parasite that parasitizes the liver and bile ducts of humans and many animals. This parasite exerts a high burden due to diverse hepatobiliary morbidities (e.g., cholangitis, cholecystitis, cholelithiasis, and cholangiocarcinoma), and an effective detection strategy is urgently needed. CRISPR/Cas12a exhibits nonspecific trans-cleavage activity upon binding to its specific target and has been widely used for nucleic acid detection. In this study, an RPA-CRISPR/Cas12a-based dual readout portable detection platform was established, which shows high sensitivity (one copy/μl) and specificity (no cross-reactivity with common pathogens) by rapid preamplification and combines lateral flow strips and visual fluorescence for visualization of results by the naked eye within 1 h. Moreover, 50 human fecal swabs and 50 fish flesh samples were detected by this platform and nested PCR. The CRISPR/Cas12a-based dual readout portable platform showed 10.0 % (5/50) *C. sinensis*-positive samples in human fecal swabs and 28.0 % (14/50) in fish flesh, which was consistent with the results of nested PCR. The results demonstrate that our portable platform has the advantages of stability, sensitivity, accuracy, and low equipment requirements. Furthermore, we provide novel point-of-care testing (POCT) for clinical use in remote rural and resource-constrained areas.

A Rare Factor in the Etiology of Löffler's Pneumonia: *Fasciola hepatica*.

Kerget B, Kerget F, Tuna ME.
24-07-2023
Rev Soc Bras Med Trop.
<https://pubmed.ncbi.nlm.nih.gov/37493748/>

Neutrophils form extracellular traps in response to *Opisthorchis viverrini* crude antigens and these traps are elevated in neutrophils from opisthorchiasis patients with hepatobiliary abnormalities.

Watakulsin K, Chuenchom C, Donsa W, Thapphan C, Thai TD, Chareonsudjai S, Faksri K, Suttiaprapa S, Tangkawatana S, Sripa B, Edwards SW, Salao K.

26-07-2023

Biol Open.

<https://pubmed.ncbi.nlm.nih.gov/37493409/>

Paragonimus westermani preadult fluke in a pulmonary necrotizing granulomatous lesion: A case associated with eating soy sauce-marinated raw freshwater crab, "gejang".

Maekawa K, Nagayasu E, Hata Y, Hanamure F, Maruyama H, Yamashita A.

26-07-2023

Pathol Int.

<https://pubmed.ncbi.nlm.nih.gov/37493110/>

Recombinant protein EBI3 attenuates Clonorchis sinensis-induced liver fibrosis by inhibiting hepatic stellate cell activation in mice.

Zhao L, Li J, Mo G, Cao D, Li C, Huang G, Jiang L, Chen G, Yao H, Peng X.

21-07-2023

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/37480105/>

Morphological and molecular characterization of Fasciola isolates from livestock in Golestan province, northern Iran.

Sharbatkhori M, Nasibi S, Mohammadi MA, Aryaeipour M, Raeghi S, Fasihi Harandi M.

Juil-2023

Vet Med Sci.

<https://pubmed.ncbi.nlm.nih.gov/37317979/>

Background: Fascioliasis, caused by the liver flukes *Fasciola hepatica* and *Fasciola gigantica*, is a global zoonotic helminthic disease. The livestock and human are the final hosts of the parasites. Northern Iran is an important endemic region for fascioliasis. Few studies have been conducted on the characterization of *Fasciola* isolates from eastern regions of the Caspian littoral of the country.

Objective: The aim of the present study was to identify *F. hepatica*, *F. gigantica* and intermediate/hybrid forms of *Fasciola* isolates from livestock in Golestan province, northern Iran, using morphometric and molecular tools.

Methods: Livestock livers naturally infected with *Fasciola* spp. were collected from Golestan slaughterhouse during 2019-2020. The worms were morphometrically studied using a calibrated stereomicroscope. Genomic DNA was extracted from all samples, and polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was performed on internal transcribed spacer (ITS1) region using *RsaI* restriction enzyme. All the isolates were then analysed by multiplex PCR on *Pepck* region. **Results:** A total of 110 *Fasciola* isolates were collected from the infected livers, including 94 sheep, 12 cattle and 4 goats. Morphometric analysis of 61 adult *Fasciola* isolates indicated that, 44 and 17 isolates belonged to *F. hepatica*

and *F. gigantica*, respectively. Eighty-one and 29 isolates belonged to *F. hepatica* and *F. gigantica* using ITS1-RFLP, respectively. However, *Pepck* Multiplex PCR indicated 72 *F. hepatica*, 26 *F. gigantica* and 12 intermediate/hybrid forms. All 12 hybrid isolates were found in sheep host. Two isolates were identified as *F. gigantica* using morphometry and *F. hepatica* using both molecular methods.

Conclusion: The present study confirmed the existence of both *F. hepatica* and *F. gigantica* species and reported the first molecular evidence of hybrid *Fasciola* isolates in ruminants of Golestan province.

Effects of Health Literacy Promotion Programs for Preventing Opisthorchiasis and Cholangiocarcinoma: a Systematic Review and Meta-analysis.

Moonsan S, Songserm N, Woradet S, Suksatan W.

Aug-2023

J Cancer Educ.

<https://pubmed.ncbi.nlm.nih.gov/36637714/>

An Unusual Case of Intermittent Fever With Multiple Liver Lesions.

Zhang XF, Yin ZK, Zhang JY.

Aug-2023

Gastroenterology.

<https://pubmed.ncbi.nlm.nih.gov/36502865/>

Trypanosomes (trypanosomiasis et maladie de Chagas)

The impact of vaccine-linked chemotherapy on liver health in a mouse model of chronic *Trypanosoma cruzi* infection.

Nguyen DM, Poveda C, Pollet J, Gusovsky F, Bottazzi ME, Hotez PJ, Jones KM.

12-07-2023

bioRxiv.

<https://pubmed.ncbi.nlm.nih.gov/37503013/>

Background: Chagas disease, chronic infection with *Trypanosoma cruzi*, mainly manifests as cardiac disease. However, the liver is important for both controlling parasite burdens and metabolizing drugs. Notably, high doses of anti-parasitic drug benznidazole (BNZ) causes liver damage. We previously showed that combining low dose BNZ with a prototype therapeutic vaccine is a dose sparing strategy that effectively reduced *T. cruzi* induced cardiac damage. However, the impact of this treatment on liver health is unknown. Therefore, we evaluated several markers of liver health after treatment with low dose BNZ plus the vaccine therapy in comparison to a curative dose of BNZ. **Methodology:** Female BALB/c mice were infected with a bioluminescent *T. cruzi* H1 clone for approximately 70 days, then randomly divided into groups of 15 mice each. Mice were treated with a 25mg/kg BNZ, 25µg Tc24-

C4 protein/ 5µg E6020-SE (Vaccine), 25mg/kg BNZ followed by vaccine, or 100mg/kg BNZ (curative dose). At study endpoints we evaluated hepatomegaly, parasite burden by quantitative PCR, cellular infiltration by histology, and expression of B-cell translocation gene 2(BTG2) and Peroxisome proliferator-activated receptor alpha (PPARα) by RT-PCR. Levels of alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) were quantified from serum. **Results:** Curative BNZ treatment significantly reduced hepatomegaly, liver parasite burdens, and the quantity of cellular infiltrate, but significantly elevated serum levels of ALT, AST, and LDH. Low BNZ plus vaccine did not significantly affect hepatomegaly, parasite burdens or the quantity of cellular infiltrate, but only elevated ALT and AST. Low dose BNZ significantly decreased expression of both BTG2 and PPARα, and curative BNZ reduced expression of BTG2 while low BNZ plus vaccine had no impact. **Conclusions:** These data confirm toxicity associated with curative doses of BNZ and suggest that the dose sparing low BNZ plus vaccine treatment better preserves liver health. **Author summary:** Chagas disease is a neglected tropical disease caused by the protozoal parasite *Trypanosoma cruzi*, which has long-term deleterious health effects. The current treatment for Chagas disease is administering the antiparasitic drug, benznidazole. While benznidazole effectively treats the disease during the acute phase, its efficacy is reduced during chronic infection. In addition, benznidazole therapy causes significant side effects, including liver toxicity. Texas Children's Hospital Center for Vaccine Development at Baylor College of Medicine has developed a treatment strategy that combines a prototype therapeutic vaccine with a lower dose of Benznidazole to promote a protective immune response, ameliorate the deleterious effects of the parasite, and limit the harmful side effect of the drug. We call this vaccine-linked chemotherapy, which has shown promising results regarding heart health by reducing parasite burden and pathology in the heart and improving cardiac function. This study evaluated the strategy's effectiveness in the liver since it is the prime metabolizer of the benznidazole drug, as well as the organ of parasite clearance. Results from this study demonstrated that vaccine-linked chemotherapy causes less damage to the liver compared to curative doses of benznidazole and may be a desirable treatment strategy to preserve overall health while retaining efficacy.

Gene editing of putative cAMP and Ca²⁺-regulated proteins using an efficient cloning-free CRISPR/Cas9 system in *Trypanosoma cruzi*.

Chiurillo MA, Ahmed M, González C, Raja A, Lander N.
10-07-2023
bioRxiv.
<https://pubmed.ncbi.nlm.nih.gov/37502958/>

Trypanosoma cruzi, the agent of Chagas disease, must adapt to a diversity of environmental conditions that it faces during its life cycle. The adaptation to these changes is mediated by signaling pathways that coordinate the cellular responses to the new environmental settings. Cyclic AMP (cAMP) and Calcium (Ca²⁺) signaling pathways

regulate critical cellular processes in this parasite, such as differentiation, osmoregulation, host cell invasion and cell bioenergetics. Although the use of CRISPR/Cas9 technology prompted reverse genetics approaches for functional analysis in *T. cruzi*, it is still necessary to expand the toolbox for genome editing in this parasite, as for example to perform multigene analysis. Here we used an efficient T7RNAP/Cas9 strategy to tag and delete three genes predicted to be involved in cAMP and Ca²⁺ signaling pathways: a putative Ca²⁺/calmodulin-dependent protein kinase (*CAMK*), Flagellar Member 6 (*FLAM6*) and Cyclic nucleotide-binding domain/C2 domain-containing protein (*CC2CP*). We endogenously tagged these three genes and determined the subcellular localization of the tagged proteins. Furthermore, the strategy used to knockout these genes allow us to presume that *TcCC2CP* is an essential gene in *T. cruzi* epimastigotes. Our results will open new venues for future research on the role of these proteins in *T. cruzi*.

Efficacy of oral administration of ascofuranone with and without glycerol against *Trypanosoma congolense*.

Yamazaki A, Suganuma K, Tanaka Y, Watanabe K, Kawazu SI, Kita K, Inoue N.
25-07-2023
Exp Parasitol.
<https://pubmed.ncbi.nlm.nih.gov/37499895/>

Prevalence of blood and skin trypanosomes in domestic and wild fauna from two sleeping sickness foci in Southern Cameroon.

Magang EMK, Kamga RMN, Telleria J, Tichit M, Crouzols A, Kaboré J, Hardy D, Bouaka CUT, Jamonneau V, Rotureau B, Kuete V, Bart JM, Simo G.
27-07-2023
PLoS Negl Trop Dis.
<https://pubmed.ncbi.nlm.nih.gov/37498955/>

How much (ATP) does it cost to build a trypanosome? A theoretical study on the quantity of ATP needed to maintain and duplicate a bloodstream-form *Trypanosoma brucei* cell.

Nascimento JF, Souza ROO, Alencar MB, Marsiccobetre S, Murillo AM, Damasceno FS, Girard RBMM, Marchese L, Luévano-Martinez LA, Achjian RW, Haanstra JR, Michels PAM, Silber AM.
27-07-2023
PLoS Pathog.
<https://pubmed.ncbi.nlm.nih.gov/37498954/>

Health economic evaluation of strategies to eliminate gambiense human African trypanosomiasis in the Mandoul disease focus of Chad.

Antillon M, Huang CI, Sutherland SA, Crump RE, Bessell PR, Shaw APM, Tirados I, Picado A, Biéler S, Brown PE,

Solano P, Mbainda S, Darnas J, Wang-Steversding X, Crowley EH, Peka M, Tediosi F, Rock KS.

27-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37498938>

Human African trypanosomiasis, caused by the gambiense subspecies of *Trypanosoma brucei* (gHAT), is a deadly parasitic disease transmitted by tsetse. Partners worldwide have stepped up efforts to eliminate the disease, and the Chadian government has focused on the previously high-prevalence setting of Mandoul. In this study, we evaluate the economic efficiency of the intensified strategy that was put in place in 2014 aimed at interrupting the transmission of gHAT, and we make recommendations on the best way forward based on both epidemiological projections and cost-effectiveness. In our analysis, we use a dynamic transmission model fit to epidemiological data from Mandoul to evaluate the cost-effectiveness of combinations of active screening, improved passive screening (defined as an expansion of the number of health posts capable of screening for gHAT), and vector control activities (the deployment of Tiny Targets to control the tsetse vector). For cost-effectiveness analyses, our primary outcome is disease burden, denominated in disability-adjusted life-years (DALYs), and costs, denominated in 2020 US\$. Although active and passive screening have enabled more rapid diagnosis and accessible treatment in Mandoul, the addition of vector control provided good value-for-money (at less than \$750/DALY averted) which substantially increased the probability of reaching the 2030 elimination target for gHAT as set by the World Health Organization. Our transmission modelling and economic evaluation suggest that the gains that have been made could be maintained by passive screening. Our analysis speaks to comparative efficiency, and it does not take into account all possible considerations; for instance, any cessation of ongoing active screening should first consider that substantial surveillance activities will be critical to verify the elimination of transmission and to protect against the possible importation of infection from neighbouring endemic foci.

Massive invasion on a Triatominae insectarium (Hemiptera: Heteroptera: Reduviidae) by *Attagenus fasciatus* (Thunberg, 1795) (Coleoptera: Dermestidae: Attageninae).

Oliveira J, Háva J, Rosa JAD, Gil-Santana HR.

24-07-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/37493742/>

First record of *Triatoma longipennis*, Usinger, 1939 (Hemiptera: Reduviidae: Triatominae) in Tecozautla, Hidalgo.

Rivas N, Antonio-Campos A, Noguez-García J, Alejandro-Aguilar R.

24-07-2023

Rev Soc Bras Med Trop.

<https://pubmed.ncbi.nlm.nih.gov/37493734/>

Background: We report the presence of *Triatoma longipennis* for the first time in two localities in Hidalgo, Mexico. **Methods:** This study was conducted at Tecozautla municipality, Hidalgo. Collection was performed in April 2022. **Results:** We collected eight triatomines from Guadalupe: two fourth-instar nymphs, three fifth-instar nymphs, one female, and two males. In San Miguel Caltepanitla, a female was collected inside a dwelling. One sample tested positive for *Trypanosoma cruzi*. **Conclusions:** These findings suggest the need to investigate the dynamics of this species with respect to the inhabitants of the study area.

Mother-to-child Chagas disease transmission: The challenge of detection and prevention in areas without the risk of vectorial transmission.

Palacios Gil-Antuñano S, Gold S, Abril M, Segovia Hernández M, Cancelo-Hidalgo MJ, Flores-Chávez M, Pelayo-Delgado I.

26-07-2023

Int J Gynaecol Obstet.

<https://pubmed.ncbi.nlm.nih.gov/37493222/>

Structure-based drug designing against *Leishmania donovani* using docking and molecular dynamics simulation studies: exploring glutathione synthetase as a drug target.

Sarma M, Borkotoky S, Dubey VK.

25-07-2023

J Biomol Struct Dyn.

<https://pubmed.ncbi.nlm.nih.gov/37491862/>

In the pursuit of developing novel anti-leishmanial agents, we conducted an extensive computational study to screen inhibitors from the FDA-approved ZINC database against *Leishmania donovani* glutathione synthetase. The three-dimensional structure of *Leishmania donovani* glutathione synthetase was constructed by homology modeling, using the crystallographic structure of *Trypanosoma brucei* glutathione synthetase as a template. Subsequently, molecular docking studies were carried out for a large number of compounds using AutoDock Vina. Among the screened compounds, we selected the top five with strong binding affinity to *Leishmania donovani* glutathione synthetase but having a very low affinity to its human homolog. Further investigations on protein-ligand complexes were done by conducting molecular dynamics (MD) simulation and MM/PBSA analysis. The results revealed that Olysio (Simeprevir) exhibited the lowest binding energy (-89.21 kcal/mol), followed by Telithromycin (-45.34 kcal/mol). These findings showed that these compounds have the potential to act as inhibitors of glutathione synthetase. Hence, our study provides valuable insights for the development of a novel therapeutic strategy against *Leishmania donovani* by targeting the glutathione synthetase enzyme. Communicated by Ramaswamy H. Sarma.

CD4+ T cells regulate sickness-induced anorexia and fat wasting during a chronic parasitic infection.

Redford SE, Varanasi SK, Sanchez KK, Thorup NR, Ayres JS.

19-07-2023

Cell Rep.

<https://pubmed.ncbi.nlm.nih.gov/37490905/>

Phenothiazine-based virtual screening, molecular docking, and molecular dynamics of new trypanothione reductase inhibitors of *Trypanosoma cruzi*.

Rivera G, González-González A, Vázquez C, Encalada R, Saavedra E, Vázquez-Jiménez LK, Ortiz-Pérez E, Bolognesi M.

25-07-2023

Mol Inform.

<https://pubmed.ncbi.nlm.nih.gov/37490403/>

Oral transmission of Chagas disease from a One Health approach: A systematic review.

López-García A, Gilabert JA.

24-07-2023

Trop Med Int Health.

<https://pubmed.ncbi.nlm.nih.gov/37488635/>

Objective: To analyse acute Chagas disease (CD) outbreaks through a qualitative systematic review and discuss the determinants for its prevention and control. **Methods:** Review of studies in which clinical cases of oral transmission were confirmed by parasitological and/or serological tests that included an epidemiological investigation of sources of infection, vectors and reservoirs. **Results:** Thirty-two outbreaks (1965-2022) were analysed. The main foods involved in oral transmission outbreaks are homemade fruit juices. Different species of vectors were identified. Reservoirs were mainly dogs, rodents and large American opossums (didelphids). **Conclusion:** Under a One Health approach, environmental changes are one of the factors responsible of the rise of oral transmission of CD. Entomological surveillance of vectors and control of the changes in wild and domestic reservoirs and reinforcement of hygiene measures around food in domestic and commercial sites are needed.

Unnixin is a protein subunit of a large-pore channel expressed by unicellular organisms.

Güiza J, Solís F, Valenzuela B, Arancibia D, Zamorano P, González J, Saavedra J, Neely A, Salgado M, Martínez AD, Sáez JC, Vega JL.

Août-023

Proc Natl Acad Sci U S A.

<https://pubmed.ncbi.nlm.nih.gov/37487087/>

CRISPR Genome Editing and the Study of Chagas Disease.

Burle-Caldas GA, Grazielle-Silva V, Faustino LP, Teixeira SMR.

2023

Adv Exp Med Biol.

<https://pubmed.ncbi.nlm.nih.gov/37486519/>

The unified theory of sleep: Eukaryotes endosymbiotic relationship with mitochondria and REM the push-back response for awakening.

Adams GJ, O'Brien PA.

06-07-2023

Neurobiol Sleep Circadian Rhythms.

<https://pubmed.ncbi.nlm.nih.gov/37484687/>

The Unified Theory suggests that sleep is a process that developed in eukaryotic animals from a relationship with an endosymbiotic bacterium. Over evolutionary time the bacterium evolved into the modern mitochondrion that continues to exert an effect on sleep patterns, e.g. the bacterium *Wolbachia* establishes an endosymbiotic relationship with *Drosophila* and many other species of insects and is able to change the host's behaviour by making it sleep. The hypothesis is supported by other host-parasite relationships, e.g., *Trypanosoma brucei* which causes day-time sleepiness and night-time insomnia in humans and cattle. For eukaryotes such as Monocercomonoids that don't contain mitochondria we find no evidence of them sleeping. Mitochondria produce the neurotransmitter gamma aminobutyric acid (GABA), and ornithine a precursor of the neurotransmitter GABA, together with substances such as 3,4-dihydroxy phenylalanine (DOPA) a precursor for the neurotransmitter dopamine: These substances have been shown to affect the sleep/wake cycles in animals such as *Drosophila* and *Hydra*. Eukaryote animals have traded the very positive side of having mitochondria providing aerobic respiration for them with the negative side of having to sleep. NREM (Quiet sleep) is the process endosymbionts have imposed upon their host eukaryotes and REM (Active sleep) is the push-back adaptation of eukaryotes with brains, returning to wakefulness.

In vitro trypanocidal activities and structure-activity relationships of ciprofloxacin analogs.

Janse van Rensburg HD, Suganuma K, N'Da DD.

23-07-2023

Mol Divers.

<https://pubmed.ncbi.nlm.nih.gov/37481633/>

Tropical diseases, such as African trypanosomiasis, by their nature and prevalence lack the necessary urgency regarding drug development, despite the increasing need for novel, structurally diverse antitrypanosomal drugs, using different mechanisms of action that would improve drug efficacy and safety. Traditionally antibacterial agents, the fluoroquinolones, reportedly possess in vitro trypanocidal activities against *Trypanosoma brucei* organisms. During our research, the fluoroquinolone, ciprofloxacin (1), and its analogs (2-24) were tested against bloodstream forms of *T. brucei brucei*, *T. b. gambiense*, *T. b. rhodesiense*, *T. evansi*, *T. equiperdum*, and *T.*

congolense and Madin-Darby bovine kidney cells (cytotoxicity). Ciprofloxacin [CPX (1)] demonstrated selective trypanocidal activity against *T. congolense* (IC₅₀ 7.79 μM; SI 39.6), whereas the CPX derivatives (2-10) showed weak selective activity (25 < IC₅₀ < 65 μM; 2 < SI < 4). Selectivity and activity of the CPX and 1,2,3-triazole (TZ) hybrids (11-24) were governed by their chemical functionality at C-3 (carboxylic acid, or 4-methylpiperazinyl amide) and their electronic effect (electron-donating or electron-withdrawing para-benzyl substituent), respectively. Trypanocidal hits in the micromolar range were identified against bloodstream forms of *T. congolense* [CPX (1); CPX amide derivatives 18: IC₅₀ 8.95 μM; SI 16.84; 22: IC₅₀ 5.42 μM; SI 25.2] and against *T. brucei rhodesiense* (CPX acid derivative 13: IC₅₀ 4.51 μM; SI 10.2), demonstrating more selectivity toward trypanosomes than mammalian cells. Hence, the trypanocidal hit compound 22 may be optimized by retaining the 4-methylpiperazine amide functional group (C-3) and the TZ moiety at position N-15 and introducing other electron-withdrawing ortho-, meta-, and/or para-substituents on the aryl ring in an effort to improve the pharmacokinetic properties and increase the trypanocidal activity. Structure-activity relationships of ciprofloxacin-1,2,3-triazole hybrids were governed by the chemical functionality at C-3 and electronic effect.

Mapping diversity in African trypanosomes using high resolution spatial proteomics.

Moloney NM, Barylyuk K, Tromer E, Crook OM, Breckels LM, Lilley KS, Waller RF, MacGregor P.

21-07-2023

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/37479728/>

African trypanosomes are dioxenous eukaryotic parasites that impose a significant human and veterinary disease burden on sub-Saharan Africa. Diversity between species and life-cycle stages is concomitant with distinct host and tissue tropisms within this group. Here, the spatial proteomes of two African trypanosome species, *Trypanosoma brucei* and *Trypanosoma congolense*, are mapped across two life-stages. The four resulting datasets provide evidence of expression of approximately 5500 proteins per cell-type. Over 2500 proteins per cell-type are classified to specific subcellular compartments, providing four comprehensive spatial proteomes. Comparative analysis reveals key routes of parasitic adaptation to different biological niches and provides insight into the molecular basis for diversity within and between these pathogen species.

In vitro anti-trypanosomal activity of synthetic nitrofurantoin-triazole hybrids against Trypanosoma species causing human African trypanosomiasis.

Seetsi A, N'da D, Molefe-Nyembe N, Sukanuma K, Ramatla T, Thekisoe O.

21-07-2023

Fundam Clin Pharmacol.

<https://pubmed.ncbi.nlm.nih.gov/37479675/>

Development of chimeric protein as a multivalent vaccine for human Kinetoplastid infections: Chagas disease and leishmaniasis.

Clímaco MC, de Figueiredo LA, Lucas RC, Pinheiro GRG, Dias Magalhães LM, Oliveira ALG, Almeida RM, Barbosa FS, Castanheira Bartholomeu D, Bueno LL, Mendes TA, Zhan B, Jones KM, Hotez P, Bottazzi ME, Oliveira FMS, Fujiwara RT.

19-07-2023

Vaccine.

<https://pubmed.ncbi.nlm.nih.gov/37479612/>

Leishmania spp. and *Trypanosoma cruzi* are parasitic kinetoplastids of great medical and epidemiological importance since they are responsible for thousands of deaths and disability-adjusted life-years annually, especially in low- and middle-income countries. Despite efforts to minimize their impact, current prevention measures have failed to fully control their spread. There are still no vaccines available. Taking into account the genetic similarity within the Class Kinetoplastida, we selected CD8⁺ T cell epitopes preserved among *Leishmania* spp. and *T. cruzi* to construct a multivalent and broad-spectrum chimeric polyprotein vaccine. In addition to inducing specific IgG production, immunization with the vaccine was able to significantly reduce parasite burden in the colon, liver and skin lesions from *T. cruzi*, *L. infantum* and *L. mexicana* challenged mice, respectively. These findings were supported by histopathological analysis, which revealed decreased inflammation in the colon, a reduced number of degenerated hepatocytes and an increased proliferation of connective tissue in the skin lesions of the corresponding *T. cruzi*, *L. infantum* and *L. mexicana* vaccinated and challenged mice. Collectively, our results support the protective effect of a polyprotein vaccine approach and further studies will elucidate the immune profile associated with this protection. Noteworthy, our results act as conceptual proof that a single multi-kinetoplastida vaccine can be used effectively to control different infectious etiologies, which in turn can have a profound impact on the development of a new generation of vaccines.

Surveillance and Control of Trypanosoma evansi in the Canary Islands: A Descriptive Analysis.

Tejedor-Junco MT, Henríquez AM, Puerto PP, Ramos MD, González-Martín M, Doreste MM, Gimonneau G, Desquesnes M, Martel SM, Corbera JA.

19-07-2023

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/37479160/>

Dual localization of receptor-type adenylate cyclases and cAMP response protein 3 unveils the presence of two putative signaling microdomains in Trypanosoma cruzi.

Chiurillo MA, Carlson J, Bertolini MS, Raja A, Lander N.

21-07-2023

mBio.

<https://pubmed.ncbi.nlm.nih.gov/37477489/>

Differential expression profile of genes involved in the immune response associated to progression of chronic Chagas disease.

Gómez I, López MC, Egui A, Palacios G, Carrilero B, Benítez C, Simón M, Segovia M, Carmelo E, Thomas MC. 13-07-2023

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/37440604/>

Trypanosome RNA helicase KREH2 differentially controls non-canonical editing and putative repressive structure via a novel proposed 'bifunctional' gRNA in mRNA A6.

Meehan J, McDermott SM, Ivens A, Goodall Z, Chen Z, Yu Z, Woo J, Rodshagen T, McCleskey L, Sechrist R, Stuart K, Zeng L, Rouskin S, Savill NJ, Schnauffer A, Zhang X, Cruz-Reyes J. 21-07-2023

Nucleic Acids Res.

<https://pubmed.ncbi.nlm.nih.gov/37246647/>

U-insertion/deletion (U-indel) RNA editing in trypanosome mitochondria is directed by guide RNAs (gRNAs). This editing may developmentally control respiration in bloodstream forms (BSF) and insect procyclic forms (PCF). Holo-editosomes include the accessory RNA Editing Substrate Binding Complex (RESC) and RNA Editing Helicase 2 Complex (REH2C), but the specific proteins controlling differential editing remain unknown. Also, RNA editing appears highly error prone because most U-indels do not match the canonical pattern. However, despite extensive non-canonical editing of unknown functions, accurate canonical editing is required for normal cell growth. In PCF, REH2C controls editing fidelity in RESC-bound mRNAs. Here, we report that KREH2, a REH2C-associated helicase, developmentally controls programmed non-canonical editing, including an abundant 3' element in ATPase subunit 6 (A6) mRNA. The 3' element sequence is directed by a proposed novel regulatory gRNA. In PCF, KREH2 RNAi-knockdown up-regulates the 3' element, which establishes a stable structure hindering element removal by canonical initiator-gRNA-directed editing. In BSF, KREH2-knockdown does not up-regulate the 3' element but reduces its high abundance. Thus, KREH2 differentially controls extensive non-canonical editing and associated RNA structure via a novel regulatory gRNA, potentially hijacking factors as a 'molecular sponge'. Furthermore, this gRNA is bifunctional, serving in canonical CR4 mRNA editing whilst installing a structural element in A6 mRNA.

Novel kinetoplastid-specific cAMP binding proteins identified by RNAi screening for cAMP resistance in *Trypanosoma brucei*.

Bachmaier S, Gould MK, Polatoglou E, Omelianczyk R, Brennand AE, Aloraini MA, Munday JC, Horn D, Boshart M, de Koning HP.

05-07-2023

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/37475965/>

Cyclic AMP signalling in trypanosomes differs from most eukaryotes due to absence of known cAMP effectors and cAMP independence of PKA. We have previously identified four genes from a genome-wide RNAi screen for resistance to the cAMP phosphodiesterase (PDE) inhibitor NPD-001. The genes were named cAMP Response Protein (CARP) 1 through 4. Here, we report an additional six CARP candidate genes from the original sample, after deep sequencing of the RNA interference target pool retrieved after NPD-001 selection (RIT-seq). The resistance phenotypes were confirmed by individual RNAi knockdown. Highest level of resistance to NPD-001, approximately 17-fold, was seen for knockdown of CARP7 (Tb927.7.4510). CARP1 and CARP11 contain predicted cyclic AMP binding domains and bind cAMP as evidenced by capture and competition on immobilised cAMP. CARP orthologues are strongly enriched in kinetoplastid species, and CARP3 and CARP11 are unique to *Trypanosoma*. Localization data and/or domain architecture of all CARPs predict association with the *T. brucei* flagellum. This suggests a crucial role of cAMP in flagellar function, in line with the cell division phenotype caused by high cAMP and the known role of the flagellum for cytokinesis. The CARP collection is a resource for discovery of unusual cAMP pathways and flagellar biology.

Ulcère de Buruli

Type-I interferons promote innate immune tolerance in macrophages exposed to *Mycobacterium ulcerans* vesicles.

Bernard Q, Goumeidane M, Chaumond E, Robbe-Saule M, Boucaud Y, Esnault L, Croué A, Jullien J, Marsollier L, Marion E.

10-07-2023

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/37428812/>

Buruli ulcer is a chronic infectious disease caused by *Mycobacterium ulcerans*. The pathogen persistence in host skin is associated with the development of ulcerative and necrotic lesions leading to permanent disabilities in most patients. However, few of diagnosed cases are thought to resolve through an unknown self-healing process. Using in vitro and in vivo mouse models and *M. ulcerans* purified vesicles and mycolactone, we showed that the development of an innate immune tolerance was only specific to macrophages from mice able to heal spontaneously. This tolerance mechanism depends on a type I interferon response and can be induced by interferon beta. A type I interferon signature was further detected during in vivo infection in mice as well as in skin samples from patients under antibiotics regiment. Our results indicate that type I interferon-related genes expressed in macrophages may promote tolerance and healing during infection with skin damaging pathogen.

Alternative boronic acids in the detection of Mycolactone A/B using the thin layer chromatography (f-TLC) method for diagnosis of Buruli ulcer.

Akolgo GA, Partridge BM, D Craggs T, Amewu RK.

27-07-2023

BMC Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/37501134/>