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Veille scientifique Maladies tropicales négligées

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Dengue, chikungunya et maladie à virus Zika

Climate change and the increased burden of dengue fever in Pakistan.

Abid MA, Abid MB.

05-12-2022

Lancet Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36480945/>

Interfer(on)ing with Zika virus.

Alvarado AG, Kornblum HI.

07-12-2022

Neuron.

<https://pubmed.ncbi.nlm.nih.gov/36480937/>

In this issue of *Neuron*, Bulstrode et al. demonstrate that glioblastoma slice cultures, unlike neural progenitors, are refractory to Zika virus infection. The anti-infective mechanism is myeloid-lineage cell-secreted interferon beta. These studies have implications for therapeutics in both glioblastoma and Zika virus infections.

Severe dengue associated with *Staphylococcus aureus* sepsis in pediatric patients: a case series.

Sudeep KC, Kumar S, Randhawa MS, Angurana SK, Nallasamy K, Bansal A, Muralidharan J.

05-12-2022

J Trop Pediatr.

<https://pubmed.ncbi.nlm.nih.gov/36480785/>

Development and evaluation of recombinant E2 protein based IgM capture enzyme-linked immunosorbent assay (ELISA) and double antigen sandwich ELISA for detection of antibodies to Chikungunya virus.

Guo M, Du S, Lai L, Wu W, Huang X, Li A, Li H, Li C, Wang Q, Sun L, Liu T, Tian T, Wang S, Liang M, Li D, Xie C, Li J.

08-12-2022

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36480572/>

Thermodynamic characterization of a macrocyclic Zika virus NS2B/NS3 protease inhibitor and its acyclic analogs.

Hammerschmidt SJ, Huber S, Braun NJ, Lander M, Steinmetzer T, Kersten C.

08-12-2022

Arch Pharm (Weinheim).

<https://pubmed.ncbi.nlm.nih.gov/36480352/>

Cyclization of small molecules is a widely applied strategy in drug design for ligand optimization to improve affinity, as it eliminates the putative need for structural preorganization of the ligand before binding, or to improve pharmacokinetic properties. In this work, we

provide a deeper insight into the binding thermodynamics of a macrocyclic Zika virus NS2B/NS3 protease inhibitor and its linear analogs. Characterization of the thermodynamic binding profiles by isothermal titration calorimetry experiments revealed an unfavorable entropy of the macrocycle compared to the open linear reference ligands. Molecular dynamic simulations and X-ray crystal structure analysis indicated only minor benefits from macrocyclization to fixate a favorable conformation, while linear ligands retained some flexibility even in the protein-bound complex structure, possibly explaining the initially surprising effect of a higher entropic penalty for the macrocyclic ligand.

Dengue and COVID-19 co-infections: an important consideration in the tropics.

Dalugama C, Seneviratne SL.

08-12-2022

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/36479900/>

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has affected >370 million individuals worldwide. Dengue is endemic in many countries and leads to epidemics at frequent intervals. In the tropics and subtropics, it is possible that individuals may be concurrently infected with both dengue and SARS-CoV-2. Differentiation between the two infections may be difficult from both a clinical and laboratory perspective. We have outlined the currently published findings (as of the end of December 2021) on patients with dengue and SARS-CoV-2 co-infections and have discussed the observed outcomes and management of such patients. Co-infections were more common in males >25 y of age, fever was not universal, 30-50% had medical comorbidities such as diabetes mellitus or hypertension and the case fatality rate was 16-28%.

Regulation of ribonucleoprotein condensates by RNase L during viral infection.

Burke JM.

07-12-2022

Wiley Interdiscip Rev RNA.

<https://pubmed.ncbi.nlm.nih.gov/36479619/>

In response to viral infection, mammalian cells activate several innate immune pathways to antagonize viral gene expression. Upon recognition of viral double-stranded RNA, protein kinase R (PKR) phosphorylates the alpha subunit of eukaryotic initiation factor 2 (eIF2 α) on serine 51. This inhibits canonical translation initiation, which broadly antagonizes viral protein synthesis. It also promotes the assembly of cytoplasmic ribonucleoprotein complexes termed stress granules (SGs). SGs are widely thought to promote cell survival and antiviral signaling. However, co-activation of the OAS/RNase L antiviral pathway inhibits the assembly of SGs and promotes the assembly of an alternative ribonucleoprotein complex termed an RNase L-dependent body (RLB). The formation of RLBs has been observed in response to double-stranded RNA, dengue virus infection, or SARS-CoV-2 infection.

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

Temporal and spatial analysis of municipal dengue cases in Paraná and social and environmental indicators, 2012 to 2021: ecological study.

Leandro GCW, Cicchelerio LM, Procopiuk M, Correa FOB, Santos PCFD, Lopes AR, Nihei OK.

05-12-2022

Rev Bras Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/36478212/>

Transcriptomic reveals the ferroptosis features of host response in a mouse model of Zika virus infection.

Yan Q, Zheng W, Jiang Y, Zhou P, Lai Y, Liu C, Wu P, Zhuang H, Huang H, Li G, Zhan S, Lao Z, Liu X.

08-12-2022

J Med Virol.

<https://pubmed.ncbi.nlm.nih.gov/36477858/>

Potential in vitro anti-periodontopathogenic, anti-Chikungunya activities and in vivo toxicity of Brazilian red propolis.

Silva NBS, de Souza JH, Santiago MB, da Silva Aguiar JR, Martins DOS, da Silva RA, de Andrade Santos I, Aldana-Mejía JA, Jardim ACG, Dos Santos Pedroso R, Ambrósio SR, Veneziani RCS, Bastos JK, Pires RH, Martins CHG.

07-12-2022

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/36477635/>

Bacterial and viral infections are serious public health issue. Therefore, this study aimed to evaluate the antibacterial, antibiofilm and antiviral potential of the Brazilian Red Propolis (BRP) crude hydroalcoholic extract, fractions, and isolated compounds, as well as their in vivo toxicity. The antibacterial activity was evaluated by determining the Minimum Inhibitory Concentration and the antibiofilm activity by determining the Minimum Inhibitory Concentration of Biofilm (MICB50). The viable bacteria count (Log₁₀ UFC/mL) was also obtained. The antiviral assays were performed by infecting BHK-21 cells with Chikungunya (CHIKV) nanoluc. The toxicity of the BRP was evaluated in the *Caenorhabditis elegans* animal model. The MIC values for the crude hydroalcoholic extract sample ranged from 3.12 to 100 µg/mL, while fractions and isolated compounds the MIC values ranged from 1.56 to 400 µg/mL. The BRP crude hydroalcoholic extract, oblongifolin B, and gutiferone E presented MICB50 values ranging from 1.56 to 100 µg/mL against monospecies and multispecies biofilms. Neovestitol and vestitol inhibited CHIKV infection by 93.5 and 96.7%, respectively. The tests to evaluate toxicity in *C. elegans* demonstrated that the BRP was not toxic below the

concentrations 750 µg/mL. The results constitute an alternative approach for treating various infectious diseases.

Genetic diversity of *Aedes aegypti* in the central-upper Paraná Cross-Border axis in Paraguay.

Brítez SC, Herrera L, Ferreira MC, Rolón LM, Ruiz V, González-Brítez N.

Apr-Jun 2022

Rev Peru Med Exp Salud Publica.

<https://pubmed.ncbi.nlm.nih.gov/36477317/>

Correlation of cGAS, STING, INF- α and INF- β gene expression with Zika virus kinetics in primary culture of microglia and neurons from BALB/c mice.

Souza MPM, Freitas BCG, Holanda GM, Diniz Junior JAP, Cruz ACR.

02-12-2022

An Acad Bras Cienc.

<https://pubmed.ncbi.nlm.nih.gov/36477233/>

Pattern recognition receptors participate in the innate immune response. Among PRRs, the cGAS/STING pathway is known to detect cytosolic DNA and cyclic dinucleotides, but it's also important in RNA virus infection. We aimed to evaluate the gene expression of some important genes of cGAS/STING pathway and to correlate this expression with Zika virus kinetics in mice microglia and neurons. Cells were infected by MOI = 1.0. Indirect immunofluorescence, plaque titration of supernatant, extraction, and quantification of total intracellular RNA, RT-qPCR and Western blotting were performed. Plaque titration profile in microglia and neurons was similar, including higher titers of plaque forming units at 24, 48, 72 and 96 hpi, respectively. ZIKV kinetics evaluated by RT-qPCR was similar in both cells, with highest viral titers at 48, 72, 24 and 96 hpi, respectively. Expression profile of cGAS, STING, INF- α and INF- β was quite different between the cells, including gene suppression, as observed for cGAS in neurons. Our results showed a differentiated expression profile of cGAS/STING pathway genes in mice microglia and neurons, which can be explained by the different mechanisms that ZIKV uses to bypass the immune response of these cells. Furthermore, each cell type responds differently to combat the viral infection.

Nucleo-Cytoplasmic Transport of ZIKV Non-Structural 3 Protein Is Mediated by Importin- α/β and Exportin CRM-1.

De Jesús-González LA, Palacios-Rápalo SN, Reyes-Ruiz JM, Osuna-Ramos JF, Farfán-Morales CN, Cordero-Rivera CD, Cisneros B, Gutiérrez-Escolano AL, Del Ángel RM.

08-12-2022

J Virol.

<https://pubmed.ncbi.nlm.nih.gov/36475764/>

Flaviviruses have a cytoplasmic replicative cycle, and crucial events, such as genome translation and replication, occur in the endoplasmic reticulum. However, some viral proteins, such as C, NS1, and NS5 from Zika virus (ZIKV)

containing nuclear localization signals (NLSs) and nuclear export signals (NESs), are also located in the nucleus of Vero cells. The NS2A, NS3, and NS4A proteins from dengue virus (DENV) have also been reported to be in the nucleus of A549 cells, and our group recently reported that the NS3 protein is also located in the nucleus of Huh7 and C636 cells during DENV infection. However, the NS3 protease-helicase from ZIKV locates in the perinuclear region of infected cells and alters the morphology of the nuclear lamina, a component of the nuclear envelope. Furthermore, ZIKV NS3 has been reported to accumulate on the concave face of altered kidney-shaped nuclei and may be responsible for modifying other elements of the nuclear envelope. However, nuclear localization of NS3 from ZIKV has not been substantially investigated in human host cells. Our group has recently reported that DENV and ZIKV NS3 alter the nuclear pore complex (NPC) by cleaving some nucleoporins. Here, we demonstrate the presence of ZIKV NS3 in the nucleus of Huh7 cells early in infection and in the cytoplasm at later times postinfection. In addition, we found that ZIKV NS3 contains an NLS and a putative NES and uses the classic import (importin- α/β) and export pathway via CRM-1 to be transported between the cytoplasm and the nucleus. IMPORTANCE Flaviviruses have a cytoplasmic replication cycle, but recent evidence indicates that nuclear elements play a role in their viral replication. Viral proteins, such as NS5 and C, are imported into the nucleus, and blocking their import prevents replication. Because of the importance of the nucleus in viral replication and the role of NS3 in the modification of nuclear components, we investigated whether NS3 can be localized in the nucleus during ZIKV infection. We found that NS3 is imported into the nucleus via the importin pathway and exported to the cytoplasm via CRM-1. The significance of viral protein nuclear import and export and its relationship with infection establishment is highlighted, emphasizing the development of new host-directed antiviral therapeutic strategies.

Transfusion transmitted virus and dengue virus among healthy blood donors: A prevalence report from Jordan.

Swedan S, Al-Saleh D.

06-12-2022

Bosn J Basic Med Sci.

<https://pubmed.ncbi.nlm.nih.gov/36475356/>

Transfusion transmitted virus (TTV) is thought to contribute to non-A non-E hepatitis and other diseases. Dengue virus (DENV) is a serious mosquito-borne pathogen. Reports on TTV and DENV in Jordan and the Middle East and North Africa region are limited. Herein, the prevalence of TTV antigen and anti-DENV IgG antibodies among apparently healthy blood donors from Northern Jordan and the Northern Agwar region of Jordan was investigated using an enzyme-linked immunosorbent assay. Chi-square test and binary logistic regression were used to correlate positivity with possible infection risk factors (age, sex, residence location, and occupation). One hundred ninety apparently healthy blood donors were included in the study (age 18 - 54 years). TTV antigen was detected in 17.9% of the samples. Lower antigen positivity

was observed among Agwar residents than non-residents (7.1% vs 24.5%; chi-square test $P < 0.001$), which was confirmed by regression analysis (odds ratio 0.262 [95% confidence interval 0.086-0.805]; $P = 0.019$). Antigen positivity did not differ by age, sex, or occupation. Seropositivity for anti-DENV IgG was 17.9%. Seropositivity did not differ by age, sex, or occupation. Higher seropositivity was observed among Agwar residents than non-residents (36.1% vs 9.4%; chi-square test $P < 0.001$), which was confirmed by regression analysis (odds ratio 5.420 [95% confidence interval 2.377-12.359]; $P < 0.001$). Overall, low TTV antigen prevalence and DENV seroprevalence were found among blood donors from Northern Jordan and the Northern Agwar region of Jordan.

A cross-tabulated analysis for the influence of climate conditions on the incidence of dengue fever in Jeddah City, Saudi Arabia during 2006-2009.

Alkhalidy I, Basu A.

Nov-Dec 2022

Int J Health Sci (Qassim).

<https://pubmed.ncbi.nlm.nih.gov/36475033/>

Meteorological indicators of dengue epidemics in non-endemic Northwest Argentina.

Gutierrez JA, Laneri K, Aparicio JP, Sibona GJ.

27-10-2022

Infect Dis Model.

<https://pubmed.ncbi.nlm.nih.gov/36474869/>

In the last two decades dengue cases increased significantly throughout the world, giving place to more frequent outbreaks in Latin America. In the non-endemic city of San Ramón de la Nueva Orán, located in Northwest Argentina, large dengue outbreaks alternate with several years of smaller ones. This pattern, as well as the understanding of the underlying mechanisms, could be essential to design proper strategies to reduce epidemic size. We develop a stochastic model that includes climate variables, social structure, and mobility between a non-endemic city and an endemic area. Climatic variables were input of a mosquito population ecological model, which in turn was coupled to a meta-population, spatially explicit, epidemiological model. Human mobility was included into the model given the high border crossing to the northern country of Bolivia, where dengue transmission is sustained during the whole year. We tested different hypotheses regarding people mobility as well as climate variability by fitting numerical simulations to weekly clinical data reported from 2009 to 2016. After assessing the number of imported cases that triggered the observed outbreaks, our model allows to explain the observed epidemic pattern. We found that the number of vectors per host and the effective reproductive number are proxies for large epidemics. Both proxies are related with climate variability such as rainfall and temperature, opening the possibility to test these meteorological variables for forecast purposes.

Transcriptome profiling and Calreticulin expression in Zika virus -infected *Aedes aegypti*.

de Almeida LS, Nishiyama-Jr MY, Junior AP, Costa-da-Silva AL, Ioshino RS, de Lara Capurro M, Suesdek L.
03-12-2022

Infect Genet Evol.

<https://pubmed.ncbi.nlm.nih.gov/36473637/>

Zika virus (ZIKV) may cause febrile illness and neurological damage, such as microcephaly in fetuses. ZIKV is transmitted to humans by *Aedes aegypti*, a nearly cosmopolitan mosquito. Understanding the virus-vector molecular interactions has been promising to enhance the knowledge towards disease mitigation. Since ZIKV infection alters gene physiology of mosquitoes, we examined the expression profile of ZIKV-infected *Ae. aegypti* by several approaches to identify genes altered by viral infection. Transcriptomics were performed by comparing between ZIKV-infected and uninfected *Ae. aegypti* females, which revealed some differentially expressed genes. Most of these genes appear to be involved with immune response as evidenced by an interactome analysis, and a prominent finding was a calreticulin-like (CRT) gene, which was upregulated during the infection. Expression of CRT was also experimentally quantified by qPCR, however, it revealed no significant differences between infected and uninfected females. Instead, expression levels were highly variable among individuals and negatively correlated to viral load. We also tested the possibility of this gene to be silenced, but the double-stranded RNA did not reduce CRT expression, and actually increased the inter-individuals' expressional variability. Present results differed from our original hypothesis of upregulation by infection. They also diverged between them (comparing qPCR to Transcriptomics) and from the literature which reported augmented CRT levels in *Aedes* species during viral infection. Present case probably underlies a more complex virus-host interaction system than we expected. Regulation of this gene seems not to be a linear correlation between expression and viremia. As infection takes place, a complex homeostatic mechanism may act to prevent expression and other cellular tasks from drifting. It is also possible that CRT expression is simply randomly disturbed by viral infection. Taken together, results show that CRT expression profile during ZIKV infection is complex and requires different investigative approaches to be understood. Studies focused on the biochemical function of CRT protein and on its role in the native mosquito metabolic network could unravel how it is actually influenced by ZIKV. Current work contributes more by getting incidental findings and by posing new hypotheses than by answering the original questions.

Predicting the Effects of Climate Change on Dengue Vector Densities in Southeast Asia through Process-Based Modeling.

Bonnin L, Tran A, Herbreteau V, Marcombe S, Boyer S, Mangeas M, Menkes C.
Dec-2022

Environ Health Perspect.

<https://pubmed.ncbi.nlm.nih.gov/36473499/>

Surface decorated reporter-tagged chikungunya virus-like particles for clinical diagnostics and identification of virus entry inhibitors.

Singh VA, Kumar CS, Khare B, Kuhn RJ, Banerjee M, Tomar S.

27-11-2022

Virology.

<https://pubmed.ncbi.nlm.nih.gov/36473281/>

The ever-evolving and versatile VLP technology is becoming an increasingly popular area of science. This study presents surface decorated reporter-tagged VLPs of CHIKV, an enveloped RNA virus of the genus alphavirus and its applications. Western blot, IFA and live-cell imaging confirm the expression of reporter-tagged CHIK-VLPs from transfected HEK293Ts. CryoEM micrographs reveal particle diameter as ~67nm and 56-70 nm, respectively, for NLuc CHIK-VLPs and mCherry CHIK-VLPs. Our study demonstrates that by exploiting NLuc CHIK-VLPs as a detector probe, robust ratiometric luminescence signal in CHIKV-positive sera compared to healthy controls can be achieved swiftly. Moreover, the potential activity of the Suramin drug as a CHIKV entry inhibitor has been validated through the reporter-tagged CHIK-VLPs. The results reported in this study open new avenues in the eVLPs domain and offer potential for large-scale screening of clinical samples and antiviral agents targeting entry of CHIKV and other alphaviruses.

STAT3 inhibition mediated upregulation of multiple immune response pathways in dengue infection.

Srivastava S, Chaudhary N, Dhembla C, Sundd M, Gupta S, Patel AK.

25-11-2022

Virology.

<https://pubmed.ncbi.nlm.nih.gov/36473280/>

Dengue infection is a world-wide public health threat infecting millions of people annually. Till date no specific antiviral or vaccine is available against dengue virus. Recent evidence indicates that targeting host STAT3 could prove to be an effective antiviral therapy against dengue infection. To explore the potential of STAT3 inhibition as an antiviral strategy, we utilized a STAT3 inhibitor stattic as antiviral agent and performed whole proteome analysis of mammalian cells by mass spectrometry. Differentially expressed proteins among the infected and stattic treated groups were sorted based on their fold change expression and their functional annotation studies were carried out to establish their biological networks. The results presented in the current study indicated that treatment with stattic induces several antiviral pathways to counteract dengue infection. Together with this, we also observed that treatment with stattic downregulates pathways involved in viral transcription and translation thus establishing STAT3 as a suitable target for the development of antiviral interventions. This study establishes the role of STAT3 inhibition as an alternative strategy to counteract DENV pathogenesis. Targeting STAT3 by stattic or similar

molecules may help in identifying novel therapeutic interventions against DENV and probably other flaviviruses.

Epidemiological characteristics of imported acute infectious diseases in Guangzhou, China, 2005-2019.

Liu WH, Shi C, Lu Y, Luo L, Ou CQ.

06-12-2022

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36472963/>

A Review: The Antiviral Activity of Cyclic Peptides.

Chia LY, Kumar PV, Maki MAA, Ravichandran G, Thilagar S.

2023

Int J Pept Res Ther.

<https://pubmed.ncbi.nlm.nih.gov/36471676/>

In the design and development of therapeutic agents, macromolecules with restricted structures have stronger competitive edges than linear biological entities since cyclization can overcome the limitations of linear structures. The common issues of linear peptides include susceptibility to degradation of the peptidase enzyme, off-target effects, and necessity of routine dosing, leading to instability and ineffectiveness. The unique conformational constraint of cyclic peptides provides a larger surface area to interact with the target at the same time, improving the membrane permeability and in vivo stability compared to their linear counterparts. Currently, cyclic peptides have been reported to possess various activities, such as antifungal, antiviral and antimicrobial activities. To date, there is emerging interest in cyclic peptide therapeutics, and increasing numbers of clinically approved cyclic peptide drugs are available on the market. In this review, the medical significance of cyclic peptides in the defence against viral infections will be highlighted. Except for chikungunya virus, which lacks specific antiviral treatment, all the viral diseases targeted in this review are those with effective treatments yet with certain limitations to date. Thus, strategies and approaches to optimise the antiviral effect of cyclic peptides will be discussed along with their respective outcomes. Apart from isolated naturally occurring cyclic peptides, chemically synthesized or modified cyclic peptides with antiviral activities targeting coronavirus, herpes simplex viruses, human immunodeficiency virus, Ebola virus, influenza virus, dengue virus, five main hepatitis viruses, termed as type A, B, C, D and E and chikungunya virus will be reviewed herein.

Vaccination with a Zika virus envelope domain III protein induces neutralizing antibodies and partial protection against Asian genotype in immunocompetent mice.

Shin M, Kim K, Lee HJ, Jung YJ, Park J, Hahn TW.

05-12-2022

Trop Med Health.

<https://pubmed.ncbi.nlm.nih.gov/36471432/>

PCR investigation of infections in patients consulting at a healthcare centre over a four-year period during the Grand Magal of Touba.

Goumballa N, Sambou M, Samba DF, Bassene H, Bedotto M, Aidara A, Dieng M, Hoang VT, Parola P, Sokhna C, Gautret P.

02-12-2022

Travel Med Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36470351/>

Unraveling the Metabolic Alterations Induced by Zika Infection in Prostate Epithelial (PNT1a) and Adenocarcinoma (PC-3) Cell Lines.

Delafiori J, Faria AVS, de Oliveira AN, Sales GM, Dias-Audibert FL, Catharino RR.

05-12-2022

J Proteome Res.

<https://pubmed.ncbi.nlm.nih.gov/36469742/>

The outbreak of Zika virus infection in 2016 led to the identification of its presence in several types of biofluids, including semen. Later discoveries associated Zika infection with sexual transmission and persistent replication in cells of the male reproductive tract. Prostate epithelial and carcinoma cells are favorable to virus replication, with studies pointing to transcriptomics alterations of immune and inflammation genes upon persistence. However, metabolome alterations promoted by the Zika virus in prostate cells are unknown. Given its chronic effects and oncolytic potential, we aim to investigate the metabolic alterations induced by the Zika virus in prostate epithelial (PNT1a) and adenocarcinoma (PC-3) cells using an untargeted metabolomics approach and high-resolution mass spectrometry. PNT1a cells were viable up to 15 days post ZIKV infection, in contrast to its antiproliferative effect in the PC-3 cell lineage. Remarkable alterations in the PNT1a cell metabolism were observed upon infection, especially regarding glycerolipids, fatty acids, and acylcarnitines, which could be related to viral cellular resource exploitation, in addition to the over-time increase in oxidative stress metabolites associated with carcinogenesis. The upregulation of FA20:5 at 5 dpi in PC-3 cells corroborates the antiproliferative effect observed since this metabolite was previously reported to induce PC-3 cell death. Overall, Zika virus promotes extensive lipid alterations on both PNT1a and PC-3 cells, promoting different outcomes based on the cellular metabolic state.

In silico and in vitro arboviral MHC class I-restricted-epitope signatures reveal immunodominance and poor overlapping patterns.

Lopes-Ribeiro Á, Araujo FP, Oliveira PM, Teixeira LA, Ferreira GM, Lourenço AA, Dias LCC, Teixeira CW, Retes HM, Lopes ÉN, Versiani AF, Barbosa-Stancioli EF, da Fonseca FG, Martins-Filho OA, Tsuji M, Peruhype-Magalhães V, Coelho-Dos-Reis JGA.

17-11-2022

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36466864/>

Immune response to arbovirus infection in obesity.

Hameed M, Geerling E, Pinto AK, Miraj I, Weger-Lucarelli J.

18-11-2022

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36466818/>

Obesity is a global health problem that affects 650 million people worldwide and leads to diverse changes in host immunity. Individuals with obesity experience an increase in the size and the number of adipocytes, which function as an endocrine organ and release various adipocytokines such as leptin and adiponectin that exert wide ranging effects on other cells. In individuals with obesity, macrophages account for up to 40% of adipose tissue (AT) cells, three times more than in adipose tissue (10%) of healthy weight individuals and secrete several cytokines and chemokines such as interleukin (IL)-1 β , chemokine C-C ligand (CCL)-2, IL-6, CCL5, and tumor necrosis factor (TNF)- α , leading to the development of inflammation. Overall, obesity-derived cytokines strongly affect immune responses and make patients with obesity more prone to severe symptoms than patients with a healthy weight. Several epidemiological studies reported a strong association between obesity and severe arthropod-borne virus (arbovirus) infections such as dengue virus (DENV), chikungunya virus (CHIKV), West Nile virus (WNV), and Sindbis virus (SINV). Recently, experimental investigations found that DENV, WNV, CHIKV and Mayaro virus (MAYV) infections cause worsened disease outcomes in infected diet induced obese (DIO) mice groups compared to infected healthy-weight animals. The mechanisms leading to higher susceptibility to severe infections in individuals with obesity remain unknown, though a better understanding of the causes will help scientists and clinicians develop host directed therapies to treat severe disease. In this review article, we summarize the effects of obesity on the host immune response in the context of arboviral infections. We have outlined that obesity makes the host more susceptible to infectious agents, likely by disrupting the functions of innate and adaptive immune cells. We have also discussed the immune response of DIO mouse models against some important arboviruses such as CHIKV, MAYV, DENV, and WNV. We can speculate that obesity-induced disruption of innate and adaptive immune cell function in arboviral infections ultimately affects the course of arboviral disease. Therefore, further studies are needed to explore the cellular and molecular aspects of immunity that are compromised in obesity during arboviral infections or vaccination, which will be helpful in developing specific therapeutic/prophylactic interventions to prevent immunopathology and disease progression in individuals with obesity.

Histopathological and immunological characteristics of placentas infected with chikungunya virus.

Salomão N, Rabelo K, Avvad-Portari E, Basílio-de-Oliveira C, Basílio-de-Oliveira R, Ferreira F, Ferreira L, de Souza TM, Nunes P, Lima M, Sales AP, Fernandes R, de Souza LJ, Dias L, Brasil P, Dos Santos F, Paes M.

17-11-2022

Front Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36466642/>

Although vertical transmission of CHIKV has been reported, little is known about the role of placenta in the transmission of this virus and the effects of infection on the maternal-fetal interface. In this work we investigated five placentas from pregnant women who became infected during the gestational period. Four formalin-fixed paraffin-embedded samples of placenta (cases 1-4) were positive for CHIKV by RT-PCR. One (case 5) had no positive test of placenta, but had positive RT-PCR for CHIKV in the serum of the mother and the baby, confirming vertical transmission. The placentas were analyzed regarding histopathological and immunological aspects. The main histopathological changes were: deciduitis, villous edema, deposits, villous necrosis, dystrophic calcification, thrombosis and stem vessel obliteration. In infected placentas we noted increase of cells (CD8⁺ and CD163⁺) and pro- (IFN- γ and TNF- α) and anti-inflammatory (TGF- β and IL-10) cytokines compared to control placentas. Moreover, CHIKV antigen was detected in decidual cell, trophoblastic cells, stroma villi, Hofbauer cells, and endothelial cells. In conclusion, CHIKV infection seems to disrupt placental homeostasis leading to histopathological alterations in addition to increase in cellularity and cytokines overproduction, evidencing an altered and harmful environment to the pregnant woman and fetus.

COVID-19 Vaccination a Cause of Guillain-Barré Syndrome? A Case Series.

Nagdev G, Chavan G, Sahu G, Devasilpa Raju PD.

30-10-2022

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36465787/>

Guillain-Barré syndrome (GBS) is a rare autoimmune neuropathic disorder of peripheral nerves usually following an infection or on rarer occasions following vaccinations, but the exact underlying pathophysiology is still unclear. The most common etiology of GBS is a bacterial infection caused by *Campylobacter jejuni*. Viral infections like Zika virus, Epstein-Barr virus, and Cytomegalovirus also add to the list of GBS etiology. COVID-19 (SARS-CoV-2) has also been reported to cause GBS. Vaccines like the rabies vaccine, influenza vaccine, and poliovirus vaccine account for a very small fraction of Guillain-Barré syndrome. GBS as an adverse effect of COVID-19 vaccination was not reported by the Vaccine Adverse Event Reporting System (VAERS), but an update was later released in the course of the pandemic from FDA news, reporting several patients developing GBS after receiving the COVID-19 vaccine. In this case series, we discuss five cases that developed the GBS post-COVID-19 AstraZeneca vaccine, along with its pathophysiology, management, and outcome.

Estimating Zika virus attack rates and risk of Zika virus-associated neurological complications in Colombian capital cities with a Bayesian model.

Charniga K, Cucunubá ZM, Walteros DM, Mercado M, Prieto F, Ospina M, Nouvellet P, Donnelly CA.
30-11-2022
R Soc Open Sci.
<https://pubmed.ncbi.nlm.nih.gov/36465672/>

Computational study of nitro-benzylidene phenazine as dengue virus-2 NS2B-NS3 protease inhibitor.

Salin NH, Hariono M, Khalili NSD, Zakaria II, Saqallah FG, Mohamad Taib MNA, Kamarulzaman EE, Wahab HA, Khawory MH.
17-11-222
Front Mol Biosci.
<https://pubmed.ncbi.nlm.nih.gov/36465554/>

According to the World Health Organisation (WHO), as of week 23 of 2022, there were more than 1,311 cases of dengue in Malaysia, with 13 deaths reported. Furthermore, there was an increase of 65.7% during the same period in 2021. Despite the increase in cumulative dengue incidence, there is no effective antiviral drug available for dengue treatment. This work aimed to evaluate several nitro-benzylidene phenazine compounds, especially those that contain 4-hydroxy-3,5-bis((2-(4-nitrophenyl)hydrazinylidene)-methyl)benzoate through pharmacophore queries selection method as potential dengue virus 2 (DENV2) NS2B-NS3 protease inhibitors. Herein, molecular docking was employed to correlate the energies of selected hits' free binding and their binding affinities. Pan assay interference compounds (PAINS) filter was also adopted to identify and assess the drug-likeness, toxicity, mutagenicity potentials, and pharmacokinetic profiles to select hit compounds that can be considered as lead DENV2 NS2B-NS3 protease inhibitors. Molecular dynamics assessment of two nitro-benzylidene phenazine derivatives bearing dinitro and hydroxy groups at the benzylidene ring showed their stability at the main binding pocket of DENV2 protease, where their MM-PBSA binding energies were between -22.53 and -17.01 kcal/mol. This work reports those two nitro-benzylidene phenazine derivatives as hits with 52-55% efficiency as antiviral candidates. Therefore, further optimisation is required to minimise the lead compounds' toxicity and mutagenicity.

Knowledge, attitude, and practices of the community toward dengue fever in Shabwah Governorate, Yemen: a descriptive study.

Saghir MA, Ahmed WAM, Dhaiban MMA, Osman ME, Abduljabbar NI.
05-12-2022
J Egypt Public Health Assoc.
<https://pubmed.ncbi.nlm.nih.gov/36464718/>

Toxicity of the essential oil from *Tetradenia riparia* (Hochstetter.) Codd (Lamiaceae) and its principal constituent against malaria and dengue vectors and non-target animals.

de Oliveira AC, Simões RC, Tavares CPS, Lima CAP, Costa Sá IS, da Silva FMA, Figueira EAG, Nunomura SM, Nunomura RCS, Roque RA.
Npov-2022
Pestic Biochem Physiol.
<https://pubmed.ncbi.nlm.nih.gov/36464370/>

Malaria and dengue are diseases transmitted by mosquitoes of the genera *Anopheles* and *Aedes* resistant to commercial insecticides, which are toxic to non-target animals. Alternatively, eco-friendly strategies have focused on searching for essential oil (EO) from plants to control these mosquitoes. In this aspect, this study was carried out to investigate the toxicity of the EO from *Tetradenia riparia* and its main constituent against *Anopheles* and *Aedes* larvae and non-target animals *Toxorhynchites haemorrhoidalis* and *Gambusia affinis*. The mechanism of the larvicidal action of the EO and its main compound was investigated by the acetylcholinesterase (AChE) inhibition. The EO from *T. riparia* was extracted by hydrodistillation with yield of $1.4 \pm 0.17\%$. The analysis of the EO by GC-MS and GC-FID revealed fenchone (38.62%) as the main compound. The EO (100 ppm) showed larvicidal activity against *Anopheles* and *Aedes* larvae (91 to 100% of mortality) (LC50 from 29.31 to 40.76 ppm). On the other hand, fenchone (10 ppm) showed more activity (89 to 100% of mortality) (LC50 from 5.93 to 7.00 ppm) than the EO. The EO and fenchone caused the inhibition of AChE (IC50 from 1.93 to 2.65 ppm), suggesting the inhibition of this enzyme as a possible mechanism of larvicidal action. Regarding toxicity, the EO (1000 ppm) and fenchone (100 ppm) showed low toxicity against *T. haemorrhoidalis* and *G. affinis* (9 to 74% of mortality) (LC50 from 170.50 to 924.89 ppm) (SI/PSF from 17.99 to 31.91) than the α -cypermethrin (0.52 ppm) which was extremely toxic against these non-target animals (100% of mortality, LC50 from 0.22 to 0.29 ppm). This significant larvicidal activity of the *T. riparia* EO and its main constituent, along with the low toxicity towards non-target organisms indicate these samples as a possible eco-friendly alternative for the control of malaria and dengue vectors.

RBM24 inhibits the translation of SARS-CoV-2 polyproteins by targeting the 5'-untranslated region.

Yao Y, Sun H, Chen Y, Tian L, Huang D, Liu C, Zhou Y, Wang Y, Wen Z, Yang B, Chen X, Pei R.
01-12-2022
Antiviral Res.
<https://pubmed.ncbi.nlm.nih.gov/36464077/>

SARS-CoV-2 is a betacoronavirus with single-stranded positive-sense RNA, which is a serious global threat to human health. Understanding the molecular mechanism of viral replication is crucial for the development of antiviral drugs. The synthesis of viral polyproteins is a crucial step in viral progression. The synthesis of viral polyproteins in coronaviruses is regulated by the 5'-untranslated region (UTR); however, the detailed regulatory mechanism needs further investigation. The present study demonstrated that the RNA binding protein, RBM24, interacts with the RNA genome of SARS-CoV-2 via its RNA recognition submotifs (RNPs). The findings

revealed that RBM24 recognizes and binds to the GUGUG element at stem-loop 4 (SL4) in the 5'-UTR of SARS-CoV-2. The interaction between RBM24 and 5'-UTR prevents 80S ribosome assembly, which in turn inhibits polyproteins translation and the replication of SARS-CoV-2. Notably, other RNA viruses, including SARS-CoV, MERS-CoV, Ebola virus, rhinovirus, West Nile virus, Zika virus, Japanese encephalitis virus, yellow fever virus, hepatitis C virus, and human immunodeficiency virus-1 also contain one or several G(U/C/A)GUG sequences in the 5'-UTR, which is also targeted by RBM24. In conclusion, the present study demonstrated that RBM24 functions by interacting with the 5'-UTR of SARS-CoV-2 RNA, and elucidated that RBM24 could be a host restriction factor for SARS-CoV-2 and other RNA viruses.

A peptide derived from the N-terminal of NS2A for the preparation of ZIKV NS2A recognition polyclonal antibody.

Yu Y, Chen Y, Wang J, Fan X, He Z, Qiao S, Hou S, Zou P.
01-12-2022

J Immunol Methods.

<https://pubmed.ncbi.nlm.nih.gov/36463933/>

Zika virus non-structural protein NS2A participates in viral replication, organization, and budding, as well as escaping host immunity. NS2A also involved in the induction of microcephaly by ZIKV. However, the above studies were mainly performed through NS2A with a tag due to the lack of available antibodies against NS2A. ZIKV NS2A is a multiplex transmembrane protein, which leads to difficulties in the preparation of its recognition antibodies, thus seriously affecting the study of ZIKV NS2A. In this study, we found that a peptide (GSTDHMDHFSLGVLC) derived from the N-terminal of ZIKV NS2A coupled to KLH induced antibodies recognizing ZIKV NS2A in rabbits. The purified polyclonal antibody recognized ZIKV NS2A in ZIKV-infected cells with high efficiency and specificity, as detected by western blot and immunofluorescence assay. Our study has important implications for the preparation of ZIKV NS2A antibodies and the in-depth study of ZIKV NS2A.

The Impact of COVID-19 Pandemic and Social Distancing on Motor Function and Growth of Children with Congenital Zika Syndrome: A Prospective Cohort Study.

Gama GL, Salvino AS, Tavares JS, Gregorio JGR, Moreira KMA, Amorim MMR, Melo A.

04-12-2022

Dev Neurorehabil.

<https://pubmed.ncbi.nlm.nih.gov/36463499/>

This article describes the impact of social distancing during the COVID-19 pandemic on the motor function and growth of children with congenital Zika syndrome (CZS). Children's motor function, weight, height and joint range of movement (ROM) were evaluated before the onset of the pandemic and soon after their return to face-to-face activities at a rehabilitation center. Fifty-two children (Mean 46.07 months, SD 3.76 months) were assessed. Results showed a reduction in proportion of children with adequate body mass index ($p = .04$), an increase in

proportion with adequate height ($p < 0.001$), deterioration in gross motor function in children with severe motor impairment ($p < .01$), and a reduction in the maximum ROM for shoulder ($p < .01$) and wrist flexion ($p = .046$), elbow ($p = .01$), knee ($p = .03$) and ankle extension ($p < .01$), and an increase in hip flexion ($p = .04$). The social distancing period appears to have contributed to important losses in motor function and joint mobility of children with CZS; however, this period of time appeared to have less impact on their growth.

Malaria and dengue outbreaks during a national disaster in Pakistan: A rising concern for public health.

Arshad T, Wajahat A, Jabeen A, Ali SH.

03-12-2022

J Glob Health.

<https://pubmed.ncbi.nlm.nih.gov/36462206/>

Antibodies Produced in Response to a Live-Attenuated Dengue Vaccine are Functional in Activating the Complement System.

Nascimento EJM, Norwood B, Kpamegan E, Parker A, Fernandes J, Perez-Guzman E, Tricou V, Braun R, Sharma M, Dean HJ.

03-12-2022

J Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36461942/>

A competition smFRET assay to study ligand-induced conformational changes of the dengue virus protease.

Maus H, Hinze G, Hammerschmidt SJ, Basché T, Schirmeister T.

03-12-2022

Protein Sci.

<https://pubmed.ncbi.nlm.nih.gov/36461913/>

Ligand binding to proteins often is accompanied by conformational transitions. Here, we describe a competition assay based on single molecule Förster resonance energy transfer (smFRET) to investigate the ligand-induced conformational changes of the dengue virus (DENV) NS2B-NS3 protease, which can adopt at least two different conformations. First, a competitive ligand was used to stabilize closed conformation of the protease. Subsequent addition of the allosteric inhibitor reduced the fraction of the closed conformation and simultaneously increased the fraction of the open conformation, demonstrating that the allosteric inhibitor stabilizes the open conformation. In addition, the proportions of open and closed conformations at different concentrations of the allosteric inhibitor were used to determine its binding affinity to the protease. The K_D value observed is in accordance with the IC_{50} determined in the fluorometric assay. Our novel approach appears to be a valuable tool to study conformational transitions of other proteases and enzymes. This article is protected by copyright. All rights reserved.

Differential expression of interferon inducible protein: Guanylate binding protein (GBP1 & GBP2) in severe dengue.

Mariappan V, Adikari S, Shanmugam L, Easow JM, Balakrishna Pillai A.

29-11-2022

Free Radic Biol Med.

<https://pubmed.ncbi.nlm.nih.gov/36460216/>

Dengue virus is reported to activate endothelial cells (EC), but the precise cause for severe dengue (SD) is not known. Guanylate binding proteins (GBPs) are IFN-inducible proteins secreted by ECs and are involved in the anti-oxidant and anti-viral response. The involvement of GBPs in the pathogenesis of dengue remains under explored. In the present study, we quantified the mRNA and protein levels of GBP1 and 2 during acute, defervescence and convalescent phase in SD-10, dengue without warning sign-15 and dengue with warning sign-25 compared to other febrile illnesses-10 and healthy controls-8 using RT-PCR and ELISA respectively. Lipid peroxidation in plasma samples were measured using the Kei Satoh method. Protein and DNA oxidation were determined by ELISA. The efficacy of the proteins in predicting disease severity was done by Support Vector Machine (SVM) model. A significant ($P \leq 0.01$) decrease in the levels of mRNA and protein of both GBP1 and GBP2 was observed during defervescence in both SD and DWW cases. The levels were significantly ($P \leq 0.05$) tapered off in SD cases from acute till critical phases compared to other study groups. DNA, protein and lipid oxidation markers showed an increasing trend in SD ($P \leq 0.01$). Both GBP1 & 2 were found to be negatively associated plasma leakage and oxidative stress markers. EC's activated with SD serum showed a reduced expression of GBP 1 and 2. Nevertheless, the SVM model revealed that plasma levels of proteins along with clinical symptoms could predict the disease outcomes with higher precision. This is the first study reporting a downregulated expression of GBP1 & 2 and their association with oxidative stress and plasma leakage in dengue cases. This suggests the importance of GBPs in regulating disease manifestation. However, further investigations are required to ascertain its role as a biomarker or therapeutic target in dengue infection.

Epidemiological and Clinical Characteristics of Patients with Dengue Fever in a Recent Outbreak in Oman: A Single Center Retrospective-cohort Study.

Al Awaidy ST, Khamis F, Al-Zakwani I, Al Kindi S, Al Busafi S, Al Sulaimi K, Al Sidiari H.

30-11-2022

Oman Med J.

<https://pubmed.ncbi.nlm.nih.gov/36458248/>

Pharmacological Manipulation of UPR: Potential Antiviral Strategy Against Chikungunya Virus.

Agrawal N, Saini S, Khanna M, Dhawan G, Dhawan U.

Dec-2022

Indian J Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36458214/>

Viruses invade the host cells and maneuver the cellular translation machinery to translate the viral proteins in substantial amounts, which may disturb Endoplasmic Reticulum homeostasis leading to induction of Unfolded Protein Response (UPR), a host response pathway involved in viral pathogenesis. Here, we investigated the effect of UPR pathways on the pathogenesis of chikungunya virus infection. We observed that chikungunya virus mediated the modulation of UPR. A positive modulation was observed in the activation of IRE1 and ATF6 branch while the PERK branch of UPR observed suppressed upon virus infection. We further investigated the effect of the inhibition of UPR pathways on chikungunya virus replication using inhibitors for each branch. Cells treated with 3-ethoxy-5,6-dibromosalicylaldehyde (IRE1 inhibitor) and AEBSF (ATF6 inhibitor) significantly inhibits the viral replication process. This study has provided a novel perspective in designing antivirals against chikungunya virus.

The Role of Infection and Inflammation in the Pathogenesis of Pediatric Arterial Ischemic Stroke.

Cornet MC, Grose C, Vexler Z, Wu YW, Fullerton HJ.

Dec-2022

Semin Pediatr Neurol.

<https://pubmed.ncbi.nlm.nih.gov/36456035/>

Infections play an important role in the pathogenesis of acute ischemic stroke (AIS) in neonates and children. In neonates, chorioamnionitis or intrauterine inflammation has been implicated as a common risk factor for AIS. In infants and children, recent investigations demonstrated that even minor childhood infections are associated with subsequent increased risk for AIS. Post-infectious inflammatory mechanisms following infections with herpesviruses may lead to focal cerebral arteriopathy (FCA), one of the most common causes of AIS in a previously healthy child. Other agents such as parvovirus B19, dengue virus, and SARS-CoV-2 have recently been implicated as other potential triggers. Infections are compelling treatable stroke risk factors, with available therapies for both pathogens and downstream inflammatory effects. However, infections are common in childhood, while stroke is uncommon. The ongoing VIPS II (Vascular effects of Infection in Pediatric Stroke) study aims to identify the array of pathogens that may lead to childhood AIS and whether either unusual strains or unusual combinations of pathogens explain this paradox. Immune modulation with corticosteroids for FCA is another active area of research, with European and U.S. trials launching soon. The results of these new pediatric stroke studies combined with findings emerging from the larger field of immune-mediated post-infectious diseases will likely lead to new approaches to the prevention and treatment of pediatric stroke. This review highlights recent developments from both clinical and animal model research enhancing our understanding of this relationship between infection, inflammation, and stroke in neonates and children.

Viewing teratogens through the lens of nicotinamide adenine dinucleotide (NAD+).

Mark PR, Dunwoodie SL.

01-12-2022

Birth Defects Res.

<https://pubmed.ncbi.nlm.nih.gov/36453269/>

[Family typologies for dengue prevention in Colombia].

Valencia-Jiménez NN, Ortega-Montes JE, Puello-Alcocer EC.

28-11-2022

Cad Saude Publica.

<https://pubmed.ncbi.nlm.nih.gov/36449843/>

The aim of this study was to analyze the relationship between sociodemographic characteristics and risk factors of the context to establish family typologies based on the control and prevention of dengue in the Department of Córdoba, Colombia, through a cross-sectional analytical study carried out during the year 2021 with 328 families. For this purpose, the proportional random stratified sampling technique was used, with a 90% confidence level and 7% error. Associations between pairs of variables were measured using the chi-square test at a significance level of 5%. For the joint measurement of the associations between variables, a multiple correspondence analysis was used. The grouping of families was done using a conglomerate analysis (cluster) and Ward's hierarchical agglomerative method. Four types of families were determined, highlighting two among them. The first, with 163 households, mainly from Montería, groups families with better educational levels, higher income, greater participation in preventive programs, better access to public services and less presence of stagnant water; the second group is composed by families with incomplete elementary school, precarious access to drinking water and/or sewage services, lower economic income and higher prevalence of the triggers for the spread of the vector. The analysis of the link family/dengue prevention justifies further studies on the subject for the implementation of comprehensive contextualized strategies that address the particularities of the territory and the variability of sociodemographic characteristics.

Zika virus noncoding RNA cooperates with the viral protein NS5 to inhibit STAT1 phosphorylation and facilitate viral pathogenesis.

Slonchak A, Wang X, Aguado J, Sng JDJ, Chaggar H, Freney ME, Yan K, Torres FJ, Amarilla AA, Balea R, Setoh YX, Peng N, Watterson D, Wolvetang E, Suhrbier A, Khromykh AA.

02-12-2022

Sci Adv.

<https://pubmed.ncbi.nlm.nih.gov/36449607/>

All flaviviruses, including Zika virus, produce noncoding subgenomic flaviviral RNA (sfRNA), which plays an important role in viral pathogenesis. However, the exact

mechanism of how sfRNA enables viral evasion of antiviral response is not well defined. Here, we show that sfRNA is required for transplacental virus dissemination in pregnant mice and subsequent fetal brain infection. We also show that sfRNA promotes apoptosis of neural progenitor cells in human brain organoids, leading to their disintegration. In infected human placental cells, sfRNA inhibits multiple antiviral pathways and promotes apoptosis, with signal transducer and activator of transcription 1 (STAT1) identified as a key shared factor. We further show that the production of sfRNA leads to reduced phosphorylation and nuclear translocation of STAT1 via a mechanism that involves sfRNA binding to and stabilizing viral protein NS5. Our results suggest the cooperation between viral noncoding RNA and a viral protein as a novel strategy for counteracting antiviral responses. [Defective viral genomes from Chikungunya virus: A new broad-spectrum antiviral approach?].

Khau S, Lopatynski C.

Nov-2022

Med Sci (Paris).

<https://pubmed.ncbi.nlm.nih.gov/36448905/>

Identification of the corticotropin-releasing factor receptor 1 antagonists as inhibitors of Chikungunya virus replication using a Gaussia luciferase-expressing subgenomic replicon.

Watanabe Y, Suzuki Y, Emi A, Murakawa T, Hishiki T, Kato F, Sakaguchi S, Wu H, Yano T, Lim CK, Takasaki T, Nakano T.

31-12-2022

Biochem Biophys Res Commun.

<https://pubmed.ncbi.nlm.nih.gov/36403481/>

The Chikungunya virus (CHIKV), an enveloped RNA virus that has been identified in over 40 countries and is considered a growing threat to public health worldwide. However, there is no preventive vaccine or specific therapeutic drug for CHIKV infection. To identify a new inhibitor against CHIKV infection, this study constructed a subgenomic RNA replicon expressing the secretory Gaussia luciferase (Gluc) based on the CHIKV SL11131 strain. Transfection of in vitro-transcribed replicon RNA to BHK-21 cells revealed that Gluc activity in culture supernatants was correlated with the intracellular replication of the replicon genome. Through a chemical compound library screen using the Gluc reporter CHIKV replicon, we identified several compounds that suppressed CHIKV infection in Vero cells. Among the hits identified, CP-154,526, a non-peptide antagonist of the corticotropin-releasing factor receptor type-1 (CRF-R1), showed the strongest anti-CHIKV activity and inhibited CHIKV infection in Huh-7 cells. Interestingly, other CRF-R1 antagonists, R121919 and NGD 98-2, also exhibited inhibitory effects on CHIKV infection. Time-of-drug addition and virus entry assays indicated that CP-154,526 suppressed a post-entry step of infection, suggesting that CRF-R1 antagonists acted on a target in the intracellular replication process of CHIKV. Therefore, the Gluc reporter replicon system established in this study would greatly

facilitate the development of antiviral drugs against CHIKV infection.

Challenges and lessons learned from the rapid operationalization of a prospective cohort to study the natural history and neurodevelopmental outcomes of postnatal Zika virus infection among infants and children in rural Guatemala.

Paniagua-Avila A, Olson D, Connery A, Calvimontes DM, Bolanos GA, Lamb MM, Bauer D, Ralda A, Rojop N, Barrios E, Chacon A, Gomez M, Arroyave P, Hernandez S, Martinez MA, Bunge-Montes S, Colbert A, Arias K, Brazeale G, Holliday A, Tomashak KM, El Sahly HM, Keitel W, Munoz FM, Asturias EJ.

16-11-2022

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36383617/>

During the course of the 2015-2017 outbreak of Zika virus (ZIKV) in the Americas, the emerging virus was recognized as a congenital infection that could damage the developing brain. As the Latin American ZIKV outbreak advanced, the scientific and public health community questioned if this newly recognized neurotropic flavivirus could affect the developing brain of infants and young children infected after birth. We report here the study design, methods and the challenges and lessons learned from the rapid operationalization of a prospective natural history cohort study aimed at evaluating the potential neurological and neurodevelopmental effects of postnatal ZIKV infection in infants and young children, which had become epidemic in Central America. This study enrolled a cohort of 500 mothers and their infants, along with nearly 400 children 1.5-3.5 years of age who were born during the initial phase of the ZIKV epidemic in a rural area of Guatemala. Our solutions and lessons learned while tackling real-life challenges may serve as a guide to other researchers carrying out studies of emerging infectious diseases of public health priority in resource-constrained settings.

Importance of NF κ B, IL-10 serum levels and DC-SIGN polymorphic haplotypes in determining dengue disease severity among eastern Indian patients.

Ghosh P, Mukherjee S, Saha B, Tripathi A.

Dec-2022

Microb Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36356794/>

Evaluation of Zika virus DNA vaccines based on NS1 and domain III of E.

Xiong G, Li Y, Chen F, Xiong X, Wang Q, Zhang L, Dong H, Zhu C, Cui J, He M, Cheng H, Hu A, Cheng C, Pang J, Liu G, Chen H.

Dec-2022

Int Immunopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/36274487/>

Assessing single-locus CRISPR/Cas9-based gene drive variants in the mosquito *Aedes aegypti* via single-generation crosses and modeling.

Reid W, Williams AE, Sanchez-Vargas I, Lin J, Juncu R, Olson KE, Franz AWE.

01-12-2022

G3 (Bethesda).

<https://pubmed.ncbi.nlm.nih.gov/36250791/>

The yellow fever mosquito *Aedes aegypti* is a major vector of arthropod-borne viruses, including dengue, chikungunya, and Zika viruses. A novel approach to mitigate arboviral infections is to generate mosquitoes refractory to infection by overexpressing antiviral effector molecules. Such an approach requires a mechanism to spread these antiviral effectors through a population, for example, by using CRISPR/Cas9-based gene drive systems. Critical to the design of a single-locus autonomous gene drive is that the selected genomic locus is amenable to both gene drive and appropriate expression of the antiviral effector. In our study, we used reverse engineering to target 2 intergenic genomic loci, which had previously shown to be highly permissive for antiviral effector gene expression, and we further investigated the use of 3 promoters (nanos, β 2-tubulin, or zpg) for Cas9 expression. We then quantified the accrual of insertions or deletions (indels) after single-generation crossings, measured maternal effects, and assessed fitness costs associated with various transgenic lines to model the rate of gene drive fixation. Overall, MGDriVE modeling suggested that when an autonomous gene drive is placed into an intergenic locus, the gene drive system will eventually be blocked by the accrual of gene drive blocking resistance alleles and ultimately be lost in the population. Moreover, while genomic locus and promoter selection were critically important for the initial establishment of the autonomous gene drive, it was the fitness of the gene drive line that most strongly influenced the persistence of the gene drive in the simulated population. As such, we propose that when autonomous CRISPR/Cas9-based gene drive systems are anchored in an intergenic locus, they temporarily result in a strong population replacement effect, but as gene drive-blocking indels accrue, the gene drive becomes exhausted due to the fixation of CRISPR resistance alleles.

Anti-Müllerian hormone concentrations in female rabbits and its relation to spay status, pseudopregnancy and ovarian follicle numbers.

Böhmer F, Erber K, Ewringmann A, Klein R, Reese S, Böhmer C, Meyer-Lindenberg A, Walter B.

Dec-2022

Reprod Domest Anim.

<https://pubmed.ncbi.nlm.nih.gov/36052807/>

Anti-Müllerian hormone (AMH), known for its role during foetal sexual differentiation, is secreted by the Sertoli cells in males and the granulosa cells in females during post-natal life. As serum AMH concentrations correlate with follicle numbers, AMH is utilized as a marker of ovarian reserve in many species. In dogs and cats, AMH is used as a diagnostic tool to determine spay or neuter status. In the

available literature, no research regarding serum AMH levels in rabbits has been published yet. The objectives of the present study were to (1) measure serum AMH concentrations in female rabbits and investigate the value of AMH as a diagnostic tool to differentiate between spayed and intact does and (2) relate measured AMH levels to pseudopregnancy and ovarian follicle numbers. For AMH measurement, serum samples were obtained from sexually intact (n = 64) and spayed (n = 22) female rabbits. Spayed does were of various breeds; intact rabbits were Zika hybrid rabbits. In the intact does, AMH measurement was complemented by determination of progesterone levels, gynaecological examination and histopathological evaluation of the uterus and ovaries, including follicle counts. Serum AMH and progesterone concentrations were measured using a human-based chemiluminescence immunoassay (CLIA) and an enzyme-linked fluorescence assay (ELFA), respectively. Depending on progesterone levels, sexually intact does were classified into follicular (n = 52) or luteal phase (n = 12). Median serum AMH levels were 1.53 ng/ml (range 0.77-3.36 ng/ml) in intact and 0.06 ng/ml (range \leq 0.01-0.23 ng/ml) in spayed does. AMH concentrations between the intact and spayed rabbits differed significantly and did not overlap ($p < .001$). Receiver operating characteristic (ROC) curve analysis yielded a sensitivity and specificity of 100% for a cut-off level of 0.50 ng/ml. Follicular or luteal phase had no significant influence on measured AMH levels ($t = 0.061$, $df = 62$, $p = .951$). While the number of secondary follicles correlated significantly with AMH concentrations ($r_s = 0.410$, $p = .001$), the number of primary or antral follicles did not ($r_s = 0.241$, $p = .055$ and $r_s = 0.137$, $p = .281$, respectively). In conclusion, a single determination of serum AMH concentrations was adequate to distinguish spayed from intact female rabbits. Among sexually intact individuals, whether does were in follicular or luteal phase had no significant influence on measured serum AMH concentrations. The relationship between small growing follicles and AMH levels as described in other species could be partially confirmed, as secondary follicles correlated significantly with AMH.

Behavioral and game-theoretic modeling of dengue epidemic: Comment on "Mathematical models for dengue fever epidemiology: A 10-year systematic review" by M. Aguiar et al.

Banerjee M, Ghosh S.

Dec-2022

Phys Life Rev.

<https://pubmed.ncbi.nlm.nih.gov/36029602/>

Visualization of the Linear and Spatial Organization of Chromosomes in Mosquitoes.

Liang J, Bondarenko SM, Sharakhov IV, Sharakhova MV.

01-12-2022

Cold Spring Harb Protoc.

<https://pubmed.ncbi.nlm.nih.gov/35960626/>

Mosquitoes are vectors of dangerous human diseases such as malaria, dengue, Zika, West Nile fever, and

lymphatic filariasis. Visualization of the linear and spatial organization of mosquito chromosomes is important for understanding genome structure and function. Utilization of chromosomal inversions as markers for population genetics studies yields insights into mosquito adaptation and evolution. Cytogenetic approaches assist with the development of chromosome-scale genome assemblies that are useful tools for studying mosquito biology and for designing novel vector control strategies. Fluorescence in situ hybridization is a powerful technique for localizing specific DNA sequences within the linear chromosome structure and within the spatial organization of the cell nucleus. Here, we introduce protocols used in our laboratories for chromosome visualization and their application in mosquitoes.

Rage

Properties of rabies virus phosphoprotein and nucleoprotein biocondensates formed in vitro and in cellulo.

Nevers Q, Scrima N, Glon D, Le Bars R, Decombe A, Garnier N, Ouldali M, Lagaudrière-Gesbert C, Blondel D, Albertini A, Gaudin Y.

08-12-2022

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36480574/>

Rabies virus (RABV) transcription and replication take place within viral factories having liquid properties, called Negri bodies (NBs), that are formed by liquid-liquid phase separation (LLPS). The co-expression of RABV nucleoprotein (N) and phosphoprotein (P) in mammalian cells is sufficient to induce the formation of cytoplasmic biocondensates having properties that are like those of NBs. This cellular minimal system was previously used to identify P domains that are essential for biocondensates formation. Here, we constructed fluorescent versions of N and analyzed by FRAP their dynamics inside the biocondensates formed in this minimal system as well as in NBs of RABV-infected cells using FRAP. The behavior of N appears to be different of P as there was no fluorescence recovery of N proteins after photobleaching. We also identified arginine residues as well as two exposed loops of N involved in condensates formation. Corresponding N mutants exhibited distinct phenotypes in infected cells ranging from co-localization with NBs to exclusion from them associated with a dominant-negative effect on infection. We also demonstrated that in vitro, in crowded environments, purified P as well as purified N^o-P complex (in which N is RNA-free) form liquid condensates. We identified P domains required for LLPS in this acellular system. P condensates were shown to associate with liposomes, concentrate RNA, and undergo a liquid-gel transition upon ageing. Conversely, N^o-P droplets were disrupted upon incubation with RNA. Taken together, our data emphasize the central role of P in NBs formation and reveal some physicochemical features of P and N^o-P droplets relevant for explaining NBs properties such as their envelopment by cellular membranes at late stages of

infection and nucleocapsids ejections from the viral factories.

Human Rabies - Texas, 2021.

Blackburn D, Minhaj FS, Al Hammoud R, Orciari L, Miller J, Maness T, Stewart J, Singletary B, Ledezma E, Ellsworth M, Carlo-Angleró A, Niezgoda M, Gigante CM, Rao AK, Satheshkumar PS, Heresi GP, Kieffer A, Wallace RM.
09-12-2022

MMWR Morb Mortal Wkly Rep.

<https://pubmed.ncbi.nlm.nih.gov/36480462/>

In late August 2021, a boy aged 7 years was bitten by a bat while he was playing outside his apartment home in Medina County, Texas. He informed his parents; however, no rabies postexposure prophylaxis (PEP) was sought because there were no visible bite marks, and the family was unaware that contact with a bat, including in the absence of visible bite marks, might cause rabies. Approximately 2 months later, the child was hospitalized for altered mental status, seizures, and hypersalivation and ultimately received a diagnosis of rabies. Experimental therapies were attempted; however, the child died 22 days after symptom onset. Fifty-seven persons who met criteria for suspected or known exposure to infectious secretions in this case were advised to consult with a medical provider about the need for rabies PEP in accordance with Advisory Committee on Immunization Practices (ACIP) guidelines (1). Rabies, an acute, progressive neuroencephalitis, is nearly always fatal. Although dogs are the most common source of human rabies deaths worldwide and account for an estimated 59,000 annual cases of human rabies globally (2), bats are the most common source of domestically acquired rabies in the United States and have been implicated in 31 (81.6%) of 38 human infections since 2000 (3). Attempts to prevent death or poor neurologic outcomes once rabies symptoms develop have been largely unsuccessful (4). Administration of rabies PEP, comprising rabies immunoglobulin and a series of doses of rabies vaccine, is critical to preventing rabies after an exposure; enhanced public education about the risk posed by bats, and the availability of PEP to prevent rabies, is needed.

Henipaviruses and lyssaviruses target nucleolar Treacle protein and regulate ribosomal RNA synthesis.

Rawlinson SM, Zhao T, Ardipradja K, Zhang Y, Veugelers PF, Harper JA, David CT, Sundaramoorthy V, Moseley GW.

08-12-2022

Traffic

<https://pubmed.ncbi.nlm.nih.gov/36479968/>

The nucleolus is a common target of viruses and viral proteins, but for many viruses the functional outcomes and significance of this targeting remains unresolved. Recently, the first intranucleolar function of a protein of a cytoplasmically-replicating negative-sense RNA virus (NSV) was identified, with the finding that the matrix (M) protein of Hendra virus (HeV) (genus Henipavirus, family Paramyxoviridae) interacts with Treacle protein within nucleolar subcompartments and mimics a cellular

mechanism of the nucleolar DNA-damage response (DDR) to suppress ribosomal RNA (rRNA) synthesis. Whether other viruses utilise this mechanism has not been examined. We report that sub-nucleolar Treacle targeting and modulation is conserved between M proteins of multiple Henipaviruses, including Nipah virus and other potentially zoonotic viruses. Furthermore, this function is also evident for P3 protein of rabies virus, the prototype virus of a different RNA virus family (Rhabdoviridae), with Treacle depletion in cells also found to impact virus production. These data indicate that unrelated proteins of viruses from different families have independently developed nucleolar/Treacle targeting function, but that modulation of Treacle has distinct effects on infection. Thus, subversion of Treacle may be an important process in infection by diverse NSVs, and so could provide novel targets for antiviral approaches with broad specificity.

Immunogenicity and one-year boostability of a 3-dose intramuscular rabies pre-exposure prophylaxis schedule in adults receiving immunosuppressive monotherapy: a prospective single-Centre clinical trial.

Garcia Garrido HM, van Put B, Terryn S, de Pijper CA, Stijnis C, D'Haens GR, Spuls PI, van de Sande MG, Gucht S, Grobusch MP, Goorhuis A.

08-12-2022

J Travel Med.

<https://pubmed.ncbi.nlm.nih.gov/36477981/>

Development of therapeutic vaccines for the treatment of diseases.

Tian Y, Hu D, Li Y, Yang L.

08-12-2022

Mol Biomed.

<https://pubmed.ncbi.nlm.nih.gov/36477638/>

Vaccines are one of the most effective medical interventions to combat newly emerging and re-emerging diseases. Prophylactic vaccines against rabies, measles, etc., have excellent effectiveness in preventing viral infection and associated diseases. However, the host immune response is unable to inhibit virus replication or eradicate established diseases in most infected people. Therapeutic vaccines, expressing specific endogenous or exogenous antigens, mainly induce or boost cell-mediated immunity via provoking cytotoxic T cells or elicit humoral immunity via activating B cells to produce specific antibodies. The ultimate aim of a therapeutic vaccine is to reshape the host immunity for eradicating a disease and establishing lasting memory. Therefore, therapeutic vaccines have been developed for the treatment of some infectious diseases and chronic noncommunicable diseases. Various technological strategies have been implemented for the development of therapeutic vaccines, including molecular-based vaccines (peptide/protein, DNA and mRNA vaccines), vector-based vaccines (bacterial vector vaccines, viral vector vaccines and yeast-based vaccines) and cell-based vaccines (dendritic cell vaccines and genetically modified cell vaccines) as well as combinatorial approaches. This review

mainly summarizes therapeutic vaccine-induced immunity and describes the development and status of multiple types of therapeutic vaccines against infectious diseases, such as those caused by HPV, HBV, HIV, HCV, and SARS-CoV-2, and chronic noncommunicable diseases, including cancer, hypertension, Alzheimer's disease, amyotrophic lateral sclerosis, diabetes, and dyslipidemia, that have been evaluated in recent preclinical and clinical studies.

Rabies: who should care?

Baker HJ, Martin DR, Gross AL, Chamorro MF, Naskou MC, Johnson AK, Brock KV, Van Kampen KR, Willoughby RE.

07-12-2022

J Am Vet Med Assoc.

<https://pubmed.ncbi.nlm.nih.gov/36476414/>

Rabies is the deadliest viral infection known, with no reliable treatment, and although it is entirely preventable, rabies continues to kill more than 60,000 people every year, mostly children in countries where dog rabies is endemic. America is only 1 generation away from the time when rabies killed more than 10,000 animals and 50 Americans every year, but 3 to 5 Americans continue to die annually from rabies. Distressingly, > 50,000 Americans undergo rabies prevention therapy every year after exposure to potentially rabid animals. While enormous progress has been made, more must be done to defeat this ancient but persistent, fatal zoonosis. In the US, lack of public awareness and ambivalence are the greatest dangers imposed by rabies, resulting in unnecessary exposures, anxiety, and risk. Veterinarians have a special role in informing and reassuring the public about prevention and protection from rabies. This summary of current facts and future advances about rabies will assist veterinarians in informing their clients about the disease.

Nonclinical Safety Assessment of Lipid Nanoparticle-and Emulsion-Based Self-Amplifying mRNA Vaccines in Rats.

Donahue DA, Ballesteros C, Maruggi G, Glover C, Ringenberg MA, Marquis M, Ben Abdeljelil N, Ashraf A, Rodriguez LA, Stokes AH.

06-12-2022

Int J Toxicol.

<https://pubmed.ncbi.nlm.nih.gov/36472205/>

Vaccines containing mRNA with the capacity to self-amplify represent an alternative to the mRNA vaccines that came to prominence during the COVID-19 pandemic. To gain further insights on the safety profile of self-amplifying mRNA- (SAM-) vaccines, this preclinical toxicology study in rats evaluated the effect of (i) the type of delivery system (lipid nanoparticle [LNP] vs cationic nano-emulsion [CNE]); (ii) antigen-encoding sequence (rabies glycoprotein G vs SARS-CoV-2 Spike); and (iii) RNA amplification. Further analyses also evaluated gene expression in peripheral blood after vaccination, and the biodistribution of vaccine RNA. The SAM vaccines administered as two doses 2-weeks apart had acceptable safety profiles in rats, with respect to clinical signs, blood biochemistry, and macroscopic and microscopic pathology. A transient increase in ALT/AST ratio occurred

only in female rats and in the absence of muscle and liver damage was dependent on RNA amplification and appeared related to the greater quantities of vaccine RNA in the muscle and livers of female rats vs male rats. The RNA and delivery-vehicle components, but not the nature of the antigen-coding sequence or the requirement for RNA amplification, affected aspects of the stimulation of innate-immune activity, which was consistent with the transient activation of type I and type II interferon signaling. The delivery vehicle, LNP, differed from CNE as vaccine RNA in CNE compositions appeared independently to stimulate innate-immune activity at 4 hours after vaccination. Our analysis supports further studies to assess whether these differences in innate-immune activity affect safety and efficacy of the SAM vaccine.

Spatial and temporal dynamic analysis of rabies: A review of current methodologies.

Chen S.

30-11-2022

Geospat Health.

<https://pubmed.ncbi.nlm.nih.gov/36468590/>

Rabies continues to be one of the deadliest, high risk diseases worldwide, posing a severe threat to public health. The lack of human-to-human transmission means that the spread of rabies is not significantly affected by the distribution of humans or migration. Thus, the spatiotemporal dynamic of cases in both wild and domestic animals is an important issue that can result in human cases. This paper gives an overview of the methodologies for the spatial and temporal dynamic analysis of this disease. It introduces the most representative research progress of spatial aggregation, dynamic transmission, spatiotemporal distribution, epidemiological analysis and application of modelling in the study of rabies transmission in recent years. This overview should be useful for investigating the spatial and temporal dynamics of rabies, as it could help understanding the spread of cases as well as contribute to the development of better prevention and control strategies in ecology and epidemiology.

Cerebrospinal fluid analysis in horses, cattle, and sheep diagnosed with rabies: A retrospective study of 62 cases.

Zakia LS, Albertino LG, Andrade DGA, Amorim RM, Takahira RR, Oliveira-Filho JP, Borges AS.

Dec-2022

Can Vet J.

<https://pubmed.ncbi.nlm.nih.gov/36467385/>

COVID-19 Vaccination a Cause of Guillain-Barré Syndrome? A Case Series.

Nagdev G, Chavan G, Sahu G, Devasilpa Raju PD.

30-10-2022

Cureus.

<https://pubmed.ncbi.nlm.nih.gov/36465787/>

Guillain-Barré syndrome (GBS) is a rare autoimmune neuropathic disorder of peripheral nerves usually

following an infection or on rarer occasions following vaccinations, but the exact underlying pathophysiology is still unclear. The most common etiology of GBS is a bacterial infection caused by *Campylobacter jejuni*. Viral infections like Zika virus, Epstein-Barr virus, and Cytomegalovirus also add to the list of GBS etiology. COVID-19 (SARS-CoV-2) has also been reported to cause GBS. Vaccines like the rabies vaccine, influenza vaccine, and poliovirus vaccine account for a very small fraction of Guillain-Barré syndrome. GBS as an adverse effect of COVID-19 vaccination was not reported by the Vaccine Adverse Event Reporting System (VAERS), but an update was later released in the course of the pandemic from FDA news, reporting several patients developing GBS after receiving the COVID-19 vaccine. In this case series, we discuss five cases that developed the GBS post-COVID-19 AstraZeneca vaccine, along with its pathophysiology, management, and outcome.

Habitat selection by free-roaming domestic dogs in rabies endemic countries in rural and urban settings.

Cunha Silva L, Friker B, Warembourg C, Kanankege K, Wera E, Berger-González M, Alvarez D, Dürr S.

03-12-2022

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/36463285/>

Domestic dogs can affect human health through bites and pathogen transmission, particularly in resource-poor countries where dogs, including owned ones, predominantly roam freely. Habitat and resource selection analysis methods are commonplace in wildlife studies but have not been used to investigate the environmental resource use of free-roaming domestic dogs (FRDD). The present study implements GPS devices to investigate habitat selection by FRDD from an urban site and a rural site in Indonesia, and one urban and two rural sites in Guatemala (N = 321 dogs). Spatial mixed effects logistic regression models, accounting for heterogeneous distribution of the resources, showed that patterns of habitat selection by FRDD were similar across study sites. The most preferred resources were anthropogenic, being buildings and roads, which implies selection for human proximity. Vegetation and open fields were less preferred and steep terrain was avoided, indicating that FRDD were synanthropic and that their space patterns likely optimised energy use. Results presented here provide novel data on FRDD habitat selection patterns, while improving our understanding of dog roaming behaviour. These findings provide insights into possible high-risk locations for pathogen transmission for diseases such as rabies, and can assist management authorities in the planning and deployment of efficient disease control campaigns, including oral vaccination.

Trachome

When the Neighboring Village is Not Treated: Role of Geographic Proximity to Communities Not Receiving Mass Antibiotics for Trachoma.

Mosenia A, Haile BA, Shiferaw A, Gebresillasie S, Gebre T, Zerihun M, Tadesse Z, Emerson PM, Callahan EK, Zhou Z, Lietman TM, Keenan JD.

07-12-2022

Clin Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36477547/>

Detection of trachoma using machine learning approaches.

Socia D, Brady CJ, West SK, Cockrell RC.

07-12-2022

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36477293/>

Background: Though significant progress in disease elimination has been made over the past decades, trachoma is the leading infectious cause of blindness globally. Further efforts in trachoma elimination are paradoxically being limited by the relative rarity of the disease, which makes clinical training for monitoring surveys difficult. In this work, we evaluate the plausibility of an Artificial Intelligence model to augment or replace human image graders in the evaluation/diagnosis of trachomatous inflammation-follicular (TF). **Methods:** We utilized a dataset consisting of 2300 images with a 5% positivity rate for TF. We developed classifiers by implementing two state-of-the-art Convolutional Neural Network architectures, ResNet101 and VGG16, and applying a suite of data augmentation/oversampling techniques to the positive images. We then augmented our data set with additional images from independent research groups and evaluated performance. **Results:** Models performed well in minimizing the number of false negatives, given the constraint of the low numbers of images in which TF was present. The best performing models achieved a sensitivity of 95% and positive predictive value of 50-70% while reducing the number images requiring skilled grading by 66-75%. Basic oversampling and data augmentation techniques were most successful at improving model performance, while techniques that are grounded in clinical experience, such as highlighting follicles, were less successful. **Discussion:** The developed models perform well and significantly reduce the burden on graders by minimizing the number of false negative identifications. Further improvements in model skill will benefit from data sets with more TF as well as a range in image quality and image capture techniques used. While these models approach/meet the community-accepted standard for skilled field graders (i.e., Cohen's Kappa >0.7), they are insufficient to be deployed independently/clinically at this time; rather, they can be utilized to significantly reduce the burden on skilled image graders.

Baseline Prevalence of Trachoma in 13 Local Government Areas of Borno State, Nigeria.

Adamu MD, Mohammed Jabo A, Orji P, Zhang Y, Isiyaku S, Olobio N, Muhammad N, Mshelia Auta L, Willis R, Bakhtiari A, Jimenez C, Solomon AW, Harding-Esch EM, Mpyet CD.

05-12-2022

Ophthalmic Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/36469560/>

Purpose: We set out to determine the baseline prevalence of trachoma in 13 Local Government Areas (LGAs) of Borno State, Nigeria. **Methods:** A population-based cross-sectional survey was conducted in each of 13 LGAs from 2017 to 2019, with the support of Tropical Data (TD). World Health Organization (WHO)-recommended protocols were used. With a probability-proportional-to-size systematic sampling method, 25 villages were selected per LGA in 2017 and 30 villages per LGA in 2019; in each village, 25 households were enrolled for 2017 surveys, while 30 were enrolled for 2019 surveys. All present, consenting residents aged ≥ 1 year were examined by TD-certified graders for trichomatous inflammation-follicular (TF) and trichomatous trichiasis (TT) using the WHO simplified grading scheme. Additionally, we collected data on household-level access to water, sanitation and hygiene (WASH) facilities. **Results:** One LGA (Magumeri) had TF prevalence in 1-9-year-olds $\geq 10\%$; two other LGAs (Monguno and Kaga) had TF prevalence between 5.0% and 9.9%. The prevalence of TT unknown to the health system was $\geq 0.2\%$ in six LGAs. The proportion of households with access to improved water sources ranged from 30% (Kwaya Kusar) to 95% (Monguno); household-level access to improved latrines was lowest in Shani (7%) and highest in Maiduguri (95%). **Conclusion:** Active TT case finding and strengthening of TT surgical services are needed in six LGAs. Mass drug administration (MDA) of antibiotics is needed in three LGAs to reduce the prevalence of active trachoma to below elimination thresholds. The trachoma elimination programme should engage WASH agencies to augment access to improved WASH facilities.

Trachoma elimination targets missed in Australia.

Barksby R.

Dec-2022

Lancet Microbe.

<https://pubmed.ncbi.nlm.nih.gov/36265506/>

Ulcère de Buruli

Buruli Ulcer and Medical Geo-Microbiology.

Manilal A, Tadesse D, Sabu KR.

25-11-2022

Infect Drug Resist.

<https://pubmed.ncbi.nlm.nih.gov/36458199/>

Buruli ulcer is a chronic debilitating infectious disease caused by the pathogen *Mycobacterium ulcerans*, which can be cured if diagnosed and treated in an early stage. However, advanced cases need antibiotic treatment followed by surgical interventions. In this context, an extremely effective and less expensive treatment modality can be developed by means of an extended topical application of certain selected natural clay minerals, most of the time containing illite-smectite having some iron content. There is a scope for developing the speciality,

medical geo-microbiology, which is truly a multidisciplinary one, for finding a cure for the severe and advanced cases of BU.

Pian

No evidence for yaws infection in a small-scale cross-sectional serosurvey in Ghanaian monkeys.

Adade E, Roos C, Chuma IS, Sylverken AA, Knauf S.

Dec-2022

Vet Med Sci.

<https://pubmed.ncbi.nlm.nih.gov/36480449/>

Yaws in Pygmy and Bantu children inhabiting the rural zones of Central Africa.

Bylicka-Szczepanowska E, Korzeniewski K, Pokorna-Kalwak D.

Oct-2022

Postepy Dermatol Alergol.

<https://pubmed.ncbi.nlm.nih.gov/36457685/>

Lèpre

Added value of the measles-rubella supplementary immunization activity in reaching unvaccinated and under-vaccinated children, a cross-sectional study in five Indian districts, 2018-20.

Prosperi C, Thangaraj JWV, Hasan AZ, Kumar MS, Truelove S, Kumar VS, Winter AK, Bansal AK, Chauhan SL, Grover GS, Jain AK, Kulkarni RN, Sharma SK, Soman B, Chaitanya IK, Kharwal S, Mishra SK, Salvi NR, Sharma NP, Sharma S, Varghese A, Sabarinathan R, Duraiswamy A, Rani DS, Kanagasabai K, Lachyan A, Gawali P, Kapoor M, Chonker SK, Cutts FT, Sangal L, Mehendale SM, Sapkal GN, Gupta N, Hayford K, Moss WJ, Murhekar MV.

05-12-2022

Vaccine.

<https://pubmed.ncbi.nlm.nih.gov/36481106/>

Assessing the Quality of the World Health Organization's Skin NTDs App as a Training Tool in Ghana and Kenya: Protocol for a Cross-sectional Study.

Frej A, Cano M, Ruiz-Postigo JA, Macharia P, Phillips RO, Amoako YA, Carrion C.

08-12-2022

JMIR Res Protoc.

<https://pubmed.ncbi.nlm.nih.gov/36480252/>

Diagnosis of New Leprosy Patients through Various Histological Findings according to Biopsy Sites.

Song S, Lim J, Park S, Lee S, Baek J, Park H, Roh JY, Kim HJ.

Dec-2022

Ann Dermatol.

<https://pubmed.ncbi.nlm.nih.gov/36478434/>

Temporal trend, distribution and spatial autocorrelation of leprosy in Brazil: ecological study, 2011 to 2021.

Lima LV, Pavinati G, Silva IGP, Moura DRO, Gil NLM, Magnabosco GT.

05-12-2022

Rev Bras Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/36478213/>

Objective: To characterize the temporal trend and spatial behavior of leprosy in Brazil, from 2011 to 2021. **Methods:** This is an ecological study, with data from the Notifiable Diseases Information System, obtained in June 2022. The annual detection rate of new leprosy cases per 100 thousand inhabitants was calculated. To estimate the trend of the 2011-2019 and 2011-2021 series, the polynomial regression model was used, testing first-, second-, and third-order polynomials. For spatiality, natural breaks were used and, later, the univariate global and local Moran's indexes. A significance level of 5% was adopted and the analyses were performed using SPSS®, GeoDa®, and QGIS® software. **Results:** The findings indicated an upward trend in the incidence of leprosy in Brazilian regions and in 20 federative units between 2011 and 2019. However, there was a decrease in most of the country when considering the COVID-19 pandemic years. Spatiality showed that the highest detection rates throughout the period were observed in the North, Midwest, and Northeast regions, with high-risk clusters, and the lowest detection rates in the South and Southeast regions, with low-risk clusters. **Conclusion:** The leprosy detection rate showed an upward trend in Brazil between 2011 and 2019, with greater spatial concentration in the North, Northeast, and Midwest regions. Nevertheless, the study raises an alert for the programmatic sustainability of leprosy control in Brazil, considering the drop in the COVID-19 pandemic, presumably due to the influence of the reorganization of the development of initiatives and provision of services in face of COVID-19.

Transverse erythronychia: A unique nail manifestation of COVID-19 infection and brief review of COVID-19 associated nail changes.

Sil A, Ghosh S, Das A, Chandra A.

08-12-2022

J R Coll Physicians Edinb.

<https://pubmed.ncbi.nlm.nih.gov/36476144/>

Over the past 2 years, a plethora of mucocutaneous manifestations have been described to be associated with coronavirus 2019 (COVID-19) infection. Nail changes attributed to COVID-19 have rarely been documented in the literature. We describe here a unique nail finding 'transverse erythronychia' due to COVID-19 and review the literature on the diverse nail pathology attributed to the disease.

[Genetic Engineering in Mycobacteria].

Armianinova DK, Karpov DS, Kotliarova MS, Goncharenko AV.

Nov-Dec 2022

Mol Biol (Mosk).

<https://pubmed.ncbi.nlm.nih.gov/36475477/>

Genetic tools for targeted modification of the mycobacterial genome contribute to the understanding of the physiology and virulence mechanisms of mycobacteria. Human and animal pathogens, such as the Mycobacterium tuberculosis complex, which causes tuberculosis, and *M. leprae*, which causes leprosy, are of particular importance. Genetic research opens up novel opportunities to identify and validate new targets for antibacterial drugs and to develop improved vaccines. Although mycobacteria are difficult to work with due to their slow growth rate and a limited possibility to transfer genetic information, significant progress has been made in developing genetic engineering methods for mycobacteria. The review considers the main approaches to changing the mycobacterial genome in a targeted manner, including homologous and site-specific recombination and use of the CRISPR/Cas system.

Non-healing ulcers over the neck.

Ghosh SK, Bhanja DB.

05-12-2022

J Paediatr Child Health.

<https://pubmed.ncbi.nlm.nih.gov/36468532/>

Thumb blister.

Sil A, Panigrahi A.

05-12-2022

J Paediatr Child Health.

<https://pubmed.ncbi.nlm.nih.gov/36468529/>

Linear erythematous papules in a young boy.

Sil A, Das S, Chakraborty S.

05-12-2022

J Paediatr Child Health.

<https://pubmed.ncbi.nlm.nih.gov/36468519/>

A young girl with curly hair.

Ghosh SK, Sil A.

05-12-2022

J Paediatr Child Health.

<https://pubmed.ncbi.nlm.nih.gov/36468497/>

Tumor targeted delivery of mycobacterial adjuvant encapsulated chitosan nanoparticles showed potential anti-cancer activity and immune cell activation in tumor microenvironment.

Chakraborty A, Roy G, Swami B, Bhaskar S.

30-11-2022

Int Immunopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/36462337/>

Targeting immunotherapeutics inside the tumor microenvironment (TME) with intact biological activity

remains a pressing issue. Mycobacterium indicus pranii (MIP), an approved adjuvant therapy for leprosy has exhibited promising results in clinical trials of lung (NSCLC) and bladder cancer. Whole MIP as well as its cell wall fraction have shown tumor growth suppression and enhanced survival in mice model of melanoma, when administered peritumorally. Clinically, peritumoral delivery remains a procedural limitation. In this study, a tumor targeted delivery system was designed, where chitosan nanoparticles loaded with MIP adjuvants, when administered intravenously showed preferential accumulation within the TME, exploiting the principle of enhanced permeability and retention effect. Bio-distribution studies revealed their highest concentration inside the tumor after 6 h of administration. Interestingly, MIP adjuvant nano-formulations significantly reduced the tumor volume in the treated groups and increased the frequency of activated immune cells inside the TME. For chemoimmunotherapeutics studies, MIP nano-formulation was combined with standard dosage regimen of Paclitaxel. Combined therapy exhibited a further reduction in tumor volume relative to either of the MIP nano formulations. From this study a three-pronged strategy emerged as the underlying mechanism; chitosan and Paclitaxel have shown direct role in tumor cell death and the MIP nano-formulation activates the tumor residing immune cells which ultimately leads to the reduced tumor growth.

Role of molecular approaches to distinguish post kala-azar dermal leishmaniasis from leprosy: A case study.

Roy S, Roy M, Nath S, Chaudhuri SJ, Ghosh MK, Mukherjee S, Chatterjee M.

10-11-2022

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/36461804/>

In-vitro anti-Mycobacterium tuberculosis effect of Eugenol.

Vidya Raj CK, Venugopal J, Muthaiah M, Chadha VK, Brammachary U, Swappna M, Sangeetha AV, Dhandapani SP, Kareedhi VR, Calivarathan L, Karthick M, Jayapal K.

Oct-2022

Indian J Tuberc.

<https://pubmed.ncbi.nlm.nih.gov/36460403/>

Case of leprosy in child.

Thaware A, Rathi R.

31-08-2022

Pan Afr Med J.

<https://pubmed.ncbi.nlm.nih.gov/36451977/>

Interactive effects of meteorological factors and air pollutants on hand, foot, and mouth disease in Chengdu, China: a time-series study.

Huang J, Ma Y, Lv Q, Liu Y, Zhang T, Yin F, Shui T.

30-11-2022

BMJ Open.

<https://pubmed.ncbi.nlm.nih.gov/36450433/>

Objectives: Hand, foot, and mouth disease (HFMD) is a viral infectious disease that poses a substantial threat in the Asia-Pacific region. It is widely reported that meteorological factors are associated with HFMD. However, the relationships between air pollutants and HFMD are still controversial. In addition, the interactive effects between meteorological factors and air pollutants on HFMD remain unknown. To fill this research gap, we conducted a time-series study. **Design:** A time-series study. **Setting and participants:** Daily cases of HFMD as well as meteorological and air pollution data were collected in Chengdu from 2011 to 2017. A total of 184 610 HFMD cases under the age of 15 were included in our study. **Outcome measures:** Distributed lag nonlinear models were used to investigate the relationships between HFMD and environmental factors, including mean temperature, relative humidity, SO₂, NO₂, and PM₁₀. Then, the relative excess risk due to interaction (*RERI*) and the proportion attributable to interaction were calculated to quantitatively evaluate the interactions between meteorological factors and air pollutants on HFMD. Bivariate response surface models were used to visually display the interactive effects. **Results:** The cumulative exposure-response curves of SO₂ and NO₂ were inverted 'V'-shaped and 'M'-shaped, respectively, and the risk of HFMD gradually decreased with increasing PM₁₀ concentrations. We found that there were synergistic interactions between mean temperature and SO₂, relative humidity and SO₂, as well as relative humidity and PM₁₀ on HFMD, with individual *RERIs* of 0.334 (95% CI 0.119 to 0.548), 0.428 (95% CI 0.214 to 0.642) and 0.501 (95% CI 0.262 to 0.741), respectively, indicating that the effects of SO₂ and PM₁₀ on HFMD were stronger under high temperature (>17.3°C) or high humidity (>80.0%) conditions. **Conclusions:** There were interactive effects between meteorological factors and air pollutants on HFMD. Our findings could provide guidance for targeted and timely preventive and control measures for HFMD.

Stigma towards leprosy across seven life domains in Indonesia: a qualitative systematic review.

Marpaung YM, Ernawati E, Dwivania AT.

30-11-2022

BMJ Open.

<https://pubmed.ncbi.nlm.nih.gov/36450432/>

Hypermobility Ehlers-Danlos syndrome: a video demonstration of Beighton score.

Sadhasivamohan A, Palaniappan V, Karthikeyan K.

30-11-2022

BMJ Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36450411/>

Social Reproduction as a methodological perspective for contextualized analysis of living and health conditions.

Medeiros MS, Augusto LGDS, Costa AM, Barca S, Santos SLD, Gonçalves ICM, Martinez-Espinosa FE, Rocha DFD.

28-11-2022

Cad Saude Publica.

<https://pubmed.ncbi.nlm.nih.gov/36449849/>

This article aims to discuss the use of Social Reproduction, proposed by Juan Samaja, in the analysis of living and health conditions in a context of an sustainable development reserve in the Brazilian Amazon. This study uses a comprehensive approach to Social Reproduction processes that comprise the network of hierarchically organized structures using the analysis of social interactions of narrated and observable events, applied to the data matrix. The Ecological Reproduction of life in the riverside forest is negatively expressed in bio-communal life, as the strategic actions provided by the Political, Economic and Cultural Reproductions, that is, the environmental policy actions, do not value the local way of life. The deficient access to social goods and services, including health care, from the Political and Techno-Economic Reproductions, has an impact on the material basis of the Bio-Communal Reproduction, whose outcome is high frequency of disease complaints and workplace accidents, such as infectious gastroenteritis, malaria, tuberculosis, leprosy, and poisoning by venomous animals. Ensuring access to social goods and services, in particular health care, is essential for improving resilience to the forest adversities. In conclusion, the social reproduction data matrix helped understand the processes of Social Reproduction that are part of the hierarchically organized structures, whose interactions shaped the living and health conditions of the riverside population analyzed in this study.

Phytochemical prospection and evaluation of antimicrobial, antioxidant and antibiofilm activities of extracts and essential oil from leaves of *Myrsine umbellata* Mart. (Primulaceae).

Laskoski LV, Bandeira DM, Batista JM, Costa WFD, Baeza LC, Kuo LH, Pinto FGDS.

25-11-2022

Braz J Biol.

<https://pubmed.ncbi.nlm.nih.gov/36449827/>

The species *Myrsine umbellata* is a native plant of Brazil, whose barks are traditionally used in herbal medicine to treat liver disorders and combat leprosy. Therefore, the aim of the study was to identify the phytochemical prospection of ethanolic (EE) and acetonetic (EA) extracts by colorimetric tests and by gas chromatography coupled to mass spectrometry (GC-MS) of the essential oil (EO) of *M. umbellata* leaves; evaluate the antimicrobial activity in front of standard ATCC strains by the broth microdilution technique; the antioxidant potential by DPPH reduction method and antibiofilm action by crystal violet assay and cell viability was determined using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) based on optical density. Phytochemical prospection of EE and EA detected the presence of free steroids, alkaloids, flavonoids (flavones, flavononoids, flavonols and xanthons) and tannins in both extracts (EE and EA) and saponins only in EE. In EO, the majority compounds identified were elixene, caryophyllene (E), spatulenol, d-Cadinene and aromadendrene. EA showed antimicrobial

activity with MIC and MBC/MFC values ranging from 3.12 to 100 mg.mL⁻¹, highlighting its efficiency on the Gram-positive strain *S. epidermidis*. EE showed antimicrobial potential in the range of 3.12 to 200 mg.mL⁻¹, and the Gram-negative *E. coli* strain was the most susceptible. However, OE showed bacteriostatic potential against *S. Typhimurium*, *S. Abaetetuba*, *P. aeruginosa*, and *S. epidermidis* strains. The ability to sequester free radicals was evident in EA extract with antioxidant activity of 89.55% and in EE with 63.05%. The antibiofilm potential was observed in EE extract which eradicated the mature biofilm biomass of all tested bacteria with high activity (50% to 84.28%) and EO also showed antibiofilm effect on mature biofilm of UEL enteroaggregative *E. coli*, *S. aureus* and *S. Enteritidis* strains with biomass reduction percentage of 63.74%, 68.04% and 86.19%, respectively. These results indicate the potential of *M. umbellata* extracts and as a source of plant bioactivity for the development of new alternative strategies for the control of planktonic or biofilm-resistant microorganisms.

Should we persist with the term Lazarine leprosy? A historical perspective.

Asokan N, Valsalan V.

Nov-Dec 2022

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/36332094/>

Lepromatous leprosy with central serous chorioretinopathy.

Goel S, Gogia K, Singla R, Gupta S, Patel K, Verma S.

Nov-Dec 2022

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/36331860/>

Leprosy Caused by *Mycobacterium lepromatosis*.

Romero-Navarrete M, Arenas R, Han XY, Vega-Memije ME, Castillo-Solana AD.

01-12-2022

Am J Clin Pathol.

<https://pubmed.ncbi.nlm.nih.gov/36200553/>

Strengthen the Indian dermatology services using dermatology nursing.

Nair LV, Narahari SR, Reethadevi US.

Nov-Dec 2022

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/35962513/>

Focused Cardiac Ultrasound to Guide the Diagnosis of Heart Failure in Pregnant Women in India.

Alsharqi M, Ismavel VA, Arnold L, Choudhury SS, Solomi V C, Rao S, Nath T, Rani A, Goel I, Kakoty SD, Mahanta P, Roy I, Deka R, Opondo C, Baigent C, Leeson P, Nair M; MaatHRI Collaboration.

Dec-2022

J Am Soc Echocardiogr.

<https://pubmed.ncbi.nlm.nih.gov/35934263/>

Background: Cardiac complications are a leading cause of maternal death. Cardiac imaging with echocardiography is important for prompt diagnosis, but it is not available in many low-resource settings. The aim of this study was to determine whether focused cardiac ultrasound performed by trained obstetricians and interpreted remotely by experts can identify cardiac abnormalities in pregnant women in low-resource settings. **Methods:** A cross-sectional study was conducted among 301 pregnant and postpartum women recruited from 10 hospitals across three states in India. Twenty-two obstetricians were trained in image acquisition using a portable cardiac ultrasound device following a simplified protocol adapted from focus-assessed transthoracic echocardiography protocol. It included parasternal long-axis, parasternal short-axis, and apical four-chamber views on two-dimensional and color Doppler. Independent image interpretation was performed remotely by two experts, in the United Kingdom and India, using a standard semiquantitative assessment protocol. Interrater agreement between the experts was examined using Cohen's κ . Diagnostic accuracy of the method was examined in a subsample for whom both focused and conventional scans were available. **Results:** Cardiac abnormalities identified using the focused method included valvular abnormalities (27%), rheumatic heart disease (6.6%), derangements in left ventricular size (4.7%) and function (22%), atrial dilatation (19.5%), and pericardial effusion (30%). There was substantial agreement on the cardiac parameters between the two experts, ranging from 93.6% ($\kappa = 0.84$) for left ventricular ejection fraction to 100% ($\kappa = 1$) for valvular disease. Image quality was graded as good in 79% of parasternal long-axis, 77% of parasternal short-axis and 64% of apical four-chamber views. The chance-corrected κ coefficients indicated fair to moderate agreement ($\kappa = 0.28-0.51$) for the image quality parameters. There was good agreement on diagnosis between the focused method and standard echocardiography (78% agreement), compared in 36 participants. **Conclusions:** The focused method accurately identified cardiac abnormalities in pregnant women and could be used for screening cardiac problems in obstetric settings.

Pretreatment attrition and treatment initiation delay among rifampicin-resistant tuberculosis patients in Lagos, Nigeria: a retrospective cohort study.

Adejumo OA, Daniel O, Adepoju VA, Onoh MO, Sokoya OD, Abdur-Razzaq H, Moronfolu O, Oyadotun OM, Olusola-Faley B.

02-12-2022

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/35710310/>

The Awesome Power of Human Genetics of Infectious Disease.

Gibbs KD, Schott BH, Ko DC.

30-11-2022

Annu Rev Genet.

<https://pubmed.ncbi.nlm.nih.gov/35697043/>

Since the identification of sickle cell trait as a heritable form of resistance to malaria, candidate gene studies, linkage analysis paired with sequencing, and genome-wide association (GWA) studies have revealed many examples of genetic resistance and susceptibility to infectious diseases. GWA studies enabled the identification of many common variants associated with small shifts in susceptibility to infectious diseases. This is exemplified by multiple loci associated with leprosy, malaria, HIV, tuberculosis, and coronavirus disease 2019 (COVID-19), which illuminate genetic architecture and implicate pathways underlying pathophysiology. Despite these successes, most of the heritability of infectious diseases remains to be explained. As the field advances, current limitations may be overcome by applying methodological innovations such as cellular GWA studies and phenome-wide association (PheWA) studies as well as by improving methodological rigor with more precise case definitions, deeper phenotyping, increased cohort diversity, and functional validation of candidate loci in the laboratory or human challenge studies.

In the footsteps of Albert Calmette: an ecological study of TB, leprosy and potential exposure to wild-type *Mycobacterium bovis*.

Pépin J, Fox A, LeBlanc L, De Wals P, Rousseau MC.

02-12-2022

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/35460554/>

Clinical and epidemiological trends in childhood leprosy: A 20-year retrospective analysis from a tertiary care hospital in Jammu, North India.

Sakral A, Dogra N, Dogra D, Sharma K.

Noc-Dec 2022

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/35146981/>

Background Slightly more than half the total number of childhood leprosy cases worldwide are from India. **Aim** To analyze the clinical and epidemiological trends of childhood leprosy over 20 years in a tertiary care hospital. **Methods** We retrieved the medical records of all children less than 15 years of age registered in the leprosy clinic between April 1998 and March 2018. We tabulated and analyzed data pertaining to demographic details along with clinical findings such as cutaneous lesions, nerves involved, sensory loss, deformities, reactions, smear status, histopathology and treatment. **Results** Out of total 1548 leprosy cases registered during the study period, 55 (3.55%) cases of childhood leprosy were diagnosed. Thirty five (63.6%) children were in the age group of 11-15 years and 83.7% were migrants from other states. Thirteen (23.6%) children reported contact with a diagnosed case of leprosy, mainly in close contacts. Fifty three (96.4%) children presented with cutaneous lesions while 2 (3.6%) had pure neural involvement. Borderline tuberculoid leprosy was the most common clinical presentation in 27 (49.1%) followed by borderline lepromatous leprosy in 11 (18%). Thickened peripheral nerve trunks were detected

in 42 (76.4%), most commonly the ulnar nerve. Reactional episodes occurred in 12 (21.8%) cases (Type 1 reaction, 10 (18.2%); Type 2 reaction, 2 (3.6%)). Grade 2 disability was detected in 4 (7.3%). Multidrug therapy was started in all patients, multibacillary (MB) regimen in 42 (76.3%) patients and paucibacillary (PB) regimen in 13 (23.7%). Twenty five (45.4%) children defaulted from the treatment. On comparing the data of 2008-18 with that of the previous decade (1998-2007), there was a higher proportion of migrant cases as compared to local cases (3:1-11:1) and MB cases as compared to PB cases (2:1-6:1). The proportion of treatment defaulters declined from 60% to 36%. Limitations Relapse rate could not be calculated due to inadequate follow-up period. As it is a hospital-based retrospective study with no active surveys, these findings may not reflect trends in the community. Conclusion Childhood leprosy continues to be a significant problem. There is a clear need to strengthen early detection, treatment and regular follow-up of these cases in both high and low endemic settings.

Need for modification of guidelines for systemic steroid-modified tinea.

Chakraborty A.

Noc-Dec 2022

Indian J Dermatol Venereol Leprol.

<https://pubmed.ncbi.nlm.nih.gov/34877856/>

Trypanosomes (trypanosomiase et maladie de Chagas)

Slow growing behavior in African trypanosomes during adipose tissue colonization.

Trindade S, De Niz M, Costa-Sequeira M, Bizarra-Rebello T, Bento F, Dejung M, Narciso MV, López-Escobar L, Ferreira J, Butter F, Bringaud F, Gjini E, Figueiredo LM.

08-12-2022

Nat Commun.

<https://pubmed.ncbi.nlm.nih.gov/36481558/>

When *Trypanosoma brucei* parasites, the causative agent of sleeping sickness, colonize the adipose tissue, they rewire gene expression. Whether this adaptation affects population behavior and disease treatment remained unknown. By using a mathematical model, we estimate that the population of adipose tissue forms (ATFs) proliferates slower than blood parasites. Analysis of the ATFs proteome, measurement of protein synthesis and proliferation rates confirm that the ATFs divide on average every 12 h, instead of 6 h in the blood. Importantly, the population of ATFs is heterogeneous with parasites doubling times ranging between 5 h and 35 h. Slow-proliferating parasites remain capable of reverting to the fast proliferation profile in blood conditions. Intravital imaging shows that ATFs are refractory to drug treatment. We propose that in adipose tissue, a subpopulation of *T. brucei* parasites acquire a slow growing behavior, which contributes to disease chronicity and treatment failure.

Triatoma costalimai, a neglected vector of Trypanosoma cruzi in the Cerrado savannas of South America: A comprehensive review.

Lima de Miranda V, Gurgel-Gonçalves R, Moreira de Souza RC, Abad-Franch F.

11-11-2022

Curr Res Parasitol Vector Borne Dis.

<https://pubmed.ncbi.nlm.nih.gov/36479576/>

Triatoma costalimai is a little-known triatomine-bug species whose role as a vector of Chagas disease remains poorly understood. To address this gap, we conducted a comprehensive review of the literature and assessed the evidence base from a public-health perspective. We found 89 individual documents/resources with information about *T. costalimai*. DNA-sequence and cytogenetic data indicate that *T. costalimai* belongs, together with *Triatoma jatai*, in a distinct clade within the 'pseudomaculata group' of South American *Triatoma*. *Triatoma costalimai* is probably a narrow endemic of the Cerrado on the upper Tocantins River Basin and associated ranges/plateaus; there, the species thrives in the sandstone/limestone outcrops typical of the "Cerrado rupestre" (rocky-soil savanna) and "mata seca decídua calcária" (limestone-soil dry forest) phytophysionomies. Wild *T. costalimai* appear to feed on whatever vertebrates are available in rocky outcrops, with lizards and rodents being most common. There is persuasive evidence that house invasion/infestation by *T. costalimai* has increased in frequency since the 1990s. The bugs often carry *Trypanosoma cruzi*, often defecate while feeding, have high fecundity/fertility, and, under overtly favorable conditions, can produce two generations per year. Current knowledge suggests that *T. costalimai* can transmit human Chagas disease in the upper Tocantins Basin; control-surveillance systems should 'tag' the species as a potentially important local vector in the Brazilian states of Goiás and Tocantins. Further research is needed to clarify (i) the drivers and dynamics of house invasion, infestation, and reinfestation by *T. costalimai* and (ii) the genetic structuring and vector capacity of the species, including its wild and non-wild populations.

Fatty acid uptake in Trypanosoma brucei: Host resources and possible mechanisms.

Poudyal NR, Paul KS.

21-11-2022

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36478671/>

Trypanosoma brucei spp. causes African Sleeping Sickness in humans and nagana, a wasting disease, in cattle. As *T. brucei* goes through its life cycle in its mammalian and insect vector hosts, it is exposed to distinct environments that differ in their nutrient resources. One such nutrient resource is fatty acids, which *T. brucei* uses to build complex lipids or as a potential carbon source for oxidative metabolism. Of note, fatty acids are the membrane anchoring moiety of the glycosylphosphatidylinositol (GPI)-anchors of the major surface proteins, Variant Surface Glycoprotein (VSG) and the Procyclins, which are

implicated in parasite survival in the host. While *T. brucei* can synthesize fatty acids *de novo*, it also readily acquires fatty acids from its surroundings. The relative contribution of parasite-derived vs. host-derived fatty acids to *T. brucei* growth and survival is not known, nor have the molecular mechanisms of fatty acid uptake been defined. To facilitate experimental inquiry into these important aspects of *T. brucei* biology, we addressed two questions in this review: (1) What is known about the availability of fatty acids in different host tissues where *T. brucei* can live? (2) What is known about the molecular mechanisms mediating fatty acid uptake in *T. brucei*? Finally, based on existing biochemical and genomic data, we suggest a model for *T. brucei* fatty acid uptake that proposes two major routes of fatty acid uptake: diffusion across membranes followed by intracellular trapping, and endocytosis of host lipoproteins.

Serial magnetic resonance imaging of splenomegaly in the *Trypanosoma brucei* infected mouse.

Paterson S, Holmes WM, Rodgers J.

07-12-2022

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36477669/>

Splenomegaly, an enlargement of the spleen, is a known clinical sign of the parasitic disease, human African trypanosomiasis. This study follows the development of splenomegaly in a group of mice over multiple infection points, using a non-invasive imaging modality, magnetic resonance imaging (MRI). CD-1 mice infected with GVR35 *T. brucei* demonstrated a significant increase in spleen size from day 7 post-infection, with changes in the spleen tracked in individual animals over five time points. At the final time point, the mean spleen weight calculated using the spleen volume from the MR images was compared with the post-mortem gross spleen weight. No significant difference was detected between the two methods ($1.62 \pm 0.06\text{g}$ using MRI and $1.51 \pm 0.04\text{g}$ gross weight, $p = 0.554$). Haematology and histological analysis were also performed, giving additional insight into splenomegaly for the GVR35 strain of infection. The study demonstrates that MRI is a useful tool when examining changes in organ volume throughout HAT infection and may be applicable in the investigation of a range of conditions where changes in organ volume occur and MRI has not been used previously.

Effect of benznidazole on cerebral microcirculation during acute *Trypanosoma cruzi* infection in mice.

Gonzaga BMS, Horita SIM, Beghini DG, Gomes F, Nisimura LM, Dos Santos IB, Estado V, de Araújo-Jorge TC, Garzoni LR.

06-12-2022

Sci Rep.

<https://pubmed.ncbi.nlm.nih.gov/36473897/>

Central nervous system alterations was described in Chagas disease in both human and experimental models, leading to meningoencephalitis, stroke and cognitive impairment. Recently, our group demonstrated that acute

infection by *Trypanosoma cruzi* leads to cerebral microvasculopathy in mice with endothelial dysfunction, capillary rarefaction, increased rolling and leukocyte adhesion. Only benznidazole and nifurtimox are available for clinical treatment, they have an efficiency of 80% in the acute phase and less than 20% in chronic phase. However, the effect of these drugs on brain microcirculation has not yet been evaluated. We hypothesized that early treatment with benznidazole could protect brain microcirculation during acute experimental Chagas disease. Swiss Webster mice were inoculated with 104 trypomastigotes forms of *T. cruzi*, and after 24 h they were treated with 50 or 100 mg/kg/day of benznidazole for 14 consecutive days. In untreated infected mice, we observed cerebral microvascular rarefaction, increase in leukocyte rolling and adhesion, reduced cerebral blood flow, and increased CD3+ and F4-80+ cells in brain tissue. Early treatment with benznidazole at 100 mg/kg/day and 50 mg/kg/day prevented the occurrence of the alterations mentioned. Here, we show that BZ is able to protect the microcirculation and reduced brain inflammation in acute experimental Chagas disease

Extracellular vesicles from *Trypanosoma cruzi*-dendritic cell interaction show modulatory properties and confer resistance to lethal infection as a cell-free based therapy strategy.

Gutierrez BC, Ancarola ME, Volpato-Rossi I, Marcilla A, Ramirez MI, Rosenzvit MC, Cucher M, Poncini CV.

16-11-2022

Front Cell Infect Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36467728/>

Extracellular vesicles (EVs) include a heterogeneous group of particles. Microvesicles, apoptotic bodies and exosomes are the most characterized vesicles. They can be distinguished by their size, morphology, origin and molecular composition. To date, increasing studies demonstrate that EVs mediate intercellular communication. EVs reach considerable interest in the scientific community due to their role in diverse processes including antigen-presentation, stimulation of anti-tumoral immune responses, tolerogenic or inflammatory effects. In pathogens, EV shedding is well described in fungi, bacteria, protozoan and helminths parasites. For *Trypanosoma cruzi* EV liberation and protein composition was previously described. Dendritic cells (DCs), among other cells, are key players promoting the immune response against pathogens and also maintaining self-tolerance. In previous reports we have demonstrate that *T. cruzi* downregulates DCs immunogenicity in vitro and in vivo. Here we analyze EVs from the in vitro interaction between blood circulating trypomastigotes (Tp) and bone-marrow-derived DCs. We found that Tp incremented the number and the size of EVs in cultures with DCs. EVs displayed some exosome markers and intracellular RNA. Protein analysis demonstrated that the parasite changes the DC protein-EV profile. We observed that EVs from the interaction of Tp-DCs were easily captured by unstimulated-DCs in comparison with EVs from DCs cultured without the parasite, and also modified the activation status of LPS-stimulated DCs. Noteworthy, we

found protection in animals treated with EVs-DCs+Tp and challenged with *T. cruzi* lethal infection. Our goal is to go deep into the molecular characterization of EVs from the DCs-Tp interaction, in order to identify mediators for therapeutic purposes.

Trypanosoma evansi secretome carries potential biomarkers for Surra diagnosis.

Moreira RS, Calomeno NA, das Neves GB, do Nascimento LFN, Filho VB, Wagner G, Miletti LC.

01-12-2022

J Proteomics.

<https://pubmed.ncbi.nlm.nih.gov/36464092/>

Trypanosoma evansi is a parasite that is phylogenetically close to *Trypanosoma brucei* and is the causative agent of a disease known as surra. Surra is responsible for a high mortality rate in livestock and large economic losses in the Americas, Africa, and Asia. This work aimed to analyze in vitro secreted proteins from *T. evansi* and identify potential treatment and diagnostic biomarkers for surra diagnosis. Two groups were used. In one group the parasites were purified using a DEAE-Cellulose column and maintained in a secretion medium while in the other group the parasites were not purified. Each group was further divided to be maintained at either 37 °C or 27 °C. We identified 246 proteins through mass spectrometry and found that the temperature appears to modulate protein secretion. We found minimal variations in the protein pools from pure and non-purified sets. We observed an emphasis on proteins associated to vesicles, glycolysis, and cellular homeostasis through the enrichment of GO. Also, we found that most secretome proteins share homologous proteins with *T. b. brucei*, *T. b. gambiense*, *T. vivax*, *T. equiperdum*, and *T. b. rhodesiense* secretome but unique *T. evansi* epitopes with potential biomarkers for surra diagnosis were detected. SIGNIFICANCE: *Trypanosoma evansi* is a parasite of African origin that is phylogenetically close to *Trypanosoma brucei*. As with other trypanosomatids and blood parasites, its infection causes non-pathognomonic symptoms, which makes its diagnosis difficult. One great problem is the fact that no diagnostic test differentiates between *Trypanosoma equiperdum* and *T. evansi*, which is a problem in South America and Asia, and Africa. Thus, it is urgent to study the biochemistry of the parasite to discover proteins that can be used for differential diagnosis or be possible therapeutic targets. In addition, the study of the secretome can point out proteins that are used by the parasite in its interactions with the host, helping to understand the progression of the disease.

Opportunistic or selective? Stage-dependent feeding behavior in a wild vector of Chagas disease.

De Bona S, Correa JP, San Juan E, Estay-Olea D, Quiroga N, Bacigalupo A, Araya-Donoso R, Botto-Mahan C.

30-11-2022

Int J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36462561/>

The composition and contribution of different host species in the dynamics of vector-borne zoonotic parasites are particularly relevant for public health. Hence, the study of host selection by vectors is fundamental. Developmental stage and infection status are factors that may modulate vector feeding behavior. In the semi-arid Mediterranean ecosystem of South America, the transmission of *Trypanosoma cruzi*, the protozoan causing Chagas disease, includes the triatomine vector *Mepraia spinolai* and several vertebrate species. In this field study, we examined whether *M. spinolai* exhibits an opportunistic feeding behavior dependent upon developmental stage and/or infection status. We found that *M. spinolai* does not feed according to the relative availability of vertebrate species. In addition, early stage nymphs (first/second instars) fed on twice as many different species as middle (third/fourth instars) and late (fifth instars and adults) *M. spinolai*, with the former feeding on native rodents and lizards and the latter mostly on rabbits. Infected and uninfected *M. spinolai* showed similar feeding profiles. Wild triatomine species might be described as stage-dependent selective blood feeders, as a consequence of the temporal and spatial scale at which host-vector interactions occur, highlighting that all developmental stages might be infected and capable of transmitting *T. cruzi*.

Efficacy and safety of acoziborole in patients with human African trypanosomiasis caused by Trypanosoma brucei gambiense: a multicentre, open-label, single-arm, phase 2/3 trial.

Betu Kumeso VK, Kalonji WM, Rembry S, Valverde Mordt O, Ngolo Tete D, Prêtre A, Delhomme S, Ilunga Wa Kyhi M, Camara M, Catusse J, Schneitter S, Nusbaumer M, Mwamba Miaka E, Mahenzi Mbembo H, Makaya Mayawula J, Layba Camara M, Akwaso Massa F, Kaninda Badibabi L, Kasongo Bonama A, Kavunga Lukula P, Mutanda Kalonji S, Mariero Philemon P, Mokilifi Nganyonyi R, Embana Mankiara H, Asuka Akongo Nguba A, Kobo Muanza V, Mulenge Nasandhel E, Fifi Nzeza Bambuwu A, Scherrer B, Strub-Wourgaft N, Tarral A.

29-11-2022

Lancet Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36460027/>

Hit-to-lead optimization of a 2-aminobenzimidazole series as new candidates for chagas disease.

de Oliveira Rezende Júnior C, Martinez PDG, Ferreira RAA, Koovits PJ, Miranda Soares B, Ferreira LLG, Michelin-Duarte S, Chelucci RC, Andricopulo AD, Matheussen A, Van Pelt N, Caljon G, Maes L, Campbell S, Kratz JM, Mowbray CE, Dias LC.

15-11-2022

Eur J Med Chem.

<https://pubmed.ncbi.nlm.nih.gov/36459758/>

Chagas disease is a neglected tropical disease caused by *Trypanosoma cruzi*. Because current treatments present several limitations, including long duration, variable efficacy and serious side effects, there is an urgent need

to explore new antitrypanosomal drugs. The present study describes the hit-to-lead optimization of a 2-aminobenzimidazole hit 1 identified through in vitro phenotypic screening of a chemical library against intracellular *Trypanosoma cruzi* amastigotes, which focused on optimizing potency, selectivity, microsomal stability and lipophilicity. Multiparametric Structure-Activity Relationships were investigated using a set of 277 derivatives. Although the physicochemical and biological properties of the initial hits were improved, a combination of low kinetic solubility and in vitro cytotoxicity against mammalian cells prevented progression of the best compounds to an efficacy study using a mouse model of Chagas disease.

CRISPR-Cas9: Taming protozoan parasites with bacterial scissor.

Pal S, Dam S.

Dec-2022

J Parasit Dis.

<https://pubmed.ncbi.nlm.nih.gov/36457766/>

The invention of CRISPR-Cas9 technology has opened a new era in which genome manipulation has become precise, faster, cheap and more accurate than previous genome editing strategies. Despite the intricacies of the genomes associated with several protozoan parasites, CRISPR-Cas9 has made a substantial contribution to parasitology. The study of functional genomics through CRISPR-Cas9 mediated gene knockout, insertion, deletion and mutation has helped in understanding intrinsic parasite biology. The invention of CRISPR-dCas9 has helped in the programmable control of protozoan gene expression and epigenetic engineering. CRISPR and CRISPR-based alternatives will continue to thrive and may aid in the development of novel anti-protozoan strategies to tame the protozoan parasites in the imminent future.

Sodalis glossinidius and Wolbachia infections in wild population of Glossina morsitans submorsitans caught in the area of Lake Iro in the south of Chad.

Djoukzoumka S, Mahamat Hassane H, Khan Payne V, Ibrahim MAM, Tagueu Kanté S, Mouliom Mfopit Y, Berger P, Kelm S, Simo G.

Nov-2022

J Invertebr Pathol.

<https://pubmed.ncbi.nlm.nih.gov/36244506/>

Investigations on the bacterial fauna and their association with trypanosome infections in tsetse fly have revealed contrasting results. This study aimed to detect *Wolbachia* and *S. glossinidius* in wild populations of *G. m. submorsitans* and subsequently, understand the influence that these bacteria may have on the vectorial competence of this tsetse species. Tsetse flies were captured in the area of Lake Iro in the south of Chad using biconical traps. After DNA extraction from each tsetse fly, *Sodalis glossinidius* and *Wolbachia* were detected using specific primers. *Sodalis glossinidius* and *Wolbachia* infection rates were compared and association studies involving trypanosome infections and *S. glossinidius* or *Wolbachia* were performed. From 345 *G. m. submorsitans*

analyzed, 9.0% and 14.5% were respectively infected with *S. glossinidius* and *Wolbachia*. Only 2.31% of all tsetse flies were co-infected by the 2 bacteria. Of all trypanosome-infected flies, 7.1% and 9.8% harbored, respectively, *S. glossinidius* and *Wolbachia*. No association was observed between *Wolbachia* and trypanosome infections while a significant association ($r = 4.992$; $P = 0.025$) was found between *S. glossinidius* and the presence of trypanosomes. A significant association ($r = 3.147$; $P = 0.043$) was also observed between *S. glossinidius* and *T. simiae*; and none with *T. congolense* or *T. godfreyi*. This study revealed *S. glossinidius* and *Wolbachia* in *G. m. submorsitans* of the area of lake Iro. It showed that co-infections between *Wolbachia* and *S. glossinidius* are rare in wild populations of *G. m. submorsitans* and that the tripartite associations vary according to trypanosome species as well as symbiotic microorganisms.

Leishmaniose

Seroprevalence of visceral leishmaniasis and its associated factors among asymptomatic pastoral community of Dire District, Borena zone, Oromia Region, Ethiopia.

Ketema H, Weldegebreal F, Gemechu A, Gobena T.

21-12-2022

Front Public Health.

<https://pubmed.ncbi.nlm.nih.gov/36478712/>

Visceral leishmaniasis (VL) is a vector-borne protozoan neglected tropical disease. In some parts of Ethiopia, it is a public health problem and its main causative agent is the *Leishmania donovani* complex. The objective of the study was to determine the seroprevalence of VL and factors associated among the asymptomatic pastoral community of Dire District, Borena Zone, Oromia Region, Ethiopia. A community-based study was conducted among 432 pastoralist communities from June to July 2021. A systematic random sampling method was used to select households. Pretested structured questionnaires and face-to-face interviews were used to collect data. A single finger-prick blood sample was collected and tested for *Leishmania donovani* complex using an immunochromatographic test (rk39-ICT). A logistic regression model was used to assess factors associated with VL infection and a p-value of < 0.05 was considered statistically significant. A total of 432 study participants were included (their mean age was 26.69) and 218 (50.5%) were females. The overall seroprevalence of VL was 33/432 (7.6%) (95%CI: 5.32-15.60). Sero-prevalence was significantly associated with high family size (>5) (adjusted odds ratios (AOR) = 5.134; 95% CI: 2.032-9.748), sleeping or/and staying under acacia tree (AOR = 2.984; 95% CI = 1.074-8.288), presence of cracked house walls (AOR = 1.801; 95%CI: 1.026-4.926), presence of termite hills (AOR = 1.938; 95%CL: 1.002-7.050), availability of water points (AOR = 3.893; 95%CI: 1.034-7.426) and presence of domestic animals (AOR = 2.124; 95% CI: 2.341-5.108). It is recommended that community awareness on the transmission and prevention methods of *Leishmania donovani* complex and taking appropriate interventions

on the identified factors play a greater role to prevent and control infection in the area. Further investigation is also needed to characterize the pathogens and risk factors and tackle the problem.

Quinoliny β -enaminone derivatives exhibit leishmanicidal activity against *Leishmania donovani* by impairing the mitochondrial electron transport chain complex and inducing ROS-mediated programmed cell death.

Rani A, Khanikar S, Dutta M, Katiyar S, Qamar T, Seth A, Agnihotri PK, Guha R, Vishwakarma JN, Kar S.

07-12-2022

J Antimicrob Chemother.

<https://pubmed.ncbi.nlm.nih.gov/36475314/>

Supramolecular assembly of pentamidine and polymeric cyclodextrin bimetallic core-shell nanoarchitectures.

Hada AM, Burduja N, Abbate M, Stagno C, Caljon G, Maes L, Micale N, Cordaro M, Scala A, Mazzaglia A, Piperno A.

18-11-2022

Beilstein J Nanotechnol.

<https://pubmed.ncbi.nlm.nih.gov/36474926/>

Advanced nanoscale antimicrobials, originated from the combination of noble metal nanoparticles (NPs) with conventional antimicrobial drugs, are considered the next generation of antimicrobial agents. Therefore, there is an increasing demand for rapid, eco-friendly, and relatively inexpensive synthetic approaches for the preparation of nontoxic metallic nanostructures endowed with unique physicochemical properties. Recently, we have proposed a straightforward synthetic strategy that exploits the properties of polymeric β -cyclodextrin (PolyCD) to act as both the reducing and stabilizing agent to produce monodispersed and stable gold-based NPs either as monometallic (nanoG) structures or core-shell bimetallic (nanoGS) architectures with an external silver layer. Here, we describe the preparation of a supramolecular assembly between nanoGS and pentamidine, an antileishmanial drug endowed with a wide range of therapeutic properties (i.e., antimicrobial, anti-inflammatory, and anticancer). The physicochemical characterization of the supramolecular assembly (nanoGSP) in terms of size and colloidal stability was investigated by complementary spectroscopic techniques, such as UV-vis, ζ -potential, and dynamic light scattering (DLS). Furthermore, the role of PolyCD during the reduction/stabilization of metal NPs was investigated for the first time by NMR spectroscopy.

The glycoprotein gp63- a potential pan drug target for developing new antileishmanial agents.

Devsani N, Vemula D, Bhandari V.

03-12-2022

Biochimie.

<https://pubmed.ncbi.nlm.nih.gov/36473603/>

Leishmaniasis is a tropical parasitic disease caused by *Leishmania* spp. They cause several presentations of illness ranging from cutaneous leishmaniasis to visceral leishmaniasis. The current arsenal of drugs to treat leishmaniasis is limited, and drug resistance further impedes the problem. Therefore, it is necessary to revisit the available information to identify an alternative or new target for treatment. The glycoprotein 63 (gp63), is a potential anti-leishmanial target that plays a significant role in host-pathogen interaction and virulence. Many studies are ongoing to develop gp63 inhibitors or use it as a vaccine target. In this review, we will discuss the potential of gp63 as a drug target. This review summarises the studies focusing on gp63 as a drug target and its inhibitors identified using in silico approaches.

Chemical composition and biological activities of the essential oil from *Eugenia stipitata* McVaugh leaves.

Dos Santos CRB, Sampaio MG, Vandemet LCS, Dos Santos BS, de Menezes SA, Portela BYM, Gomes DWR, Correia MTS, Gomez MCV, de Alencar Menezes IR, da Silva MV.

05-12-2022

Nat Prod Res.

<https://pubmed.ncbi.nlm.nih.gov/36469681/>

In the present study, the volatile components and cytotoxic, antibacterial, antioxidant, and antiprotozoal activities of the essential oil obtained from the leaves of *Eugenia stipitata* McVaugh (Myrtaceae) grown in the Brazilian Northeast region (Araripe) were investigated. The essential oil was obtained by hydrodistillation. The leaves of *E. stipitata* provided an oil yield of $0.13 \pm 0.01\%$ (w/w). The volatile compounds in the essential oil of *E. stipitata* were analysed using gas chromatography, and the volatile chemical composition was mainly composed of β -eudesmol (15.28%), γ -eudesmol (10.85%), elemol (10.21%) and caryophyllene oxide (6.65%). The essential oil of *E. stipitata* was highly selective against *Leishmania braziliensis* and *L. infantum* promastigotes. The essential oil exhibited good antibacterial activity. *E. stipitata* essential oil showed low free-radical scavenging activity. Our results suggest that the *E. stipitata* essential oil is a relevant source of the primary compounds required for the development of antibacterial and antiprotozoal drugs.

A systematic review and global analysis of the seasonal activity of *Phlebotomus (Paraphlebotomus) sergenti*, the primary vectors of *L. tropica*.

Karmaoui A, Sereno D, El Jaafari S, Hajji L.

05-12-2022

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36469546/>

Review of the Clinical Presentation, Pathology, Diagnosis, and Treatment of Leishmaniasis.

Mathison BA, Bradley BT.

05-12-2022

Lab Med.

<https://pubmed.ncbi.nlm.nih.gov/36468667/>

Leishmaniasis is a vector-borne infection caused by kinetoplastid protozoans in the genera *Leishmania* and *Endotrypanum*. The disease occurs worldwide in the tropics and subtropics and can be particularly burdensome in resource-limited settings. Diseases caused by leishmaniasis range in severity from mild cutaneous lesions to life-threatening visceral and disfiguring mucocutaneous illnesses. Rapid and accurate diagnosis is needed to ensure proper clinical management of patients afflicted with this disease. Complicating matters of diagnosis and treatment are the diversity of species within these 2 genera and the variable specificity of diagnostic assays. This mini-review provides laboratory professionals with an overview of *Leishmania* epidemiology, biology, pathogenesis, clinical presentations, and treatments with additional emphasis placed on the nuances involved in diagnosis.

Urinary phoretograms performed by capillary electrophoresis in dogs with chronic disease with or without *Leishmania infantum* infection.

Navarro PF, Fernández-Barredo S, Gil L.

18-11-2022

Front Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/36467666/>

Seroepidemiological Study of Visceral Leishmaniasis (Kala-Azar) in Children under 12 Years Old in North of Iran: An Observational Study in 2019-2020.

Amir Niaye Shad I, Mahmoudi MR, Mohebalı M, Atrkar Roshan Z, Ashrafi K, Akhounı B, Majıdı Shad B.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466030/>

Investigation of *Leishmania* RNA Virus 2 (LRV2) in Cutaneous Leishmaniasis Strains Isolated from Hatay, Turkey.

Çulha G, Kaya T, Özpınar N.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466020/>

Polycistronic Expression of Multi-Subunit Complexes in the Eukaryotic Environment: A Narrative Review.

Abdı Ghavıdel A, Jajarmi V, Bandehpour M, Kazemi B.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466018/>

Protein complexes are involved in many vital biological processes. Therefore, researchers need these protein complexes for biochemical and biophysical studies. Several methods exist for expressing multi-subunit proteins in eukaryotic cells, such as 2A sequences, IRES, or intein. Nevertheless, each of these elements has several

disadvantages that limit their usage. In this article, we suggest a new system for expressing multi-subunit proteins, which have several advantages over existing methods meanwhile it, lacks most of their disadvantages. *Leishmania* is a unicellular eukaryote and member of the Trypanosomatidae family. In the expression system of *Leishmania*, pre-long RNAs that contain several protein sequences transcribe. Then these long RNAs separate into mature mRNAs in the process named trans splicing. For producing multi-subunit protein, *Leishmania* transformed with a vector containing the sequences of all subunits. Therefore, those subunits translate and form the complex under eukaryotic cell conditions. The sequence of each protein must separate by the spatial sequence needed for trans splicing. Based on a *Leishmania* expression pattern, not only is it possible to produce the complexes with the correct structures and post-translational modifications, but also it is possible to overcome previous method problems.

Development of an Indirect Fluorescent Antibody (IFA) Assay for the Detection of *Leishmania* RNA Virus 2 (LRV2) in *Leishmania* Parasites.

Hajjaran H, Ebadizadeh M, Ataei-Pirkooh A, Mohebalı M, Samimi-Rad K, Saberi R, Naddaf SR.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466016/>

[Prevalence of mountain-zoonotic type visceral leishmaniasis in Yangquan City of Shanxi Province from 2015 to 2020].

Zhang PJ, Zhou ZB, Li YY, Hao YW, Luo ZW, Li HY, Li ZQ, Yang LM, Zhang Y, Wu B, Li SZ.

14-11-2022

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36464261/>

Detection of parasite-derived tRNA and rRNA fragments in the peripheral blood of mice experimentally infected with *Leishmania donovani* and *Leishmania amazonensis* using next-generation sequencing analysis.

Kusakisako K, Nakao R, Katakura K.

01-12-2022

Parasitol Int.

<https://pubmed.ncbi.nlm.nih.gov/36464229/>

All prokaryotes and eukaryotes, including parasites, release extracellular vesicles or exosomes that contain selected proteins, lipids, nucleic acids, glycoconjugates, and metabolites. *Leishmania* exosomes are highly enriched in small RNAs derived from the rRNAs and tRNAs of the protozoan parasite species. Here, using plasma exosomes isolated by a kit and next-generation sequencing, we report the detection of fragments of parasite-derived rRNAs and tRNAs in the peripheral plasma samples of mice experimentally infected with *Leishmania donovani* and *Leishmania amazonensis*, the causative agents of Old World visceral leishmaniasis and

New World disseminated cutaneous leishmaniasis, respectively. Detected RNA molecules of 28S rRNA, 5.8S rRNA, tRNA-Glu, and tRNA-Thr were common to both plasma samples of mice inoculated with *L. donovani* and *L. amazonensis*, whereas tRNA-Ile and tRNA-Trp were only detected in *L. amazonensis*-infected mice. The detected rRNAs and tRNA isotypes were matched with the exosomal components reported in a previous key study. Our preliminary results suggested that parasite-derived small RNAs were circulating in the blood of mice infected with *Leishmania* species, providing a better understanding of the roles of exosomal components in leishmaniasis and also new insights into exosome-based biomarkers for *Leishmania* infection.

Ecology and natural infection of phlebotomine sand flies in different ecotopes and environments in the municipality of Pains, Minas Gerais, Brazil.

Capucci DC, Campos AM, Soares JVR, Ramos VDV, Binder C, Lima MA, Margonari C, Filho JDA.

01-12-2022

Acta Trop.

<https://pubmed.ncbi.nlm.nih.gov/36463952/>

Phlebotomines (Diptera: Psychodidae) are vectors of protozoa of the genus *Leishmania* and distributed throughout Brazil, formerly restricted to rural areas, have expanded including to periurban and urban regions, been recorded in different habitats. This study aimed to understand the dynamics of sand flies in different ecotopes in the municipality of Pains. Sand flies were captured during thirty samplings using HP light traps installed in seven different ecotopes for two consecutive nights, once a month, from August 2018 to July 2019. A total of 1,352 sand flies were captured, representing 24 species belong to ten genera. *Evandromyia edwardsi* was the most abundant species, followed by *Evandromyia lenti* and *Micropygomyia quinquefer*. *Leishmania* DNA was detected in seven female sand flies in four ecotopes, for an infection rate of 0.9%. Sand flies were collected in all seven ecotopes, although forest (23.04%), cave (20.88%) and pasture (17.75%) had higher abundance and richness. Similarity was found among ecotopes, indicating that they are all important for the maintenance of the sand fly community. Spatial analysis indicated high densities of sand flies in areas with natural characteristics. All ecotopes in the municipality were evidenced to have an adequate and harmonious epidemiological profile for the transmission and expansion of leishmaniasis throughout the territory. Because of the increasing environmental changes and deforestation in the municipality, the risk of generating ecological imbalance and increased cases of leishmaniasis is imminent, which highlights the importance of developing preventive and control strategies.

Centrin-deficient *Leishmania mexicana* confers protection against Old World visceral leishmaniasis.

Karmakar S, Volpedo G, Zhang WW, Lypaczewski P, Ismail N, Oliveira F, Oristian J, Meneses C, Gannavaram S, Kamhawi S, Hamano S, Valenzuela JG, Matlashewski G, Satoskar AR, Dey R, Nakhasi HL.

03-12-2022

NPJ Vaccines.

<https://pubmed.ncbi.nlm.nih.gov/36463228/>

Leishmaniasis is one of the top neglected tropical diseases with significant morbidity and mortality in low and middle-income countries (LMIC). However, this disease is also spreading in the developed world. Currently, there is a lack of effective strategies to control this disease. Vaccination can be an effective measure to control leishmaniasis and has the potential to achieve disease elimination. Recently, we have generated centrin gene-deleted new world *L. mexicana* (*LmexCen*^{-/-}) parasites using CRISPR/Cas9 and showed that they protect mice against a homologous *L. mexicana* infection that causes cutaneous disease. In this study, we tested whether *LmexCen*^{-/-} parasites can also protect against visceral leishmaniasis caused by *L. donovani* in a hamster model. We showed that immunization with *LmexCen*^{-/-} parasites is safe and does not cause lesions. Furthermore, such immunization conferred protection against visceral leishmaniasis caused by a needle-initiated *L. donovani* challenge, as indicated by a significant reduction in the parasite burdens in the spleen and liver as well as reduced mortality. Similar control of parasite burden was also observed against a sand fly mediated *L. donovani* challenge. Importantly, immunization with *LmexCen*^{-/-} down-regulated the disease promoting cytokines IL-10 and IL-4 and increased pro-inflammatory cytokine IFN- γ resulting in higher IFN- γ /IL-10 and IFN- γ /IL4 ratios compared to non-immunized animals. *LmexCen*^{-/-} immunization also resulted in long-lasting protection against *L. donovani* infection. Taken together, our study demonstrates that immunization with *LmexCen*^{-/-} parasites is safe and efficacious against the Old World visceral leishmaniasis.

3'Nucleotidase/nuclease is required for *Leishmania infantum* clinical isolate susceptibility to miltefosine.

Carnielli JBT, Dave A, Romano A, Forrester S, de Faria PR, Monti-Rocha R, Costa CHN, Dietze R, Graham IA, Mottram JC.

30-11-2022E

BioMedicine.

<https://pubmed.ncbi.nlm.nih.gov/36462405/>

Phlebotominae Fauna (Diptera: Psychodidae) and the Spatial Distribution of Species in Sergipe, Brazil.

Andrade DC, Lima AFVA, Jeraldo VLS, de Melo CM, Pinto MC, Madi RR.

03-12-2022

J Med Entomol.

<https://pubmed.ncbi.nlm.nih.gov/36462189/>

Some sand fly species are the vectors responsible for the transmission of *Leishmania* spp. (Kinetoplastida: Trypanosomatidae), the etiological agent of leishmaniasis, and in the state of Sergipe, the two main forms of the

disease (visceral and cutaneous) are recorded. Few works show information about the species that form the Phlebotominae fauna in Sergipe. This study aimed to update and determine how they are distributed throughout the state. The study used data from surveys about phlebotomines in Sergipe, from the Program of Surveillance and Control of Visceral Leishmaniasis, carried out by the Central Public Health Laboratory of Sergipe, from 2008 to 2018, along with review and original data from 2022. The commentary on this information was developed with focus on the species that can be vectors for the disease. Sergipe has, up to now, 27 registered species of phlebotomines from 12 genera, 15 of them are of sanitary relevance. Twenty two of these species are in the mesoregion East, 19 in the Agreste, and 11 in the Sertão of Sergipe. The species with the greatest distribution was *Evandromyia lenti* (Mangabeira, 1938), present in 74.6% of the municipalities of Sergipe, followed by *Lutzomyia longipalpis* (Lutz & Neiva, 1912), the main vector of the etiological agent of visceral leishmaniasis in Brazil, present in 68% of the municipalities studied. This study expands the number and distribution of species recorded in the state. This information can contribute to disease containment plans and support health education actions aimed at the control of leishmaniasis in Sergipe.

Synthesis, antimalarial, antileishmanial evaluation, and molecular docking study of some 3-aryl-2-styryl substituted-4(3H)-quinazolinone derivatives.

Seifu GW, Birhan YS, Beshay BY, Hymete A, Bekhit AA.
02-12-2022

BMC Chem.

<https://pubmed.ncbi.nlm.nih.gov/36461074/>

Quinazolinones are a diverse group of nitrogen-containing heterocyclic compounds with promising antimalarial and antileishmanial activities. Herein, some 3-aryl-2-styryl substituted-4(3H)-quinazolinones were synthesized via cyclization, condensation, and hydrolysis reactions. ¹H NMR, FTIR and elemental microanalysis was used to verify the structures of the synthesized compounds. The in vivo antimalarial and in vitro antileishmanial activities of the target compounds were investigated using mice infected with *Plasmodium berghi* ANKA and *Leishmania donovani* strain, respectively. Among the test compounds, 8 and 10 showed better antimalarial activities with percent suppression of 70.01 and 74.18, respectively. In addition, (E)-2-(4-nitrostyryl)-3-phenylquinazolin-4(3H)-one (6) showed promising antileishmanial activity (IC₅₀ = 0.0212 µg/mL). It is two and 150 times more active than the standard drugs amphotericin B deoxycholate (IC₅₀ = 0.0460 µg/mL) and miltefosine (IC₅₀ = 3.1911 µg/mL), respectively. Its superior in vitro antileishmanial activity was supported by a molecular docking study conducted in the active site of Lm-PTR1. Overall, the synthesized 3-aryl-2-styryl substituted-4(3H)-quinazolinones showed promising antileishmanial and antimalarial activities and are desirable scaffolds for the synthesis of different antileishmanial and antimalarial agents.

First Record of Forcipomyia (Lasiohelea) Kieffer (Diptera: Ceratopogonidae) in Uruguay.

Canneva B.

Neotrop Entomol. 2022 Dec 2

<https://pubmed.ncbi.nlm.nih.gov/36459344/>

During an insect surveillance in the Santa Lucía Wetlands, Montevideo, it was captured three specimens of *Forcipomyia* (*Lasiohelea*) *stylifera* (Lutz), being the first record for this subgenus from Uruguay. *Lasiohelea* comprise species of veterinary and medical concern, due to the hematophagous feeding nature of adult females, which cause diverse degrees of nuisance on humans and animals. In the last decade, suspicion was raised involving this taxon in the transmission of *Leishmania* parasites, but there is still no conclusive evidence.

Response to thermal and infection stresses in an American vector of visceral leishmaniasis.

Martins KA, Morais CS, Broughton SJ, Lazzari CR, Bates PA, Pereira MH, Dillon RJ.

02-12-2022

Med Vet Entomol.

<https://pubmed.ncbi.nlm.nih.gov/36458853/>

Lutzomyia longipalpis is known as one of the primary insect vectors of visceral leishmaniasis. For such ectothermic organisms, the ambient temperature is a critical life factor. However, the impact of temperature has been ignored in many induced-stress situations of the vector life. Therefore, this study explored the interaction of *Lu. longipalpis* with temperature by evaluating its behaviour across a thermal gradient, thermographic recordings during blood-feeding on mice, and the gene expression of heat shock proteins (HSP) when insects were exposed to extreme temperature or infected. The results showed that 72 h after blood ingestion, *Lu. longipalpis* became less active and preferred relatively low temperatures. However, at later stages of blood digestion, females increased their activity and remained at higher temperatures. Real-time imaging showed that the body temperature of females can adjust rapidly to the host and remain constant until the end of blood-feeding. Insects also increased the expression of HSP90(83) during blood-feeding. Our findings suggest that *Lu. longipalpis* interacts with temperature by using its behaviour to avoid temperature-induced physiological damage during the gonotrophic cycle. However, the expression of certain HSP might be triggered to mitigate thermal stress in situations where a behavioural response is not the best option.

[An In Vitro Study on Sonodynamic Therapy of *Leishmania tropica* Using Curcumin].

Özlem Çalışkan S, Özen H, Kaya İ, İlkçı Sağkan R, Ertabaklar H.

Oct-2022

Mikrobiyol Bul.

<https://pubmed.ncbi.nlm.nih.gov/36458716/>

Leishmaniasis is an infectious disease that is transmitted by Phlebotomus, 400 thousand new cases appearing every year, and approximately 350 million people are at risk, and accepted by the World Health Organization as one of the six important tropical diseases. Cutaneous leishmaniasis is a disease that occurs on exposed areas of the body and is characterized by long-term non-healing skin lesions. Although the treatment methods applied today vary according to the clinical picture of the patient, the immune system of the person and the causative agent Leishmania species, there is still no standard treatment scheme that has few side effects and can be used in the treatment of leishmaniasis. Therefore, alternative treatment methods with less side effects are being tried. Sonodynamic therapy (SDT) has also emerged as an active antimicrobial research area in recent years. SDT, a new modality for antibacterial therapy, aims to increase antibacterial effects with the simultaneous combination of low-intensity ultrasound and sonosensitizer. There is no information in the literature about the effect of SDT on parasites. In this study, it was aimed to demonstrate the anti-leishmanial effect and possible mechanisms of curcumin mediated SDT on *L.tropica* promastigotes in vitro. Parasites were incubated with 0.25, 1.0, 4.0 and 15.6 micromolar (μ M) of curcumin for one hour and subjected to 1 MHz frequency, 50% duty cycle and 3 W/cm² intensity ultrasound irradiation. XTT assay was used to evaluate the viability of the cells and morphological changes were analyzed by Giemsa staining. Flow cytometry was used to quantify the fluorescence emitted by intracellular reactive oxygen species (ROS) signal, JC-1, cell cycle, Annexin V/PI staining reagents. With the combination of curcumin (15.6 μ M) and ultrasound (3 W/cm² intensity, seven minutes), *L.tropica* promastigote viability was found to be significantly decreased compared to the control group. Giemsa staining results showed that 15.6 μ M curcumin mediated SDT induced several morphological alterations in *L.tropica* promastigotes typical for apoptosis. Late apoptosis was observed in 15.6 μ M curcumin combined SDT treated parasites according to Annexin/PI staining. Besides, curcumin mediated SDT caused mitochondrial membrane potential ($\Delta\psi$ m) loss. Cell cycle analysis data indicated that curcumin based SDT caused a subG1 arrest in the cell cycle of *L.tropica* promastigotes. The generation of intracellular ROS detected by flow cytometry was increased in *L.tropica* promastigotes treated with curcumin mediated SDT. This study provided new data elucidating the molecular mechanism underlying the anti-leishmanial effect of curcumin mediated SDT. Curcumin mediated SDT has the potential to inactivate *L.tropica* promastigotes. However, further testing with amastigote or animal models is needed.

[The Effect of Oleuropein on The Mitochondrial Membrane Potential and Generation of Reactive Oxygen Species on Leishmania tropica Promastigotes].

Ilıkçı Sağkan R, Kaya İ, Akın B, Özen H, Bulduk İ, Özlem Çalışkan S.

Oct-2022

Mikrobiyol Bul.

<https://pubmed.ncbi.nlm.nih.gov/36458715/>

Cytotoxic screening and in vitro effect of sodium chlorite against Leishmania major promastigotes.

Bahreini MS, Yazdi AR, Jowkar F, Motamedi M, Mikaeili F.

Dec-2022

J Parasit Dis.

<https://pubmed.ncbi.nlm.nih.gov/36457781/>

Cutaneous leishmaniasis (CL) is one of the most important parasitic diseases in the world. Despite the existence of many therapeutic strategies, the treatment of this infection still faces problems. Sodium chlorite as an antimicrobial agent has been shown to have acceptable tissue regenerative and wound healing properties. Therefore, the present study aimed to analyze the in vitro effects of different concentrations of sodium chlorite on *Leishmania major* promastigotes and macrophage cells. The inhibitory and toxicity effect of various concentrations (0.0035, - 1.8 mg/ml) of sodium chlorite on the standard Iranian strain of *L. major* promastigotes were evaluated via counting the cells and flow cytometry. Furthermore, cytotoxicity on promastigotes and J774 macrophage cell line were performed by MTT assay. The results of the inhibitory test demonstrated that sodium chlorite had dose-dependent, anti-leishmanial activities. The half-maximal inhibitory concentration (IC₅₀) for promastigotes and J774 cells by cytotoxicity test was detected at 0.17 mg/ml and 0.08 mg/ml after 48 h respectively. Flow cytometry results showed that 27.34% death of promastigotes was observed in 0.0035 mg/ml of sodium chlorite and 78.12% in 1.8 mg/ml. The results of the present study showed that sodium chlorite could be used as an effective treatment for CL, especially in cases resistant to treatment with pentavalent compounds. However, the toxicity of this substance in high concentrations should be considered in clinical setting.

Correction to: An outbreak of cutaneous leishmaniasis due to Leishmania major in an endemic focus in central Iran.

Soleimani H, Jafari R, Veysi A, Zahraei-Ramazani AR, Rassi Y, Mirhendi H, Arandian MH, Ghasemi A, Abdoli H, Saeidi Z, Jalalizand N, Fadaei R, Ramazanpour J, Yaghoobi-Ershadi MR, Akhavan AA.

Dec-2022

J Parasit Dis.

<https://pubmed.ncbi.nlm.nih.gov/36457770/>

An introduction to dynamic nucleoporins in Leishmania species: Novel targets for tropical-therapeutics.

Dubey AK, Kumar P, Mandal D, Ravichandiran V, Singh SK.

Dec-2022

J Parasit Dis.

<https://pubmed.ncbi.nlm.nih.gov/36457769/>

As an ailment, leishmaniasis is still an incessant challenge in neglected tropical diseases and neglected infections of poverty worldwide. At present, the diagnosis and treatment to combat *Leishmania* tropical infections are

not substantial remedies and require advanced & specific research. Therefore, there is a need for a potential novel target to overcome established medicament modalities' limitations in pathogenicity. In this review, we proposed a few ab initio findings in nucleoporins of nuclear pore complex in *Leishmania* sp. concerning other infectious protists. So, through structural analysis and dynamics studies, we hypothesize the nuclear pore molecular machinery & functionality. The gatekeepers Nups, export of mRNA, mitotic spindle formation are salient features in cellular mechanics and this is regulated by dynamic nucleoporins. Here, diverse studies suggest that Nup93/NIC96, Nup155/Nup144, Mlp1/Mlp2/Tpr of *Leishmania* Species can be a picked out marker for diagnostic, immune-modulation, and novel drug targets. In silico prediction of nucleoporin-functional interactors such as NUP54/57, RNA helicase, Ubiquitin-protein ligase, Exportin 1, putative T-lymphocyte triggering factor, and 9 uncharacterized proteins suggest few more noble targets. The novel drug targeting to importins/exportins of *Leishmania* sp. and defining mechanism of Leptomycin-B, SINE compounds, Curcumins, Selinexor can be an arc-light in therapeutics. The essence of the review in *Leishmania*'s nucleoporins is to refocus our research on noble molecular targets for tropical therapeutics.

CRISPR-Cas9: Taming protozoan parasites with bacterial scissor.

Pal S, Dam S.

Dec-2022

J Parasit Dis.

<https://pubmed.ncbi.nlm.nih.gov/36457766/>

The invention of CRISPR-Cas9 technology has opened a new era in which genome manipulation has become precise, faster, cheap and more accurate than previous genome editing strategies. Despite the intricacies of the genomes associated with several protozoan parasites, CRISPR-Cas9 has made a substantial contribution to parasitology. The study of functional genomics through CRISPR-Cas9 mediated gene knockout, insertion, deletion and mutation has helped in understanding intrinsic parasite biology. The invention of CRISPR-dCas9 has helped in the programmable control of protozoan gene expression and epigenetic engineering. CRISPR and CRISPR-based alternatives will continue to thrive and may aid in the development of novel anti-protozoan strategies to tame the protozoan parasites in the imminent future.

Prevalence and risk factors of canine leishmaniasis in Morocco: a systematic review and meta-analysis.

El-Mouhdi K, Boussaa S, Chahlaoui A, Fekhaoui M.

Dec-2022

J Parasit Dis.

<https://pubmed.ncbi.nlm.nih.gov/36457764/>

Human visceral leishmaniasis has long been associated with canine leishmaniasis (CL). However, to date, there is no clear information on the status of the disease in dogs in Morocco that could be used by policymakers for the prevention of human cases. This study aims to assess the status of CL in Morocco and its risk factors through an

exhaustive literature search. The meta-analysis was performed using RevMan 5.4. The main results showed that the overall prevalence of CL in Morocco is 17% (95% CI: 0.12-0.22), caused by two strains of *Leishmania* parasite: *Leishmania tropica* and *L. infantum*. According to the region, the maximum prevalence was reported in the coastal provinces and in the central part of the country; while, the CL risk was higher in rural area (18% [95% CI: 0.14-0.23]) and at altitude above 1000 m (23% [95% CI: 0.08-0.53]). Regarding the intrinsic factors, the prevalence of the disease increased with the age of the dog, (30% [95% CI - 0.09-0.68]) and the risk was very high in clinically asymptomatic dogs (RR = 2.08 [95% CI: 1.15-3.76]). This study is the first in Morocco indicating the CL prevalence, its geographical distribution and detailing its risk factors. These results are needed to improve management strategies for the canine reservoir of leishmaniasis in Morocco and interrupt the local transmission cycle to humans.

Discovery of novel *Leishmania major* trypanothione synthetase inhibitors by high-throughput screening.

Phan TN, Park KP, Benítez D, Comini MA, Shum D, No JH.
31-12-2022

Biochem Biophys Res Commun.

<https://pubmed.ncbi.nlm.nih.gov/36413853/>

Leishmaniasis is an infectious disease caused by obligate intracellular protozoa of the genus *Leishmania* with high infection and death rates in developing countries. New drugs with better pharmacological performance with regards to safety, efficacy, toxicity, and drug resistance than those/the ones currently used are urgently needed. Trypanothione synthetase (TryS) is an attractive target for the development of drugs against leishmaniasis because it is specific and essential to kinetoplastid parasites. In this study, *Leishmania major* TryS was expressed and purified, and the kinetic parameters of purified TryS were determined. To identify novel inhibitors of LmTryS, a high-throughput screening (HTS) assay was developed and used to screen a library of 35,040 compounds. In the confirmatory assay, 42 compounds displayed half maximal inhibitory concentration (IC50) values < 50 µM and six of them corresponded to novel structures with IC50 ranging from 9 to 19 µM against LmTryS enzyme activity. Of the six inhibitors, TS001 showed the highest activity against growth of *L. major* promastigotes, *L. donovani* promastigotes, and *Trypanosoma brucei brucei* Lister 427 with IC50 values of 17, 26, and 31 µM, respectively. An in silico docking study using a homology model of LmTryS predicted the molecular interactions between LmTryS and the inhibitors.

Roe deer (*Capreolus capreolus*) are a novel potential reservoir for human visceral leishmaniasis in the Emilia-Romagna region of northeastern Italy.

Magri A, Bianchi C, Chmelová L, Caffara M, Galuppi R, Fioravanti M, Yurchenko V, Kostygov AY.

Nov-2022

Int J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36265672/>

How I Approach Leishmaniasis: Diagnosis and Treatment in the United States.

Ness TE, Martin-Blais R, Weatherhead JE.
05-12-2022

J Pediatric Infect Dis Soc.

<https://pubmed.ncbi.nlm.nih.gov/36043874/>

Leishmaniasis is a vector-borne disease caused by over 20 species of obligate intracellular protozoa belonging to the genus *Leishmania*. Leishmaniasis has a global distribution, including in the United States, and can cause a spectrum of clinical syndromes, including cutaneous, mucosal, and visceral diseases depending on host factors and the infecting *Leishmania* spp. Accurate diagnosis, including *Leishmania* species identification, is an important step to guide the most appropriate therapeutic intervention. Antileishmanial therapy is dependent on the *Leishmania* spp. identified, the clinical syndrome, and the child's immune system. However, many treatment regimens for children have been extrapolated from adult clinical trials, which may lead to underdosing and subsequent poor outcomes in infected children. Additional research is urgently needed to help guide therapy for children and determine appropriate antileishmanial agents, doses, and treatment courses for children with leishmaniasis.

Hexane extracts from fruit of two varieties of *Capsicum chinense* Jacq.: their volatile constituents and antiacetylcholinesterase, antileishmanial and antiproliferative activities.

Toigo SEM, Fernandes CC, Squarisi IS, Ribeiro AB, Tavares DC, Candido ACBB, Magalhães LG, Moreira FF, Crotti AEM, Miranda MLD.

Dec 2022

Nat Prod Res.

<https://pubmed.ncbi.nlm.nih.gov/35357248/>

This article aims to investigate volatile constituents and antiacetylcholinesterase, antileishmanial and antiproliferative activities of hexane extracts from *Capsicum chinense* fruit (unripe bode pepper 'HE-UB' and ripe little beak pepper 'HE-RB'). HE-UB and HE-RB were screened by the microplate assay method to determine their antiacetylcholinesterase activity. Both exhibited inhibitory potential, i. e., IC₅₀ = 41.5 and 20.3 µg/mL, respectively. HE-UB (IC₅₀ = 67.19 µg/mL) and HE-RB (IC₅₀ = 38.16 µg/mL) exhibited antileishmanial activity against promastigote forms of *Leishmania* (*Leishmania*) amazonensis. In addition, HE-UB and HE-RB demonstrated cytotoxic activity against different human tumor cell lines with IC₅₀ ranging from 325.40 to 425.0 µg/mL. Both GC-FID and GC-MS analyses revealed that the major component in both extracts was E-caryophyllene. In short, HE-RB was more satisfactory than HE-UB in all in vitro activities under evaluation. These findings may be used as initial data for further studies of *Capsicum* species.

Cysticercose

Experimental brain infection with cysticercosis in sheep.

Sota KA, Bustos JA, Verastegui MR, Toribio L, Chile N, Angulo N, Cangalaya C, Calcina J, González AE, Gilman RH, García HH.

Jul-Sep 2022

Rev Peru Med Exp Salud Publica.

<https://pubmed.ncbi.nlm.nih.gov/36478166/>

New animal models of neurocysticercosis can help understand epileptogenesis in neuroinfection.

Garcia HH, Verastegui MR, Arroyo G, Bustos JA, Gilman RH; Cysticercosis Working Group in Peru.

16-11-2022

Front Mol Neurosci.

<https://pubmed.ncbi.nlm.nih.gov/36466808/>

Regulation of piglet T-cell immune responses by thioredoxin peroxidase from *Cysticercus cellulosae* excretory-secretory antigens.

He W, Sun X, Luo B, Liu M, Li L, Fan X, Ye J, Zhou B.
18-11-2022

Front Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36466695/>

Taenia solium (*T. solium*) cysticercosis is a serious threat to human health and animal husbandry. During parasitization, *Cysticercus cellulosae* (*C. cellulosae*) can excrete and secrete antigens that modulate the host's T-cell immune responses. However, the composition of *C. cellulosae* excretory-secretory antigens (ESAs) is complex. This study sought to identify the key molecules in *C. cellulosae* ESAs involved in regulating T-cell immune responses. Thus, we screened for thioredoxin peroxidase (TPx), with the highest differential expression, as the key target by label-free quantification proteomics of *C. cellulosae* and its ESAs. In addition, we verified whether TPx protein mainly exists in *C. cellulosae* ESAs. The TPx recombinant protein was prepared by eukaryotic expression, and ESAs were used as the experimental group to further investigate the effect of TPx protein on the immune response of piglet T cells *in vitro*. TPx protein induced an increase in CD4⁺ T cells in piglet peripheral blood mononuclear cells (PBMCs), while CD8⁺ T cells did not change significantly. This resulted in an imbalance in the CD4⁺/CD8⁺ T-cell ratio and an increase in CD4⁺CD25⁺Foxp3⁺ Treg cells in the PBMCs. In addition, TPx protein initiated T helper 2 (Th2)-type immune responses by secreting IL-4 and IL-10 and suppressed Th1/Th17-type immune responses. The results showed that ESAs were involved in regulating piglet T-cell immune responses cells. This suggests that TPx protein found in ESAs plays an essential role to help the parasite evade host immune attack. Moreover, this lays a foundation for the subsequent exploration of the mechanism through which TPx protein regulates signaling molecules to influence T-cell differentiation.

[Epidemic trend and control progress of taeniasis and cysticercosis in Henan Province].

Jiang TT, Ji PH, He ZQ, Zhang YL, Deng Y, Chen X, Hong Y, Zhao DY, Zhang HW, Lin XM, Chen WQ.

02-09-2022

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36464252/>

Henan Province is one of the provinces where taeniasis and cysticercosis were historically highly prevalent, and *Taenia solium* is the dominant species of tapeworm. Following the concerted efforts since 1970s, the prevalence of human taeniasis and cysticercosis has been maintained at a low level in Henan Province, which facilitates the national taeniasis and cysticercosis elimination program in China. Following the implementation of the policy of aeniasis and cysticercosis elimination and classified guidance, a great success has been achieved in aeniasis and cysticercosis control in Henan Province. With continuous promotion of the opening-up policy and the Belt and Road Initiative, there are still challenges in taeniasis and cysticercosis control. This review summarizes the control progress of taeniasis and cysticercosis and proposes the challenges of taeniasis and cysticercosis control in Henan Province.

Focus session: parasitic diseases of the central nervous system-an introduction.

Salomão JFM.

02-12-2022

Childs Nerv Syst.

<https://pubmed.ncbi.nlm.nih.gov/36459210/>

[A Histopathologically Diagnosed Neurocysticercosis Case from Türkiye].

Özer Balin Ş, Enez M, Akbulut A, Çalık M, Akgün B, Balgetir F, Yıldırım H.

Oct-2022

Mikrobiyol Bul.

<https://pubmed.ncbi.nlm.nih.gov/36458721/>

Cysticercosis is a parasitic tissue infection caused by larval cysts of *Taenia solium*. Although the disease affects many tissues, it primarily affects the brain and muscles. The most common form is neurocysticercosis, a term used for human central nervous system involvement with *T. solium* cysts. Neurocysticercosis is an important public health problem in many parts of the world. Its prevalence is particularly high in places where *T. solium* tapeworms are common, such as Mexico, Central America, South America, Southeast Asia, Africa, China, India, and Nepal. Its incidence has been increasing rapidly in recent years in non-endemic countries, due to both import and local cases, while in some highly endemic areas, numbers appear to have decreased, possibly due to better sanitation and increased public awareness. It is extremely rare in Türkiye. Cysticercosis is usually caused by drinking water or eating food containing tapeworm eggs. Clinical manifestations can range from completely asymptomatic infection to severe illness or death. Although the infection can involve any part of the central nervous system,

symptomatic patients mostly have spinal cord involvement, intracerebral lesion, intraventricular cyst or subarachnoid lesion. An intraparenchymal cerebral cyst typically grows slowly and causes minimal symptoms for years or decades after the onset of infection. The site of involvement and the symptoms experienced determine the diagnosis and treatment method. The current general consensus supports antihelminthic and corticosteroid therapy for viable parenchymal lesions. In this report, a neurocysticercosis case with a single brain lesion that was surgically removed and histologically examined was presented. The patient had complaints of lisp in the tongue, numbness in the lips and left face. The patient had no concomitant chronic disease. The patient did not have a travel history or a history of eating pork but had a history of contact with a dead pig two months ago. Upon detection of a central mass in the brain computed tomography examination, surgical procedure was performed on the patient. Based on the identification of a larval stage of *T. solium* in biopsy material neurocysticercosis was diagnosed. However, histopathologically demonstration of the parasite is not possible in most cases. The patient received an antiparasitic treatment with albendazole 1000 mg/d in combination with dexamethasone. The patient was successfully treated and is still being followed up by calling for controls.

Dracunculose

Target sequence data shed new light on the infrafamilial classification of Araceae.

Haigh AL, Gibernau M, Maurin O, Bailey P, Carlsen MM, Hay A, Leempoel K, McGinnie C, Mayo S, Wong SY, Zuluaga A, Zuntini AR, Baker WJ, Forest F.

08-12-2022

Am J Bot.

<https://pubmed.ncbi.nlm.nih.gov/36480380/>

[Identification, biological characteristics, and control of pathogen causing southern blight of *Pinellia ternata*].

Zhou J, Chen QH, Xu JW, Chen H, Huang BS, Miao YH, Liu DH.

Oct-2022

Zhongguo Zhong Yao Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36472027/>

In summer in 2020, *Pinellia ternata* in many planting areas in Hubei suffered from serious southern blight, as manifested by the yellowing and wilted leaves and rotten tubers. This study aims to identify the pathogen, clarify the biological characteristics of the pathogen, and screen fungicides. To be specific, the pathogen was isolated, purified, and identified, and the pathogenicity was detected according to the Koch's postulates. Moreover, the biological characteristics of the pathogen were analyzed. Furthermore, PDA plates and seedlings were used to determine the most effective fungicides. The results showed that the mycelia of the pathogen were

white and villous with silk luster, which produced a large number of white to black brown sclerotia. The pathogen was identified as *Athelia rolfsii* by morphological observation and molecular identification based on LSU and TEF gene sequences. The optimum growth conditions for *A. rolfsii* were 30 °C and pH 5-8, and the optimum conditions for the germination of sclerotia were 25 °C and pH 7-9. *Bacillus subtilis*, difenoconazole, and flusilazole were identified as effective fungicides with PDA, and their half maximal effective concentration (EC₅₀) was all less than 5 mg·L⁻¹. The effective fungicides screened with the seedlings were hymexazol and difenoconazole. Based on the screening experiments, difenoconazole can be used as the main agent for the prevention and treatment of southern blight.

[Preparation of monoclonal antibodies against *Pinellia ternata* lectin protein and establishment of double-antibody sandwich ELISA].

Xie YW, Yu HL, Wu H, Tao XB, Wang HP, Cheng YQ, Wang CX, Zeng P, Liu BB, Zhang P, Cui XB.

Nov-2022

Zhongguo Zhong Yao Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36471932/>

To determine the content of endogenous toxic substance *Pinellia ternata* lectin (PTL) protein in *Pinelliae Rhizoma* and the related processed products, this study prepared specific monoclonal antibodies against PTL by hybridoma cell technology, and established a quantitative double-antibody sandwich enzyme linked immunosorbent assay (ELISA) for PTL antigen. The detection conditions were 2.5 µg·mL⁻¹ working concentration of the captured antibody and 1:450 of the dilution multiple of detected antibody. The coating condition was staying overnight at 4 °C. The blocking time and incubation times of antigen and detected antibody were all 90 minutes. The incubation time of horseradish peroxidase conjugated streptavidin-horseradish peroxidase (SA-HRP) was 15 minutes. The quantitative limit of the method for PTL antigen was 0.375 ng·mL⁻¹. The linear range was 75.000-4 800.000 pg·mL⁻¹, and R²=0.997 1. The recovery rate was 90.0%-110.0%, and the variation coefficients of intra-test and inter-test precision were 2.0%-3.0% and 2.0%-8.5%. The content of PTL in three batches of *Pinelliae Rhizoma* and the related processed products was determined by the method, and the average content of PTL in *Pinelliae Rhizoma* was 35.42 mg·g⁻¹. The average content of PTL in *Pinelliae Rhizoma Praeparatum Cum Alumine*, *Pinelliae Rhizoma Praeparatum*, and *Pinelliae Rhizoma Praeparatum Cum Zingibere Et Alumine* were 1.15 mg·g⁻¹, 16.53 µg·g⁻¹, and 122.63 ng·g⁻¹, respectively, indicating that the content of PTL decreased significantly after processing. The quantitative double-antibody sandwich ELISA for PTL antigen established in this paper had good linearity, sensitive response, and high accuracy, which provided a simple and effective monitoring method for the detection of PTL content in the processing of *Pinelliae Rhizoma*.

Rare earth element scandium mitigates the chromium toxicity in *Lemna minor*

by regulating photosynthetic performance, hormonal balance and antioxidant machinery.

Alp FN, Arikan B, Ozfidan-Konakci C, Ekim R, Yildiztugay E, Turan M.

01-01-2023

Environ Pollut.

<https://pubmed.ncbi.nlm.nih.gov/36379288/>

Chromium (Cr) toxicity is a serious problem that threatens the health of living organisms and especially agricultural production. The presence of excess Cr leads to biomass loss by causing the imbalance of biochemical metabolism and inhibiting photosynthetic activity. A new critical approach to cope with Cr toxicity is the use of the rare earth elements (REEs) as an antioxidant defence system enhancer in plants. However, the effect of scandium (Sc), which is one of the REEs, is not clear enough in *Lemna minor* exposed to Cr toxicity. For this purpose, the photosynthetic and biochemical effects of scandium (50 µM and 200 µM Sc) treatments were investigated in *Lemna minor* under Cr stress (100 µM, 200 µM and 500 µM Cr). Parameters related to photosynthesis (F_v/F_m, F_v/F_o) were suppressed under Cr stress. Stress altered antioxidant enzymes activities and hormone contents. Sc applications against stress increased the activities of superoxide dismutase (SOD), NADPH oxidase (NOX), ascorbate peroxidase (APX), glutathione reductase (GR), monodehydroascorbate reductase (MDHAR), and glutathione S-transferase (GST). In addition to the antioxidant system, the contents of indole-3-acetic acid (IAA), abscisic acid (ABA) and jasmonic acid (JA) were also rearranged. However, in all treatment groups, with the provision of ascorbate (AsA) regeneration and effective hormone signaling, reactive oxygen species (ROS) retention which result in high hydrogen peroxide (H₂O₂) content and lipid peroxidation (TBARS) were effectively removed. Sc promoted the maintenance of cellular redox state by regulating antioxidant pathways included in the AsA-GSH cycle. Our results showed that Sc has great potential to confer tolerance to duckweed by reducing Cr induced oxidative damage, protecting the biochemical reactions of photosynthesis, and improving hormone signaling.

Reconstitution of an N-AChR from *Brugia malayi*, an evolved change in acetylcholine receptor accessory protein requirements in filarial parasites.

Noonan JD, Beech RN.

14-11-2022

PLoS Pathog.

<https://pubmed.ncbi.nlm.nih.gov/36374934/>

Neurotransmission is an important target for anthelmintic drugs, where receptor characteristics and response can be examined through reconstitution ex vivo in *Xenopus laevis* oocytes. The homomeric ACR-16 nicotine sensitive acetylcholine receptors (N-AChRs) of several helminth species have been characterized in this way. Our efforts to reconstitute the N-AChR from the clade III filarial parasite, *Brugia malayi* using similar conditions, initially produced no detectable response. A robust response to

acetylcholine is obtained from the closely related clade III parasite *Ascaris suum*, suggesting that specific changes have occurred between *Ascaris* and *Brugia*. N-AChRs from three species intermediate between *A. suum* and *B. malayi* were characterized to provide information on the cause. Maximal response to acetylcholine did not change abruptly, consistent with a discrete event, but rather decreased progressively from *A. suum* through *Dracunculus medinensis*, *Gongylonema pulchrum* and *Thelazia callipaeda*. Receptor responses to the characteristic nicotine, and other agonists were generally similar. The decrease in maximal current did correlate with a delayed time to reach larger response. Together, this suggested that the failure to reconstitute the *B. malayi* N-AChR was one extreme of a progressive decrease and that an issue with synthesis of the receptor in oocytes was responsible. Addition of accessory proteins EMC-6, NRA-2 and NRA-4, in addition to RIC-3, produced a small, but measurable *B. malayi* N-AChR response. Pharmacological properties of a chimeric *B. malayi* N-AChR were equivalent to the other species, confirming the receptor response remains unchanged while its production is increasingly dependent on accessory proteins. One possibility is that loss of many subunits for acetylcholine receptors from the filarial nematode genome is linked to new subunit combinations that lead to such a dependence. This novel phylogenetic approach allowed the first characterization of a *B. malayi* AChR *ex vivo* and in doing so, provides a framework for the successful characterization of other receptors that have yet to be reconstituted.

Echinococcosis

Cloning and identification of the CTLA-4IgV gene and functional application of vaccine in Xinjiang sheep.

Kong H, Zhao S, Zheng J, Liu B, Zhou Y, Li Y, Zhou W, Zhou X.

23-11-2022

Open Life Sci.

<https://pubmed.ncbi.nlm.nih.gov/36474703/>

Cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) is an important surface molecule of activated T cells that has a strong affinity with the B7 molecule on the surface of antigen-presenting cells. Among these molecules, the CTLA-4 extracellular region (CTLA-4 IgV) may be used as a novel immune adjuvant molecule for delivering antigens and inducing strong humoral and cellular immune responses. In this study, bioinformatics analysis was performed to determine and clone the extracellular region of Xinjiang sheep CTLA-4 (NM_001009214). The CTLA-4 IgV gene was amplified and ligated into the pMD19-T vector, and the positive bacteria were screened by blue-white spots for sequencing and comparison. The correctly sequenced CTLA-4 IgV was digested and then ligated into the prokaryotic expression vector pET-30a(+). The plasmid pET30a-CTLA-4 IgV was constructed to induce the expression of the recombinant protein CTLA-4 IgV. Thereafter, CTLA-4 IgV was identified. Clustal X multiple sequence alignment revealed that the protein sequence of Xinjiang sheep CTLA-4 IgV was different from that of the

known CTLA-4 extracellular region. The 3D protein structure of Xinjiang sheep CTLA-4 IgV was constructed via the bioinformatics method. Subsequently, molecular docking between the Xinjiang sheep CTLA-4 IgV protein and the B7 molecule was conducted. Results revealed multiple binding sites in the extracellular region of Xinjiang sheep CTLA-4, and two multiple interactions ensured stable binding after docking. The functionality of the Xinjiang sheep CTLA-4 IgV protein was further verified by fusing the CTLA-4 extracellular V region with EgG1Y162, a protective protein from *Echinococcus granulosus*, and the purified recombinant protein CTLA-4 IgV-EgG1Y162 was expressed with the mouse bone marrow-derived. The addition of the Xinjiang sheep CTLA-4 IgV protein at the amino terminus promoted the binding of EgG1Y162 to dendritic cells (DCs) and increased the maturation rate of these cells, further indicating that the protein could effectively improve the antigen presentation ability of DCs. The CTLA-4 extracellular domain protein of Xinjiang sheep is unique and has the potential to promote the presentation of the fusion protein by DCs as an adjuvant. The cloning and expression of this gene provide new measures and ideas for the preparation of the Xinjiang sheep vaccine to prevent zoonotic diseases.

7T Small Animal MRI Research for Hepatic Alveolar Echinococcosis.

Zhang G, Mou Y, Fan H, Li W, Cao Y, Bao H.

01-12-2022

Top Magn Reson Imaging.

<https://pubmed.ncbi.nlm.nih.gov/36469640/>

Label-free quantitative proteomics and immunoblotting identifies immunoreactive and other excretory-secretory (E/S) proteins of *Anoplocephala perfoliata*.

Hautala K, Pursiainen J, Näreaho A, Nyman T, Varmanen P, Sukura A, Nielsen MK, Savijoki K.

16-11-2022

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36466892/>

Anoplocephala perfoliata is a common tapeworm in horses causing colic and even mortalities. Current diagnostic tests to detect *A. perfoliata* infections have their limitations and an improved method is needed. Immunoreactive excretory/secretory proteins (E/S proteome) of this parasite can provide promising candidates for diagnostic tests. We compared E/S proteins produced by small (length < 20 mm, width < 5 mm) and large (length 20 to 40 mm, width 5 to 10 mm) *A. perfoliata* worms *in vitro* by label-free quantitative proteomics using a database composed of related *Hymenolepis diminuta*, *Echinococcus multilocularis/granulosus* and *Taenia aseatica* proteins for protein identifications. Altogether, 509 E/S proteins were identified after incubating the worms *in vitro* for three and eight hours. The greatest E/S proteome changes suggested both worm size- and time-dependent changes in cytoskeleton remodeling, apoptosis, and production of antigens/immunogens. The E/S proteins collected at the three-hour time point

represented the natural conditions better than those collected at the eight-hour time point, and thereby contained the most relevant diagnostic targets. Immunoblotting using antibodies from horses tested positive/negative for *A. perfoliata* indicated strongest antigenicity/immunogenicity with 13-, 30- and 100-kDa proteins, involving a thioredoxin, heat-shock chaperone 90 (Hsp90), dynein light chain component (DYNLL), tubulin-specific chaperone A (TBCA) and signaling pathway modulators (14-3-3 and Sj-Ts4). This is among the first studies identifying new diagnostic targets and *A. perfoliata* antigens eliciting a IgG-response in horses.

Evaluation of the Ability of Antigen B Originated from Echinococcus granulosus Sensu Stricto and E. canadensis for the Diagnosis of Confirmed Human Cystic Echinococcosis Using ELISA.

Sadjjadi SF, Mohammadzadeh T, Hafezi F, Sadjjadi SM.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466027/>

Multiorgan Echinococcosis with Uterine Involvement Causing Bilateral Hydronephrosis in a Child: Case Report.

Yağmur I, Kocaman OH, Dere O, Demir M, Katı B, Boleken ME.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466026/>

Hydatid cyst is a parasitic infection transmitted by oral ingestion of *Echinococcus granulosus* eggs. Hydatid cyst of the genital tract is rare and the occurrence in the uterus is an extreme rarity. We present an 8-yr-old girl with complaints of swelling of lower abdomen, pollakiuria and bilateral flank pain was brought to Emergency Department of Harran University, Turkey, in Jun 2019. The patient had simultaneous hydatid cysts of the liver, mesentery and uterus. We performed abdominal exploration and completely removed the inner germinal layer of cyst through an incision made in the anterior of the uterine fundus. Then, we applied total excision to the two cysts in the right and left colon mesentery. Finally, we performed partial cystectomy to the cyst in the liver, and we removed the cyst membrane totally. In endemic regions, hydatid cysts should be considered for the diagnosis of children with cystic mass lesions. Uterine-sparing approach should be kept in mind as an option, especially in young women. Early surgical treatment of large pelvic cysts that cause obstructive uropathy may prevent the progression of renal damage.

Mediastinal and pericardial hydatidosis: A case report with review of the literature.

Rhalem I, Haloua M, Hajjar C, El Bouardi N, Alami B, Lamrani MYA, Maaroufi M, Boubbou M.

29-11-2022

Radiol Case Rep.

<https://pubmed.ncbi.nlm.nih.gov/36465165/>

Hydatidosis is an echinococcosis caused by the development of *Echinococcus granulosus* larvae in humans. The lung is the second most frequent site after the liver. The primary mediastinal and pericardial localisations are extremely rare. Ultrasound and CT scans play an important role in the diagnosis of this disease. We report the case of an 11-year-old female patient from a rural environment with a history of dogs contact, whose symptomatology consisted of chest pain, dyspnoea, all evolving in a febrile context. The imagery showed the existence of multiple mediastinal and pericardial collections. This patient was rapidly managed with albendazole (ABZ) and scanography revealed an excellent therapeutic response. Primary mediastinal and pericardial hydatidosis is a very uncommon disease. It can be unfortunately revealed at the stage of vital prognosis complications. Ultrasound and computerized tomography (CT) are helpful for localizing and defining the morphologic features of hydatid cysts. It should be kept in mind, especially in patients from endemic areas.

'Fight the parasite': raising awareness of cystic echinococcosis in primary school children in endemic countries.

Porcu F, Cantacessi C, Dessi G, Sini MF, Ahmed F, Cavallo L, Nonnis F, Gibson K, Varcasia C, Joanny G, Scala A, Tamponi C, Varcasia A.

02-12-2022

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36461072/>

Comparative analysis of anti-relapse treatment regimens in 110 patients with hepatic and pulmonary hydatid echinococcosis.

Galyavin AV.

Nov-2022

Eur Rev Med Pharmacol Sci.

<https://pubmed.ncbi.nlm.nih.gov/36459040/>

A rare case of hydatid cyst of the neck with concurrent pulmonary hydatid disease.

Shukla AK, Peter A, Arya V, Dwivedi V, Gupta MK, Rai N, Tiwari P, Bhargava JK.

Dec-2022

J Parasit Dis.

<https://pubmed.ncbi.nlm.nih.gov/36457772/>

Echinococcosis, commonly known as hydatid disease, is a zoonotic infection caused by dog tapeworm *Echinococcus granulosus*. Hydatid disease of the head and neck region is scarcely reported even in endemic areas. We herein report a case with neck swelling and respiratory symptoms subsequently diagnosed to have disseminated echinococcosis of the neck and left lung.

Anti-helminthic effects and cellular mechanisms of *Astragalus ecbatanus*

extract against *Echinococcus granulosus* protoscoleces

Mahmoudvand H, Al-Abodi HR, Zolfagharkhani P, Ghasemian Yadegari J.

Dec-2022

J Parasit Dis

<https://pubmed.ncbi.nlm.nih.gov/36457771/>

We aimed to investigate the in vitro and ex vivo anti-helminthic effects of *Astragalus ecbatanus* chloroform extract (AECE) as well as its cellular mechanisms against *Echinococcus granulosus* protoscoleces. In vitro and ex vivo anti-helminthic effects of AECE on *E. granulosus* protoscoleces were evaluated through eosin exclusion test. Effects of AECE on induction of the caspase-3 like activity, the permeability of plasma membrane were also determined. The effects of AECE against the human hepatocyte carcinoma (HepG2) and human embryonic kidney (HEK293T) cells were determined by MTT ([3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide]]) test. The findings revealed that AECE especially at 45 mg/mL displayed potent in vitro and ex vivo anti-helminthic effects against *E. granulosus* protoscoleces ($p < 0.001$). After treatment of protoscoleces with AECE, the caspase-3 enzyme activity and the rate of permeability of plasma membrane was dose dependently ($P < 0.001$) increased. The 50% cytotoxic concentration (CC50) value of AECE for normal and cancer cells lines 4.62 mg/mL and 1.89 mg/mL, respectively. The findings of the current study revealed the favorable in vitro and ex vivo anti-helminthic effects of AECE against protoscoleces of *E. granulosus*. However, further surveys in animal model are required to elucidate different aspects of this extract before use in clinical phases.

Trématodoses d'origine alimentaire (clonorchiose, opisthorchiase, fasciolase et paragonimose)

Human and Animal Fascioliasis: Origins and Worldwide Evolving Scenario.

Mas-Coma S, Valero MA, Bargues MD.

0512-2022

Clin Microbiol Rev.

<https://pubmed.ncbi.nlm.nih.gov/36468877/>

Fascioliasis is a plant- and waterborne zoonotic parasitic disease caused by two trematode species: (i) *Fasciola hepatica* in Europe, Asia, Africa, the Americas, and Oceania and (ii) *F. gigantica*, which is restricted to Africa and Asia. Fasciolid liver flukes infect mainly herbivores as ruminants, equids, and camelids but also omnivore mammals as humans and swine and are transmitted by freshwater Lymnaeidae snail vectors. Two phases may be distinguished in fasciolid evolution. The long predomestication period includes the *F. gigantica* origin in

east-southern Africa around the mid-Miocene, the *F. hepatica* origin in the Near-Middle East of Asia around the latest Miocene to Early Pliocene, and their subsequent local spread. The short postdomestication period includes the worldwide spread by human-guided movements of animals in the last 12,000 years and the more recent transoceanic anthropogenic introductions of *F. hepatica* into the Americas and Oceania and of *F. gigantica* into several large islands of the Pacific with ships transporting livestock in the last 500 years. The routes and chronology of the spreading waves followed by both fasciolids into the five continents are redefined on the basis of recently generated knowledge of human-guided movements of domesticated hosts. No local, zonal, or regional situation showing disagreement with historical records was found, although in a few world zones the available knowledge is still insufficient. The anthropogenically accelerated evolution of fasciolids allows us to call them "peridomestic endoparasites." The multidisciplinary implications for crucial aspects of the disease should therefore lead the present baseline update to be taken into account in future research studies.

Cost-benefit ratio of anthelmintic treatment and its comparative efficacy in commercial dairy farms.

Rashid M, Zahra N, Chudhary A, Rehman TU, Aleem MT, Alouffi A, Mohammed A, Rashid MI, Ehsan M, Malik MI, Hussain Dilber G, Bakhsh A, Almutairi MM.

16-11-2022

Front Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/36467634/>

Intestinal parasitic infection is one of the major challenges in obtaining optimal production and maintaining the health and welfare of all animals including cattle and buffaloes. Anti-parasitic treatments appear to be a reliable countermeasure. However, the effectiveness and selection of suitable anthelmintics require situational assessments in a given locality. In the current study, the efficacy and impact of benzimidazole (albendazole) were assessed in a total of 400 (100 each) on the performance of buffaloes, buffalo-heifer, cattle, and cattle-heifers at two commercial dairy farms in the Province of Punjab, Pakistan. Additionally, the cost-benefit ratio was calculated by assessing the inputs (medication, feed, and labor cost) and outputs (milk and weight gain). The qualitative and quantitative examination of helminth eggs in each type of animal indicated a prevalence of 73.3, 78.3, 76.6, and 85.0% in cattle, cattle-heifers, buffaloes, and buffaloes-heifers, respectively. Specifically, a highest rate (10.0-13.3%) of *Haemonchus* sp. infection was only observed in cattle and heifers, while *Fasciola* sp. infections (10.0-11.6%) were the most often found species in buffaloes and heifers. The highest anthelmintic impacts (egg per gram of feces, $p < 0.001$) were observed on day 14 post-medication. Until 60 days of post-anthelmintic treatment, an average increase of 0.8 and 0.7 L in milk production per day in cattle and buffaloes, respectively while a total of 11.45 and 9.45 kg body weight were noticed in cattle-heifer and buffaloes-heifer, respectively. Cumulative cost-benefit analysis indicated a positive correlation between treated and non-treated animals.

These findings reiterate the importance of anthelmintic drugs in reducing the impacts of parasites on the productivity, health, and well-being of an animal under high infection challenges.

Clinical, Laboratory and Radiological Features of Paragonimiasis Misdiagnosed as Pulmonary Tuberculosis.

Poudyal BS, Paudel B, Bista B, Shrestha GS, Pudasaini P.
Jul-Sep 2022
Iran J Parasitol.
<https://pubmed.ncbi.nlm.nih.gov/36466025/>

[Prevalence of parasitic infections in fish from markets in Zhenjiang City from 2017 to 2020].

Li AH, Wang L, Li SS, Zhang WJ.
22-04-2022
Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
<https://pubmed.ncbi.nlm.nih.gov/36464250/>

Economic losses, morpho-molecular identification, and identity of Fasciola species recovered from Egypt.

Abdel-Fatah OR, Arafa WM, Wahba AA, El-Dakhly KM.
Dec-2022
J Parasit Dis.
<https://pubmed.ncbi.nlm.nih.gov/36457773/>

A retrospective study to estimate economic losses caused by livers condemnation, due to fascioliasis, of slaughtered cattle and buffaloes in Egypt during the period of 2016-2020, was done. Moreover, a morpho-molecular identification of collected liver flukes from slaughtered animals in municipal abattoirs was conducted. Livers of naturally infected carcasses were obtained from slaughtered animals in Beni-Suef, Cairo and Tanta provinces, Egypt during 2019-2020 for phenotypic characterization of recovered *Fasciola* species and molecular identification of collected worms using PCR targeting the ITS-1 region. Findings of the retrospective study revealed that percentages of livers condemnation of cattle and buffaloes ranged from 0.79 to 0.66% during the period from 2016 to 2020. The highest percentages were detected in the south Egypt (2.5-6.0%) with the highest economic losses (261850-616300 USD annually). Morphometrically, collected flukes categorized into *Fasciola hepatica* and *Fasciola gigantica*. No intermediate forms (*Fasciola* sp.-like) were detected. Sequencing analysis of ITS-1 PCR products showed that only *Fasciola hepatica* (26/34) and *F. gigantica* (8/34) isolates were found, with no intermediate forms, *Fasciola* sp.-like, could be identified. Currently, *Fasciola hepatica* was 100% identical with the Egyptian species (LC076196 and JF294998), French species (JF294999), and Iranian species (MF969009 and MK377150). Moreover, the obtained *F. gigantica* species showed 100% identity with Egyptian ones (LC076125, LC076108 and KX198619), Iranian (KF982047 and MF372919), and other GenBank specimens from Vietnam, Cameroon and India. In

conclusion, South Egypt showed the highest economic losses due to fascioliasis, especially Aswan province. *Fasciola hepatica* was more common than *F. gigantica*, while the hybrid form was not detected.

Fasciolosis prevalence, risk factors and economic losses due to bovine liver condemnation in abattoirs in Mexico.

Utrera-Quintana F, Covarrubias-Balderas A, Olmedo-Juárez A, Cruz-Aviña J, Córdova-Izquierdo A, Pérez-Mendoza N, Villa-Mancera A.
Dec-2022
Microb Pathog.
<https://pubmed.ncbi.nlm.nih.gov/36309180/>

This study investigated the prevalence of bovine liver condemnation due to *Fasciola hepatica* in abattoirs and its influence on livestock productivity. It also explored risk factors such as season, breed, age and sex in the states of Puebla and Veracruz, Mexico. A total of 5281 cattle livers were inspected in two abattoirs. The overall prevalence of the parasite in cattle throughout 2020 was 24.9% (1313 out of 5281). The highest prevalence was found in Veracruz (28.5%; tropical climate), followed by Puebla (18.4%; temperate climate). The prevalence of fluke infection during the wet season was 19.0% and 25.8% in the states of Puebla and Veracruz, respectively; during the dry season, this was 18.0% and 30.2% respectively. The annual loss caused by condemnation of the liver for both abattoirs was estimated to be US\$7502. Using multivariate logistic regression analysis, two models were constructed for potential association with the prevalence of condemned livers, using season, breed, age and sex as risk factors. The results indicate that season, age and sex were significantly associated with an increased risk of parasitic infection. Cattle age was the variable most strongly associated with *F. hepatica* infection, with the highest prevalence in cattle over three years of age as compared to younger animals, both in the states of Veracruz with a tropical climate (OR 6.443; 95% CI: 4.487-9.251) and in Puebla with a temperate climate (OR 2.854; 95% CI: 1.531-5.321). The results indicate that different factors were significantly associated with the prevalence of condemned livers, and it highlights the importance of continuous monitoring programmes for *F. hepatica* infection and preventing economic losses in cattle production.

A survey of sheep and/or cattle farmers in the UK shows confusion over the diagnosis and control of rumen fluke and liver fluke.

Hoyle RC, Rose Vineer H, Duncan JS, Williams DJL, Hodgkinson JE.
Dec-2022
Vet Parasitol.
<https://pubmed.ncbi.nlm.nih.gov/36270230/>

Calicophoron daubneyi (rumen fluke) is an emerging parasitic infection of livestock across Europe. Despite increasing in prevalence, little is known about the level of awareness of rumen fluke or current control practices used by UK farmers. *Fasciola hepatica* (liver fluke) is a common parasitic infection of cattle and sheep in the UK.

Co-infections with these parasites can present in sheep and cattle, but the only drug with reported efficacy against rumen fluke is oxcyclozanide. Between December 2019 and March 2020, 451 sheep and/or cattle farmers completed an online questionnaire, capturing their awareness and current means of control for liver fluke and rumen fluke. Most respondents (70%) were aware of rumen fluke, with 14% recording its presence on their farms and 18% having previously treated for rumen fluke. Almost all respondents (99%) were aware of liver fluke and higher numbers of respondents reported its presence on farm (67%) with 88% having previously treated for liver fluke. Respondents who were aware of rumen fluke said they were concerned about the parasite (81%), although rumen fluke was less of a concern than liver fluke ($p < 0.05$). Of respondents who reported rumen fluke presence on their farm, 42% cited incorrect diagnostic methods, including those traditionally used to detect liver fluke. Respondents were more likely to treat annually for liver fluke, as opposed to rumen fluke ($p < 0.05$). The most frequently used drug for the treatment of liver fluke infection was triclabendazole (53% sheep treatments, 34% cattle treatments) and only a minority of farmers treated with a product effective against rumen fluke (oxcyclozanide; 42% cattle treatments, 35% sheep treatments). A small proportion of farmers stated that they used a non-flukicide drug to treat sheep for liver fluke infection (1.6% sheep treatments). These results demonstrate a broad awareness of liver and rumen fluke in sheep and cattle, but reveal confusion amongst farmers about their diagnosis and treatment, highlighting the need to provide best practice advice to the livestock industry for the control of both parasites.

Filariose lymphatique

Filarial Dance Sign in Lymphatic Filariasis of the Scrotum.

Sahu AK, Aggarwal B.

08-12-2022

N Engl J Med

<https://pubmed.ncbi.nlm.nih.gov/36477034/>

Unilateral Lower Extremity Elephantiasis.

Duan X, Xiong X, Yu H, Deng L.

30-11-2022

Clin Infect Dis.

<https://pubmed.ncbi.nlm.nih.gov/36449404/>

Visualization of the Linear and Spatial Organization of Chromosomes in Mosquitoes.

Liang J, Bondarenko SM, Sharakhov IV, Sharakhova MV.

01-12-2022

Cold Spring Harb Protoc.

<https://pubmed.ncbi.nlm.nih.gov/35960626/>

Mosquitoes are vectors of dangerous human diseases such as malaria, dengue, Zika, West Nile fever, and lymphatic filariasis. Visualization of the linear and spatial organization of mosquito chromosomes is important for

understanding genome structure and function. Utilization of chromosomal inversions as markers for population genetics studies yields insights into mosquito adaptation and evolution. Cytogenetic approaches assist with the development of chromosome-scale genome assemblies that are useful tools for studying mosquito biology and for designing novel vector control strategies. Fluorescence in situ hybridization is a powerful technique for localizing specific DNA sequences within the linear chromosome structure and within the spatial organization of the cell nucleus. Here, we introduce protocols used in our laboratories for chromosome visualization and their application in mosquitoes.

Mycétome

Diagnostics to support mycetoma management-Development of two target product profiles.

Fongwen N, Asiedu KB, Bakhiet S, Bonifaz A, Cruz I, Argaw D, Estrada-Chavez G, Fahal AH, Litvintseva A, Marks M, Salinas-Carmona MC, Sow D, van de Sande WWJ.

Dec-2022

Trop Med Int Health.

<https://pubmed.ncbi.nlm.nih.gov/36329624/>

Schistosomiase

Prevalence of Bovine Schistosomiasis and Associated Risk Factors in Tis Abay District, Northwest Ethiopia.

Kifle T, Bayile T, Fesseha H, Mathewos M.

28-11-2022

Vet Med Int.

<https://pubmed.ncbi.nlm.nih.gov/36479435/>

Mapping schistosomiasis risk in Southeast Asia: a systematic review and geospatial analysis.

Luo C, Wang Y, Su Q, Zhu J, Tang S, Bergquist R, Zhang Z, Hu Y.

08-11-2022

Int J Epidemiol.

<https://pubmed.ncbi.nlm.nih.gov/36478466/>

Activation of primary hepatic stellate cells and liver fibrosis induced by targeting TGF- β 1/Smad signaling in schistosomiasis in mice.

Huang P, Ma H, Cao Y, Zhan T, Zhang T, Wang X, Zhang Y, Xu J, Xia C.

06-12-2022

Parasit Vectors.

<https://pubmed.ncbi.nlm.nih.gov/36474240/>

Development of real-time and lateral flow recombinase polymerase amplification assays for rapid detection of *Schistosoma mansoni*.

Mesquita SG, Lugli EB, Matera G, Fonseca CT, Caldeira RL, Webster B.

18-11-2022

Front Microbiol.

<https://pubmed.ncbi.nlm.nih.gov/36466644/>

A *Schistosoma Colitis* Case Misdiagnosed as Ulcerative Colitis in a Non-Endemic Area: A Case Report.

Ak Ç, Sayar S, Kılıç ET.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466017/>

The differential diagnosis of bloody diarrhea is necessary to specify etiology and plan treatment. Misdiagnosis can lead to catastrophic results with the treatments to be given. In this case report, we present a case of schistosomal colitis mimicking ulcerative colitis in a 26-year-old Guinean male patient diagnosed in 2021.

A self-purifying microfluidic system for identifying drugs acting against adult schistosomes.

Girod V, Houssier R, Sahmer K, Ghoris MJ, Caby S, Melnyk O, Dissous C, Senez V, Vicogne J.

30-11-2022

R Soc Open Sci.

<https://pubmed.ncbi.nlm.nih.gov/36465675/>

The discovery of novel antihelmintic molecules to combat the development and spread of schistosomiasis, a disease caused by several *Schistosoma* flatworm species, mobilizes significant research efforts worldwide. With a limited number of biochemical assays for measuring the viability of adult worms, the antischistosomal activity of molecules is usually evaluated by a microscopic observation of worm mobility and/or integrity upon drug exposure. Even if these phenotypical assays enable multiple parameters analysis, they are often conducted during several days and need to be associated with image-based analysis to minimize subjectivity. We describe here a self-purifying microfluidic system enabling the selection of healthy adult worms and the identification of molecules acting instantly on the parasite. The worms are assayed in a dynamic environment that eliminates unhealthy worms that cannot attach firmly to the chip walls prior to being exposed to the drug. The detachment of the worms is also used as second step readout for identifying active compounds. We have validated this new fluidic screening approach using the two major antihelmintic drugs, praziquantel and artemisinin. The reported dynamic system is simple to produce and to parallelize. Importantly, it enables a quick and sensitive detection of antischistosomal compounds in no more than one hour.

[Current status and prospects of artificial intelligence in schistosomiasis prevention and control].

Li ZA, Jiao YP, Xu J.

10-11-2022

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36464266/>

Schistosomiasis is a parasitic disease that seriously endangers human health and affects socioeconomic developments. Artificial intelligence technology has been widely used in clinical medical sciences, including tumor screening, and electrocardiogram, imaging and pathological analyses, which has potential for precision control of schistosomiasis. Currently, artificial intelligence technology has been employed for clinical assessment of schistosomiasis-associated hepatic fibrosis and ectopic schistosomiasis, prognostic prediction of advanced schistosomiasis, automated identification of *Oncomelania hupensis* and *Schistosoma japonicum* eggs and miracidia, epidemiological surveillance of schistosomiasis, and drug discovery. This review summarizes the advances in the applications of artificial intelligence technology in the management of schistosomiasis and proposes the prospects for the use of artificial intelligence in schistosomiasis elimination.

[Trends in the prevalence of schistosomiasis in Anhui Province from 2004 to 2020 based on Joinpoint regression analysis].

Gao FH, Ding SJ, Zhang SQ, Wang TP, He JC, Xu XJ, Dai B, Liu T.

21-10-2022

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36464260/>

[Watershed ecology-based rethinking of *Oncomelania* snail control].

Chen S, Lü S.

31-08-2022

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.

<https://pubmed.ncbi.nlm.nih.gov/36464254/>

Oncomelania hupensis is the only intermediate host of *Schistosoma japonicum*, and control of *O. hupensis* is of great significance in schistosomiasis control. As an amphibious mollusk, *O. hupensis* is frequently distributed in the fluctuating zones of rivers and lakes, and its distribution is along the water system and watershed. Nevertheless, there is little knowledge on the impact of watershed factors on the landscape and dynamic changes of *O. hupensis* distribution. As a novel discipline, watershed ecology will help reveal the internal relationship of snail distribution, identify the vulnerable areas of snail distribution, and define the priority areas for snail control and protection based on the specific needs of schistosomiasis control and ecological protection of the Yangtze River. In addition, watershed ecology may be used to evaluate the impact of water resource development projects on snail control from the perspective of watershed hierarchy.

[Interleukin-9 promotes the activation of hepatic stellate cells in mice infected with *Schistosoma japonicum*].

Zhan TZ, Ma HH, Li Q, Tang LL, He SS, Tang ZL, Xia CM.
21-11-2022

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi.
<https://pubmed.ncbi.nlm.nih.gov/36464253/>

Juglone: "A novel immunomodulatory, antifibrotic, and schistosomicidal agent to ameliorate liver damage in murine schistosomiasis mansoni".

Khalil RG, Ibrahim AM, Bakery HH.
Dec-2022

Int Immunopharmacol.
<https://pubmed.ncbi.nlm.nih.gov/36461604/>

Schistosomiasis remains one of the world's leading health concerns, affecting millions. The granulomatous reaction is the most significant immunopathological change associated with *Schistosoma mansoni* infection, resulting in significant mortality. Recent progress has been made in the search for new natural compounds to reduce schistosomiasis and its immunopathology. Walnuts contain the phenolic compound Juglone (5-hydroxy-1,4-naphthoquinone), which has antiparasitic, anti-inflammatory, immunoregulatory, and antioxidant properties. There were three groups of infected mice: untreated (IU), Juglone-treated (JUG T), and praziquantel-treated (PZ). In mice treated at 8 mg Juglone /kg body weight, a reduction of 63.1 % and 52.1 % were observed in the number of male and female worms, respectively. In addition, the number of eggs/g tissue was reduced by 65.7 % in the liver, 58.58 % in the intestine, and 62.31 % in the liver and intestine combined. In addition, Juglone decreased hepatic granuloma size by 55.1 % and collagen fiber deposition by 23.4 % compared to PZQ (41.18 % and 11.2 %, respectively). Interestingly, the JUG T group had significantly lower levels of IL-4, IL-13, IL-37, TNF- α , TGF- β , and IFN- γ than PZ mice ($p < 0.05$). While IL-10 and IL-17 levels rose ($p < 0.01$), Juglone could restore hepatic ALT, AST, GGT, and LDH activities following infection. In addition, it increased catalase, SOD, GSH, and GST while decreasing NO and LPO in comparison to the infected group. Moreover, anti-SWAP, SEA, and CAP IgG levels increased significantly. IgE levels did not change significantly, however. Juglone could be used as an antifibrotic, immunomodulatory, and schistosomicidal agent; thus, it could be used in place of PZQ.

Assessment of schistosomiasis transmission in the River Nile at Greater Cairo using malacological surveys and cercariometry.

El-Khayat HMM, Mossalem HS, El-Homossany K, Sayed SSM, Mohammed WA, Zayed KM, Saied M, Habib MR.
Dec-2022

J Parasit Dis.
<https://pubmed.ncbi.nlm.nih.gov/36457778/>

Continuous field studies on the abundance and distribution of freshwater snails and cercarial populations

are important for schistosomiasis control programs. In the present work, snail surveys and cercariometry were conducted for four successive seasons at 12 sites on the Nile River banks in the area of Greater Cairo to identify potential transmission foci for schistosomiasis. In addition, water physicochemical parameters were recorded. The results showed that the electrical conductivity, total dissolved solids, dissolved oxygen, and pH were within the permissible levels, except that the water temperature increased, especially in the spring season. Malacological surveys identified 10 native snail species at the studied sites of the Nile River, namely *Bulinus truncatus*, *Biomphalaria alexandrina*, *Lymnaea natalensis*, *Lanistes carinatus*, *Cleopatra bulimoides*, *Melanoides tuberculata*, *Helisoma duryi*, *Bellamya unicolor*, *Physa acuta*, *Theodoxus niloticus*, and one invasive snail species, *Thiara scabra*. The calculated diversity index indicated that the structure of snails' habitats was poor, while Evenness index indicated that the individuals were not distributed equally. Natural infection results identified no schistosome cercariae in *B. truncatus* and *B. alexandrina*. However, the cercariometry recovered *Schistosoma* cercariae in all the surveyed sites during all seasons with variable distribution. The preceding data suggest that there are still some active transmission foci for schistosomiasis infection in the Nile River. Moreover, the present finding highlights the importance of cercariometry as a complementary approach to snail samplings for identifying the transmission foci for schistosomiasis.

Praziquantel: An update on the mechanism of its action against schistosomiasis and new therapeutic perspectives.

Nogueira RA, Lira MGS, Licá ICL, Frazão GCCG, Dos Santos VAF, Filho ACCM, Rodrigues JGM, Miranda GS, Carvalho RC, Nascimento FRF.
Nov-2022

Mol Biochem Parasitol.
<https://pubmed.ncbi.nlm.nih.gov/36375598/>

Praziquantel (PZQ) is the drug of choice for the treatment of all forms of schistosomiasis, although its mechanisms of action are not completely understood. PZQ acts largely on adult worms. This narrative literature review describes what is known about the mechanisms of action of PZQ against schistosomes from in vitro and in vivo studies and highlights the molecular targets in parasites and immune responses induced in definitive hosts by this drug. Moreover, new therapeutic uses of PZQ are discussed. Studies have demonstrated that in addition to impacting voltage-operated Ca²⁺ channels, PZQ may interact with other schistosome molecules, such as myosin regulatory light chain, glutathione S-transferase, and transient receptor potential channels. Following PZQ administration, increased T regulatory type 1 (Tr1) cell differentiation and decreased inflammation were observed, indicating that PZQ promotes immunoregulatory pathways. Although PZQ is widely used in mass drug administration schemes, the existence of resistant parasites has not been proven; however, it is a concern that should be constantly investigated in human populations. In addition, we discuss studies that evaluate

health applications of PZQ (other than helminth infection), such as its effect in cancer therapy and its adjuvant action in vaccines against viruses.

Evaluation of faecal lactoferrin as a morbidity biomarker in Schistosoma mansoni infection.

Elhadad H, Mohamed MA, Mohamed MM, Abdo S.
Dec-2022

Trop Med Int Health.

<https://pubmed.ncbi.nlm.nih.gov/36264644/>

Biophysical description of Bromosulphophthalein interaction with the 28-kDa glutathione transferase from Schistosoma japonicum.

Pooe K, Thulo M, Makumbe H, Akumadu B, Otun O, Alope C, Achilonu I.

Nov-2022

Mol Biochem Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36195242/>

Glutathione transferases (GSTs) are major detoxification enzymes vital for the survival and reproduction of schistosomes during infection in humans. *Schistosoma* encode two GST isoenzymes, the 26- and 28-kDa isoforms, that show different substrate specificities and cellular localisations. Bromosulphophthalein (BSP) has been identified and characterised as a potent 26-kDa *Schistosoma japonicum* GST (Sj26GST) inhibitor with an anthelmintic potential. This study describes the structure, function, and ligand properties of the 28-kDa *Schistosoma japonicum* GST (Sj28GST) towards BSP. Enzyme kinetics show that BSP is a potent enzyme inhibitor, with a specific activity decreases from 60.4 $\mu\text{mol}/\text{min}/\text{mg}$ to 0.0742 $\mu\text{mol}/\text{min}/\text{mg}$ and an IC_{50} in the micromolar range of 0.74 μM . Far-UV circular dichroism confirmed that purified Sj28GST follows a typical GST fold, which is predominantly alpha-helical. Fluorescence spectroscopy suggests that BSP binding occurs at a site distinct from the glutathione-binding site (G-site); however, the binding does not alter the local G-site environment. Isothermal titration calorimetry studies show that the binding of BSP to Sj28GST is exergonic ($\Delta G^\circ = -33 \text{ kJ}/\text{mol}$) and enthalpically-driven, with a stoichiometry of one BSP per dimer. The stability of Sj28GST ($\Delta G_{(\text{H}_2\text{O})} = 4.7 \text{ kcal}/\text{mol}$) is notably lower than Sj26GST, owing to differences in the enzyme's dimeric interfaces. We conclude that Sj28GST shares similar biophysical characteristics with Sj26GST based on its kinetic properties and susceptibility to low concentrations of BSP. The study supports the potential benefits of re-purposing BSP as a potential drug or prodrug to mitigate the scourge of schistosomiasis.

MicroRNA-181b promotes schistosomiasis-induced hepatic fibrosis by targeting Smad7.

Wang S, Zhang J, Chen H, Zhan X, Nie H, Wang C, Zhang Y, Zheng B, Gong Q.

Nov-2022

Mol Biochem Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36195241/>

Schistosomiasis is a common parasitic disease. Hepatosplenic schistosomiasis, caused by *Schistosoma japonicum* and *Schistosoma mansoni*, involves pathological changes, including worm egg-induced hepatic granuloma and fibrosis, which can markedly affect the liver's physiological functions. Although the drug praziquantel (PZQ) is used to treat schistosomiasis, drugs against schistosomiasis-induced liver fibrosis are rare in the clinical setting. Therefore, developing effective strategies to prevent and treat schistosomiasis-induced liver fibrosis is crucial. Previous studies have shown that miRNAs are involved in various liver diseases. In this study, we found a gradual increase in miR-181b expression in the murine liver as *S. japonicum* infection progressed, while the expression of Smad7 decreased. Down-regulating miR-181b significantly alleviated *S. japonicum*-induced hepatic granuloma and liver fibrosis. In vitro experiments showed that treatment with TGF- β 1 upregulated miR-181b levels in the hepatic stellate cell (HSC) line LX2 in a concentration- and time-dependent manner. Downregulation of miR-181b significantly decreased collagen type I alpha 1 chain (COL1A1) expression in TGF- β 1-stimulated LX2 cells. These findings indicate that miR-181b promotes HSC activation by down-regulating Smad7 expression, activating the TGF- β 1/Smad signaling pathway, and leading to excess collagen expression and deposition. Our findings suggest that miR-181b might be a potentially novel therapeutic target for schistosomiasis-induced liver fibrosis.

Synthesis, in vitro schistosomicidal activity and ultrastructural alterations caused by thiosemicarbazones and thiazolidinones against juvenile and adult Schistosoma mansoni worms (Sambon, 1907).

Tavares da Rocha RE, de Almeida Júnior ASA, Júnior NCP, do Nascimento AV, Leite NMS, de Oliveira JF, Alves de Lima MDC, Feitosa APS, Bezerra de Mélo ME, Brayner FA, Alves LC.

Nov-2022

Mol Biochem Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36122704/>

Schistosomiasis is a neglected disease that affects about 258 million people worldwide. Caused by *Schistosoma mansoni*, helminth which, in Brazil, it is present on 19 states and capital. Praziquantel (PZQ) treatment presents low efficacy and adverse effects in parasites juvenile stages. Thiosemicarbazones and thiazolidinones are rising as potent chemical groups that have biological activity wide spectrum, and with radical modifications, they may become more effective and selective. Aiming to evaluate the action of these molecules against *S. mansoni*, JF series thiosemicarbazones and thiazolidinones (LqIT/UFPE) were synthesized: JF30, JF31, JF33, JF34, JF35, JF36, JF38, JF39, JF42 and JF43. Several parameters were evaluated, such as: their cytotoxicity in VERO cells, in vitro schistosomicidal activity for juvenile and adult worms and their action on worms through ultrastructural changes. Cytotoxicity indices ranged from 272 μM to 725 μM . When evaluating mortality rate, adult and juvenile worms showed 100 %

mortality rate within 24 h and 48 h, respectively, when exposed to the compounds JF31 and JF43 at a dose of 200 µM. Also, motility, mortality and oviposition parameters were evaluated: JF31 and JF43 presented a score of 0 in 24 h, meaning total absence of movement, whereas no eggs and soft tissue damage were observed under optical microscopy. Through scanning electron microscopy, integumentary alterations caused by the compounds JF31 and JF43 were observed, such as: exposure of the musculature, formation of integumentary bubbles, integuments with abnormal morphology and destruction of tubercles and spikes. The results showed that the compound JF31 was 2.39 times more selective for adult worms and JF43 was 3.74 times more selective for juvenile worms. Thus, the compounds JF43 and JF31 are the most promising for presenting schistosomicidal activity of *S. mansoni*.

Mammary schistosomiasis: A rare case.

Chen S, Falkner NM, Hardie MJ, Wylie E.

Dec-2022

J Med Imaging Radiat Oncol.

<https://pubmed.ncbi.nlm.nih.gov/35916441/>

Schistosomiasis is prevalent in some developing countries; however, it does not commonly affect the breast. Mammary schistosomiasis may present as suspicious microcalcification or a mass on mammography. Image-guided biopsy is necessary to exclude malignancy and identify calcified *Schistosoma* ova on histology. We report a case of a patient born in the Philippines who was diagnosed with mammary schistosomiasis from incidental microcalcifications seen on mammography.

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

Xu X, Wang Y, Wang C, Guo G, Yu X, Dai Y, Liu Y, Wei G, He X, Jin G, Zhang Z, Guan Q, Pain A, Wang S, Zhang W, Young ND, Gasser RB, McManus DP, Cao J, Zhou Q, Zhang Q.

Jan-2023

Mol Ecol Resour.

<https://pubmed.ncbi.nlm.nih.gov/35844053/>

Sarcopenia, body composition and factors associated with variceal gastrointestinal bleeding and splenectomy in hepatosplenic schistosomiasis mansoni.

Barbosa FA, Nardelli MJ, Caçado GGL, Silva CF, Osório FMF, Melo RFQ, Taranto DOL, Ferrari TCA, Couto CA, Faria LC.

02-12-2022

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/35748511/>

The observed relationship between the degree of parasite aggregation and the

prevalence of infection within human host populations for soil-transmitted helminth and schistosome infections.

Kura K, Truscott JE, Collyer BS, Phillips A, Garba A, Anderson RM.

02-12-2022

Trans R Soc Trop Med Hyg.

<https://pubmed.ncbi.nlm.nih.gov/35474017/>

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

Parasitism of terrestrial gastropods by medically-important nematodes in Brazil.

Thiengo SC, Ramos-de-Souza J, Silva GM, Fernandez MA, Silva EF, Sousa AKP, Rodrigues PS, Mattos AC, Costa RAF, Gomes SR.

17-11-2022

Front Vet Sci.

<https://pubmed.ncbi.nlm.nih.gov/36467665/>

An ample variety of parasitic associations are found between mollusks and nematodes, in which the mollusks may act as intermediate, paratenic or definitive hosts. Some free-living nematodes, in particular those of the order Rhabditida, are also found frequently in terrestrial mollusks. The present study reviews the results of the parasitological testing on samples of terrestrial mollusks conducted at the Brazilian National Reference Laboratory for Schistosomiasis and Malacology between 2008 and 2021. The samples were supplied primarily by the public health authorities from the different regions of Brazil, but also by research institutions and general population. The mollusks were processed individually and the obtained larvae were identified from their morphology and, whenever necessary, by molecular analysis. A total of 1,919 service orders were registered during the period, including 19,758 mollusk specimens collected from 23 of the 26 Brazilian states, as well as the Federal District, totaling 145 municipalities. There was a marked predominance of the synanthropic species that are widely distributed in Brazil: *Achatina fulica* (87.08%), *Bulimulus tenuissimus* (4.18%), *Bradybaena similaris* (2.06%), and *Sarasinula linguaeformis* (1.50%). Of the 16,750 terrestrial mollusks examined, nematodes were recorded in 1,308 service orders, with the predominance of the superfamily Metastrongyloidea, in 616 service orders. They included *Angiostrongylus cantonensis*, rat lungworm, which was found in 252 samples, and *Aelurostrongylus abstrusus* in 145 samples. Free-living nematodes were found in 952 samples, *Ancylostoma caninum* and *Cruzia tentaculata* (previously identified as *Strongyluris* sp.) in one and 275 samples, respectively, and other parasites in 210 samples (not identified). The results highlight the diversity of the associations between nematodes and terrestrial mollusks in Brazil, in particular invasive and synanthropic species, with emphasis on the giant African land snail, *Achatina*

fulica. They demonstrate the prominent role of this species of mollusk in the transmission of medically-important nematodes, which affect the health of both humans and animals, in particular eosinophilic meningitis, which is caused by *Angiostrongylus cantonensis*. This reinforces the need for more studies, and justify the growing demand for information as well as parasitological diagnosis of this mollusk, given its wide distribution in Brazil and its impact as an urban pest.

Prevalence and Associated Risk Factors of Intestinal Parasitic Infections among Patients Visiting a Referral Hospital in Tehran Province, Iran.

Zarei A, Mohebbali M, Agholi M, Jonaidi Jafari N, Mohammadzadeh T.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466024/>

The survey of soil-transmitted helminth species abundance in Slovakia with an emphasis on parameters important for their distribution.

Ihnacik L, Šmigová J, Šoltys J, Bobíková D, Kuzevičová Ž, Kuzevič Š, Schusterová I, Papajová I.

01-11-2022

Front Med (Lausanne).

<https://pubmed.ncbi.nlm.nih.gov/36465912/>

Soil-transmitted helminths (STH) can be easily dispensable in socially disadvantaged groups. The Roma people represent the group most at risk in Slovakia. This study aimed to investigate the occurrence of STH infections in minorities living with animals under low hygienic conditions and on contaminated soil. Subsequently, we identified the risk assessment factors of the STH transmissions based on parasitological results. In our study, STHs were predominantly found among the Roma communities living in unsanitary conditions. The prevalence of *Ascaris lumbricoides* among the majority was 0.79%, and *Trichuris trichiura* was 0.05 %. On the contrary, a community-based cross-sectional survey across eastern Slovakia also found a prevalence of 22.28 and 3.47% for *A. lumbricoides* and *T. trichiura* among the Roma population. Inhabitants that belong to the Roma minority had a 37.12 infection OR times higher than non-Roma inhabitants. The Roma people living in the countryside have a 2.23-fold higher chance of getting infected with STH than Roma living in the city. Therefore, soil and domestic animals were also examined for the presence of the STH eggs to show the environmental burden. In general, the presence of STH eggs was confirmed in 26.26% of the soil examined samples. The detailed description is as follows: eggs of *Toxocara* spp., *Trichuris* spp., eggs from the family *Ancylostomatidae*, and *Toxascaris leonina*. *Ascaris* eggs were detected only in the soil from localities with low hygienic standards. The probability of contracting the STH eggs in segregated settlements was 15.94 times higher compared to urban or rural areas. In addition to humans, dogs can also be a source of STH eggs in the soil. The STH eggs were

confirmed in 43.55% of dog droppings. The most interesting finding was that the eggs of the genus *Ascaris* were up to 7.93% of dog droppings from localities with a low hygienic standard were positive. This study revealed that climatic factors and the WASH conditions influenced the distribution of STHs to variable degrees. In addition, ethnicity and sanitation were crucial factors in the distribution of STH infection in eastern Slovakia.

[Spatio-temporal distribution characteristics of soil-transmitted nematodiasis in Sichuan Province from 2016 to 2021].

Wu XH, Tian HC, Luo JW, Tie L, Zhang LP, Deng X, Liu Y. 14-11-2022

Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi

<https://pubmed.ncbi.nlm.nih.gov/36464262/>

Gale

The leucine-responsive regulatory protein SCAB_Lrp modulates thaxtomin biosynthesis, pathogenicity, and morphological development in *Streptomyces scabies*.

Liu J, Wang Y, He H, Dong S, Tang L, Yang E, Wang W, Zhang B.

07-12-2022

Mol Plant Pathol.

<https://pubmed.ncbi.nlm.nih.gov/36478143/>

Streptomyces scabies is the best-characterized plant-pathogenic streptomycete, which is a special species among the large genus *Streptomyces*. The pathogenicity of *S. scabies* relies on the production of the secondary metabolite thaxtomin A. Little is known about the molecular mechanisms underlying the regulation of thaxtomin biosynthesis in *S. scabies* beyond the pathway-specific activator TtxR and the cellulose utilization repressor CebR. The leucine-responsive regulatory protein (Lrp) family modulates secondary metabolism in nonpathogenic streptomycetes. However, the regulatory relationship between the Lrp and pathogenic streptomycetes remains unknown. In this study, we demonstrated that SCAB_Lrp (SCAB_77931) from *S. scabies* significantly affects thaxtomin biosynthesis, pathogenicity, and morphological development. SCAB_Lrp deletion resulted in a dramatic decline in thaxtomin A production and a low-virulence phenotype of *S. scabies*. An in-depth dissection of the regulatory mechanism of SCAB_Lrp revealed that it positively regulates the transcription of the thaxtomin biosynthetic gene cluster by directly binding to the promoter of the cluster-situated regulator gene ttxR. SCAB_Lrp also controls the morphological development of *S. scabies* by directly activating the transcription of *amfC*, *whiB*, and *ssgB*. SCAB_Lrp directly controls the transcription of its own gene by binding a specific sequence (5'-GGACAGTCGCCGTGCTACG-3'). Moreover, phenylalanine and methionine have been characterized as SCAB_Lrp effectors by strengthening the binding affinity and

complex status between SCAB_Lrp and DNA. Our findings characterize a multifunctional regulatory protein, SCAB_Lrp, that controls secondary metabolism, pathogenicity, and sporulation in *S. scabiei* and provide new insights into the complex regulatory network that modulates thaxtomin phytotoxins in pathogenic *Streptomyces*.

Proteomic analysis of *Sarcoptes scabiei* reveals that proteins differentially expressed between eggs and female adult stages are involved predominantly in genetic information processing, metabolism and/or host-parasite interactions.

Wang T, Gasser RB, Korhonen PK, Young ND, Ang CS, Williamson NA, Ma G, Samarawickrama GR, Fernando DD, Fischer K.

06-12-2022

PLoS Negl Trop Dis.

<https://pubmed.ncbi.nlm.nih.gov/36472966/>

Presently, there is a dearth of proteomic data for parasitic mites and their relationship with the host animals. Here, using a high throughput LC-MS/MS-based approach, we undertook the first comprehensive, large-scale proteomic investigation of egg and adult female stages of the scabies mite, *Sarcoptes scabiei*-one of the most important parasitic mites of humans and other animals worldwide. In total, 1,761 *S. scabiei* proteins were identified and quantified with high confidence. Bioinformatic analyses revealed differentially expressed proteins to be involved predominantly in biological pathways or processes including genetic information processing, energy (oxidative phosphorylation), nucleotide, amino acid, carbohydrate and/or lipid metabolism, and some adaptive processes. Selected, constitutively and highly expressed proteins, such as peptidases, scabies mite inactivated protease paralogues (SMIPPs) and muscle proteins (myosin and troponin), are proposed to be involved in key biological processes within *S. scabiei*, host-parasite interactions and/or the pathogenesis of scabies. These proteomic data will enable future molecular, biochemical and physiological investigations of early developmental stages of *S. scabiei* and the discovery of novel interventions, targeting the egg stage, given its non-susceptibility to acaricides currently approved for the treatment of scabies in humans.

Dermatoparasitoses in Referral Patients to the Laboratory.

Navi Z, Najafi F, Paknezhad N, Mousavian G, Bizhani N, Naddaf SR, Mowlavi G.

Jul-Sep 2022

Iran J Parasitol.

<https://pubmed.ncbi.nlm.nih.gov/36466019/>

[[Translated article]] Diagnosis and Clinical Characteristics of Scabies in a Tertiary Care Hospital During the SARS-CoV-2 Pandemic: A Descriptive Study.

Aguado Vázquez Á, Gegúndez Hernández H, Melgosa Ramos FJ, Díaz Corpas T.

01-12-2022

Actas Dermosifiliogr.

<https://pubmed.ncbi.nlm.nih.gov/36464010/>

Epidemic Scabies: New Treatment Challenges in an Ancient Disease.

Lluch Galcerá JJ, Carrascosa Carrillo JM, Boada García A.

30-11-2022

Actas Dermosifiliogr.

<https://pubmed.ncbi.nlm.nih.gov/36462668/>

Scabies, which is among the most prevalent diseases worldwide, is becoming more frequent in Spain. The problems of this epidemic can be explained by several factors: improper application or prescription of treatments, resistance or reduced sensitivity to topical treatments, and poor understanding of the parasite and contagion. We require a new evidence-based approach to therapy that takes these problems into consideration. If symptoms persist after proper treatment, it is important to identify the reason for failure and standardize our approach. In refractory cases, the prescriber should prioritize oral medication, indicate a higher dose, combine treatments, or evaluate the use of off-label treatments in certain populations. The availability of new medications - such as spinosad or, especially, moxidectin - offer hope for bringing this disease under control.

Immunomodulatory effects of two recombinant arginine kinases in *Sarcoptes Scabiei* on host peripheral blood mononuclear cells.

Xu Y, Xu Z, Gu X, Xie Y, He R, Xu J, Jing B, Peng X, Yang G.

14-11-2022

Front Immunol.

<https://pubmed.ncbi.nlm.nih.gov/36451837/>

Morsures de serpent

Fatal infective necrotising fasciitis: Complication following *Naja nigricincta nigricincta* bite (western barred spitting cobra/zebra snake).

Saaiman EL, Buys PC.

01-12-2022

S Afr Med J.

<https://pubmed.ncbi.nlm.nih.gov/36472321/>

Wound infections following cytotoxic snakebites are common. Bites from *Naja nigricincta nigricincta* (an African spitting cobra) usually present as severe dermonecrosis spreading within the subdermal fascia layer. Primary infections can follow inoculation of the snake's oral flora during the bite, worsening the dermonecrosis into infective necrotising fasciitis. We report the case of a 2½-year-old boy who presented with infective (*Proteus vulgaris*) necrotising fasciitis after an *N. n. nigricincta* bite, resulting in multiple-organ failure and death. A *P. vulgaris*

with the same antibiotic profile was cultured from the mouth of the snake.

Ethnobotany, botany, phytochemistry and ethnopharmacology of the genus *Thalictrum* L. (Ranunculaceae): A review.

Singh H, Singh D, Lekhak MM.

02-12-2022

J Ethnopharmacol.

<https://pubmed.ncbi.nlm.nih.gov/36470306/>

Epidemiology and Characteristics of North American Crotalid Bites Reported to the National Poison Data System 2006-2020.

Thornton S, Darracq M.

Dec-2022

South Med J.

<https://pubmed.ncbi.nlm.nih.gov/36455899/>

Studies on antioxidant, anti-diabetic and GC-MS analyses of methanol extract of *Aristolochia bracteolata* root bark.

Agada R, Lydia DE, Khusro A, Abdulaziz O, Khayam Sahibzada MU, Baseer A, Farid Hassan SM.

Sep-2022

Pak J Pharm Sci.

<https://pubmed.ncbi.nlm.nih.gov/36451555/>

Aristolochia bracteolata is utilized in confronting multiple and complicated disease conditions such as cancer, lung inflammation, dysentery, syphilis, gonorrhoea, arthritis, skin diseases, snake bite and oxidative stress relating to humans due to their acceptability, affordability and proximity. This investigation seeks to determine the antioxidant and anti-diabetic effects of methanol extract of *A. bracteolata* root bark in vitro. The phytochemical screening, antioxidant, and enzymes inhibitory (alpha-amylase and alpha-glucosidase) properties of root bark extract were evaluated by standard procedures. The methanol extract indicated the presence of diverse phytochemicals (tannins, saponins, flavonoids, alkaloids, phenols, glycosides and terpenoids) and contained a remarkable amount of saponins (8.20±0.03%), phenols (6.82±0.01%), alkaloids (4.71±0.03%) and flavonoids (3.50±0.12%). The extract showed not only strong antioxidant properties against DPPH, FRAP and TBARS radicals with IC50 value of 57.87, 54.64 and 47.54 mg/ml, respectively but also anti-diabetic activity by inhibiting alpha-amylase (IC50=53.70 mg/ml) and alpha-glucosidase (IC50=49.18 mg/ml). GC-MS chromatogram identified a diverse array of active metabolites in the methanol extract of *A. bracteolata* root bark. This study suggested that the methanol extract of *A. bracteolata* root bark possessed anti-oxidative and anti-diabetic activities.

Therapeutic Plasma Exchange for Venom-Induced Thrombotic Microangiopathy Following Hump-

Nosed Pit Viper (Genus: *Hypnale*) Bites: A Prospective Observational Study.

Rathnayaka RMMKN, Nishanthi Ranathunga PEA, Kularatne SAM, Sugathadasa K.

Dec-2022

Wilderness Environ Med.

<https://pubmed.ncbi.nlm.nih.gov/36244888/>

Hump-Nosed Pit Viper Envenomation in Western Coastal India: A Case Series.

Sirur FM, Balakrishnan JM, Lath V.

Dec-2022

Wilderness Environ Med.

<https://pubmed.ncbi.nlm.nih.gov/36229382/>

The hump-nosed pit viper (HNPV) has historically been considered less medically significant, causing local envenomation, renal injury, and coagulopathy; however, now, it is known to cause life-threatening complications. We describe the clinical presentation, treatment, and complications of 3 confirmed HNPV bites from the state of Karnataka (southwest coastal India). Patient 1, an 88-y-old woman, reported with the live specimen and developed venom-induced consumption coagulopathy (VICC) and thrombotic microangiopathy leading to acute kidney injury requiring blood product transfusions and dialysis. Patient 2, a 60-y-old woman, reported 3 d after envenomation followed by treatment at another hospital where 30 vials of polyvalent anti-snake venom (ASV) were given. She developed VICC and acute kidney injury requiring dialysis. On Day 9 of treatment, she developed a pontine hemorrhage. She died after a transfer to another treatment center closer to her residence. Patient 3, a 25-y-old man, was brought to our emergency department 6 h after being envenomed. He received topical ayurvedic treatment before arrival. He was unconscious and found to have severe VICC with a massive middle cerebral artery infarct. All 3 patients received Indian polyvalent ASV, which does not cover HNPV envenomation, clearly demonstrating the absence of paraspecificity and neutralization in a clinical setting. To our knowledge, *Hypnale hypnale* envenomation has not previously been reported from Karnataka state. The diagnosis of HNPV envenomation in a country without snake venom detection kits, under-reporting despite serious complications, financial burdens on rural populations afflicted, and poor outcomes due to the lack of a specific antivenom are discussed.

Diagnostic Tests for Hypofibrinogenemia Resulting from Green Pit Viper (*Trimeresurus albolabris*) Envenomation: A Simulated In Vitro Study.

Tiyawat G, Lohajaroensub S, Othong R.

Dec-2022

Wilderness Environ Med.

<https://pubmed.ncbi.nlm.nih.gov/36216671/>

Introduction: The green pit viper (GPV) *Trimeresurus albolabris* is found in Southeast Asia. Its venom has a thrombin-like activity that can cause hypofibrinogenemia.

Fibrinogen measurement is not always available. We aimed to establish a more available diagnostic tool indicating hypofibrinogenemia caused by GPV envenomation. **Methods:** This was an in vitro study, in which healthy subjects aged 20 to 45 y were enrolled. There were 2 experiments. In Experiment 1, blood samples from 1 subject had varying amounts of T albolabris venom added to determine its effect on the fibrinogen level (FL). In Experiment 2, 3 sets of blood samples were obtained from another 25 subjects. The 2 venom doses established in Experiment 1 were used on 2 sets of the samples to simulate severe (FL $<1.0 \text{ g}\cdot\text{L}^{-1}$) and mild hypofibrinogenemia (FL $1.0\text{-}1.7 \text{ g}\cdot\text{L}^{-1}$). The third set of samples was venom-free. All samples were used for platelet counts, prothrombin time (PT)/international normalized ratio (INR)/activated partial thromboplastin time (aPTT), and 2 bedside clotting tests. Diagnostic parameters were calculated against the target FL of $<1.0 \text{ g}\cdot\text{L}^{-1}$ and $<1.7 \text{ g}\cdot\text{L}^{-1}$. **Results:** Twenty-five subjects were enrolled in Experiment 2. On referencing normal cutoff values (platelet count $>150,000 \text{ cells}/\text{mm}^3$, venous clotting time $<15 \text{ min}$, normal 20-min whole blood clotting time, INR <1.2 , aPTT <30), we found abnormalities of 5, 0, 0, 3, and 22%, respectively. The highest correlation with hypofibrinogenemia was provided by PT/INR. For an FL of $<1.0 \text{ g}\cdot\text{L}^{-1}$, PT and INR revealed the highest areas under the receiver operating characteristic curve, 0.76 (95% CI, 0.55-0.97) and 0.76 (95% CI, 0.57-0.97), respectively. The highest accuracy and the highest sensitivity were provided by PT/INR. **Conclusions:** PT/INR could be used as a diagnostic test for severe hypofibrinogenemia in GPV envenomation because of its high accuracy and area under the receiver operating characteristic curve