Réseau MTN Francophone

Veille scientifique
Maladies tropicales négligées

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Cysticercose

"Till death do us apart": The common destiny of brown hare and its parasite community.

Stancampiano L, Guarniero I, Militerno G.
18-08-2023
Int J Parasitol Parasites Wildl.
https://pubmed.ncbi.nlm.nih.gov/37654697/

Knowledge, attitudes and practices regarding porcine cysticercosis control among smallholder pig farmers in Kongwa and Songwe districts, Tanzania: A cross-sectional study.

Wilson C, Nonga HE, Mdegela RH, Churi AJ, Mkupasi EM, Winkler AS, Ngowi HA.
Sept-2023
Vet Parasitol Reg Stud Reports.
https://pubmed.ncbi.nlm.nih.gov/37652629/

Taenia solium taeniasis/cysticercosis (TSTC) is a parasitic zoonotic disease that is endemic in several developing countries, causing serious public health and economic impacts. A cross-sectional study was conducted to assess knowledge, attitudes and practices (KAP) related to porcine cysticercosis (PCC) transmission, prevention and control among smallholder pig farmers in Kongwa and Songwe Districts in Tanzania. A semi-structured questionnaire was administered to 692 smallholder pig farmers from randomly selected households. STATA software version 17 was used to analyse quantitative data, summarize farmers' KAP about PCC and calculate performance scores. Nearly half (42%) of the respondents had little knowledge regarding PCC, only 17% of the respondents had good practices towards prevention/control of PCC and 72% had a positive attitude towards PCC- prevention/control measures. The majority (73%) of smallholder pig farmers admitted deworming their pigs regularly, whereas 76% reported deworming themselves and their family members regularly. Albendazole and ivermectin are the most commonly used medications for deworming people and pigs, respectively. According to the findings, the majority of smallholder pig farmers in Kongwa and Songwe Districts showed a good attitude towards PCC prevention/control measures but had limited knowledge of the PCC life cycle and control. In addition, only one in five farmers was engaged in good practices. The findings revealed further that farmers are engaged in risky behaviours that aid the spread and perpetuation of the T. solium parasite in the study area. It is recommended that farmers should be given proper health education on the T. solium transmission cycle and preventive/control practices to limit PCC transmission.

Preformulation and Long-Term Stability Studies of an Optimized Palatable Praziquantel Ethanol-Free Solution for Pediatric Delivery.

Bedogni G, Garcia P, Seremeta K, Okulik N, Salomon C.
30-07-2023
Pharmaceutics.
https://pubmed.ncbi.nlm.nih.gov/37631264/

To date, the treatment for cysticercosis and neurocysticercosis consists of a single oral intake of praziquantel (5-10 mg/kg), which since it is only available as tablets, hinders its administration to pediatric patients. Praziquantel is a poorly water-soluble drug which represents a challenge for its formulation in solution, particularly for the pediatric population. Thus, this study aimed to develop a palatable solution for praziquantel using pharmaceutical-accepted co-solvent systems. A design of experiments approach was applied to identify the optimal conditions for achieving a suitable amount of praziquantel in solution using co-solvent mixtures. Thus, praziquantel solubility increased from 0.38 up to 43.50 mg/mL in the optimized system. A taste masking assay in healthy human volunteers confirmed a successful reduction of drug bitterness after the addition of selected flavors and a sweetener. Stability studies were also conducted at different temperatures (4, 25, and 40 °C) for 12 months Even though the presence of the three known impurities of praziquantel was observed, their amounts never exceeded the acceptance criteria of the USP. Thus, this novel approach should be considered a valuable alternative for further preclinical studies considering the high prevalence of this infection worldwide.

Dengue, chikungunya et maladie à virus Zika

Preclinical proof of concept of a tetravalent lentiviral T-cell vaccine against dengue viruses.

Nemirov K, Authié P, Souque P, Moncoq F, Noirat A, Blanc C, Bourgine M, Majlessi L, Charneau P.
15-08-2023
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/37654495/

Dengue virus (DENV) is responsible for approximately 100 million cases of dengue fever annually, including severe forms such as hemorrhagic dengue and dengue shock syndrome. Despite intensive vaccine research and development spanning several decades, a universally accepted and approved vaccine against dengue fever has not yet been developed. The major challenge associated with the development of such a vaccine is that it should induce simultaneous and equal protection against the four DENV serotypes, because past infection with one serotype may greatly increase the severity of secondary infection with a distinct serotype, a phenomenon known as antibody-dependent enhancement (ADE). Using a lentiviral vector platform that is particularly suitable for the induction of cellular immune responses, we designed a tetravalent T-cell vaccine candidate against DENV ("LV-DEN"). This vaccine candidate has a strong CD8^{+} T-cell immunogenicity against the targeted non-structural DENV proteins, without inducing antibody response against surface antigens. Evaluation of its protective potential in the preclinical flavivirus infection model, i.e., mice knockout for the receptor to the type I IFN, demonstrated

its significant protective effect against four distinct DENV serotypes, based on reduced weight loss, viremia, and viral loads in peripheral organs of the challenged mice. These results provide proof of concept for the use of lentiviral vectors for the development of efficient polyvalent T-cell vaccine candidates against all DENV serotypes.

Wolbachia wMel strain-mediated effects on dengue virus vertical transmission from Aedes aegypti to their offspring.

Duong Thi Hue K, da Silva Goncalves D, Tran Thuy V, Thi Vo L, Le Thi D, Vu Tuyet N, Nguyen Thi G, Huynh Thi Xuan T, Nguyen Minh N, Nguyen Thanh P, Yacoub S, Simmons CP.
31-08-2023
Parasit Vectors.
https://pubmed.ncbi.nlm.nih.gov/37653429/

Association of inhibitory NKG2A and activating NKG2D natural killer cell receptor genes with resistance to SARS-CoV-2 infection in a western Indian population.

Tripathy AS, Wagh P, Akolkar K, Walimbe AM, Potdar VA, Choudhary ML, Kadgi N, Nakate L, Abraham P.
31-08-2023
Arch Virol.
https://pubmed.ncbi.nlm.nih.gov/37653112/

Does ignoring transmission dynamics lead to underestimation of the impact of interventions against mosquito-borne disease?

Cavany S, Huber JH, Wieler A, Tran QM, Alkuzweny M, Elliott M, España G, Moore SM, Perkins TA.
Août-2023
BMJ Glob Health.
https://pubmed.ncbi.nlm.nih.gov/37652566/

New vector-control technologies to fight mosquito-borne diseases are urgently needed, the adoption of which depends on efficacy estimates from large-scale cluster-randomised trials (CRTs). The release of *Wolbachia*-infected mosquitoes is one promising strategy to curb dengue virus (DENV) transmission, and a recent CRT reported impressive reductions in dengue incidence following the release of these mosquitoes. Such trials can be affected by multiple sources of bias, however. We used mathematical models of DENV transmission during a CRT of *Wolbachia*-infected mosquitoes to explore three such biases: human movement, mosquito movement and coupled transmission dynamics between trial arms. We show that failure to account for each of these biases would lead to underestimated efficacy, and that the majority of this underestimation is due to a heretofore unrecognised bias caused by transmission coupling. Taken together, our findings suggest that *Wolbachia*-infected mosquitoes could be even more promising than the recent CRT suggested. By emphasising the importance of accounting for transmission coupling between arms, which requires a mathematical model, we highlight the key role that

models can play in interpreting and extrapolating the results from trials of vector control interventions.

Molecular characterization and geographical distribution of Zika virus worldwide from 1947 to 2022.

Noisumdaeng P, Dangsagul W, Sangsiriwut K, Prasertsopon J, Changsom D, Yoksan S, Ajawatanawong P, Buathong R, Puthavathana P.
29-08-2023
Int J Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37652092/

Objectives: We conducted molecular characterization, demonstrated the geographical distribution of Zika virus (ZIKV) circulating worldwide from 1947 to 2022 and explored the potential genetic recombination site in the Thailand ZIKV genomes. **Methods:** We constructed phylogenetic trees based on ZIKV coding sequences (CDS) and determined the geographical distribution of the representative viruses by genetic relationship and timeline. We determined genetic recombination among ZIKV and between ZIKV and other flaviviruses using similarity plot and bootscan analyzes, together with the phylogeny encompassing the CDS and eight subgenomic regions. **Results:** The phylogenetic trees comprising 717 CDS showed two distinct African and Asian lineages. ZIKV in the African lineage formed two sublineages, and ZIKV in the Asian lineage diversified into the Asian and American sublineages. The 1966 Malaysian isolate was designated the prototype of the Asian sublineage and formed a node of only one member, while the newer viruses formed a distinct node. We detected no genetic recombination in the Thailand ZIKV. **Conclusions:** Five Thailand isolates discovered in 2006 were the second oldest ZIKV after the Malaysian prototype. Our result suggested two independent routes of ZIKV spread from Southeast Asia to Micronesia in 2007 and French Polynesia in 2013 before further spreading to South American countries.

Secondary vectors of Zika Virus, a systematic review of laboratory vector competence studies.

Bisia M, Montenegro-Quinoñez CA, Dambach P, Deckert A, Horstick O, Kolimenakis A, Louis VR, Manrique-Saide P, Michaelakis A, Runge-Ranzinger S, Morrison AC.
31-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37651473/

Background: After the unprecedented Zika virus (ZIKV) outbreak in the western hemisphere from 2015-2018, Aedes aegypti and Ae. albopictus are now well established primary and secondary ZIKV vectors, respectively. Consensus about identification and importance of other secondary ZIKV vectors remain. This systematic review aims to provide a list of vector species capable of transmitting ZIKV by reviewing evidence from laboratory vector competence (VC) studies and to identify key knowledge gaps and issues within the ZIKV VC literature. **Methods:** A search was performed until 15th March 2022 on the Cochrane Library, Lilacs, PubMed, Web of Science, WHOLIS and Google Scholar. The search strings included

three general categories: [1] "ZIKA"; [2] "vector"; [3] "competence", "transmission", "isolation", or "feeding behavior" and their combinations. Inclusion and exclusion criteria has been predefined and quality of included articles was assessed by STROBE and STROME-ID criteria. **Findings:** From 8,986 articles retrieved, 2,349 non-duplicates were screened by title and abstracts,103 evaluated using the full text, and 45 included in this analysis. Main findings are 1) secondary vectors of interest include Ae. japonicus, Ae. detritus, and Ae. vexans at higher temperature 2) Culex quinquefasciatus was not found to be a competent vector of ZIKV, 3) considerable heterogeneity in VC, depending on the local mosquito strain and virus used in testing was observed. Critical issues or gaps identified included 1) inconsistent definitions of VC parameters across the literature; 2) equivalency of using different mosquito body parts to evaluate VC parameters for infection (mosquito bodies versus midguts), dissemination (heads, legs or wings versus salivary glands), and transmission (detection or virus amplification in saliva, FTA cards, transmission to neonatal mice); 3) articles that fail to use infectious virus assays to confirm the presence of live virus; 4) need for more studies using murine models with immunocompromised mice to infect mosquitoes. **Conclusion:** Recent, large collaborative multi-country projects to conduct large scale evaluations of specific mosquito species represent the most appropriate approach to establish VC of mosquito species.

Replication of Dengue Virus 4 in Plodia interpunctella (Lepidoptera: Pyralidae) Larvae Under Laboratory Conditions.

Zazueta-Moreno JM, Torres-Avendaño JI, Torres-Montoya EH, Ríos-Tostado JJ, Ramos-Payan R, López-Gutiérrez J, Castillo-Ureta H.

Design of a multi-epitope subunit vaccine candidate for chikungunya virus using computational methodology.

Tongco AMP, Rivera WL.

In silico screening of plant peptides against the envelope protein of dengue virus.

Reena G, Ranjani R, Goutham KD, Sangeetha K.

Peptide therapeutics are found to be an emerging and attractive class of treatment due to their highly specific and safe nature. Hence twenty plant peptides were subjected to screening by molecular docking against the envelope protein of the dengue virus using Clus Pro, Patch Dock, and HADDOCK servers. Physicochemical parameters, allergenicity, and toxicity profile of the plant peptides were estimated by Protparam analysis, AllergenFP, and ToxinPred web servers. Six potential compounds namely Ginkbilobin, Cycloviolin-D, Circulin-B, Circulin-A, Cycloviolacin-013, and Circulin-C showed the highest binding energy with both nonallergenic and nontoxic properties. They also exhibited desirable half-lives extending to 30 hrs except for Ginkbilobin, which showed the least half-life of 4.4 hours and non-polar activity. The residues of Ala-4 of Ginkbilobin; Arg-30 of Cycloviolin D; Arg-29 of Circulin A and C interacted with the Try 101 of the domain II of Envelope protein, implying the possible inhibition of the insertion process of the trimeric E protein during fusion with the host cells. Thus, the identified plant peptides could serve as potential leads upon further subjection to in vitro studies.

Dengue Virus Infection In Mice Induces Bone Marrow Myeloid Cell Differentiation And Generates Ly6glow Immature Neutrophils With Modulated Functions.

Duggal S, Rawat S, Siddqui G, Vishwakarma P, Samal S, Banerjee A, Vrati S.

[Acute myocarditis in a patient with dengue infection].

Aboukhoudir F, Dernys A, Moussa K, Kamal H, Rekik S, Andrieu S.

Designing Quantum Capacitive Peptide Interfaces for Electroanalytical Applications.

Brandão STR, Dos Santos A, Bueno PR, Cilli EM.

Redox-active moieties assembled on metallic interfaces have been shown to follow quantum mechanical rules, where the quantum capacitance of the interface (directly associated with the electronic structure of the redox-active moieties) plays a key role in the electron transfer dynamics of the interface. Modifying these interfaces with biological receptors has significant advantages (simplifying molecular diagnostics methods, reducing size, time, and cost while maintaining high sensitivity), enabling the fabrication of miniaturized electroanalytical devices that can compete with traditional ELISA and RT-PCR benchtop assay methods. Owing to their intrinsic characteristics, the use of peptide-based redox-active moieties is a promising chemical route for modifying metallic surfaces, resulting in a high quantum capacitive signal sensitivity. In the present work, different ferrocene-tagged peptides with a structure of Fc-Glu-XX-XX-Cys-NH$_2$ (XX = serine, phenylalanine, glycine) were used to form self-assembled monolayers on

gold. The feasibility of using these interfaces in an electroanalytical assay was verified by detecting the NS1 DENV (Dengue Virus) biomarker to compare the efficiency of peptide structures for biosensing purposes. Parameters such as the formal potential of the interface, normalized electronic density of states (DOS), quantum capacitance, and electron transfer rate constants were obtained for Ser-, Phe-, and Gly-peptides. The Gly-peptide structure presented the highest analytical performance for sensing NS1 with a sensitivity of 5.6% per decade and the lowest LOD (1.4 ng mL^{-1}) and LOQ (2.6 ng mL^{-1}), followed by Phe-peptide, whereas Ser-peptide had the lowest performance. This work demonstrates that the use of peptides to fabricate a self-assembled monolayer as a biosensor component has advantages for low-cost point-of-care diagnostics. It also shows that the performance of the sensing interface depends strongly on how the chemistry of the surface is designed as a whole, not only on the redox-active group.

Genomic and eco-epidemiological investigations in Uruguay reveal local Chikungunya virus transmission dynamics during its expansion across the Americas in 2023.

Burgueño A, Giovanetti M, Fonseca V, Morel N, Lima M, Castro E, Guimarães NR, Iani FCM, Bormida V, Cortinas MN, Ramas V, Coppola L, Bento AI, Franco L, Rico JM, Lourenço J, Alcantara LCJ, Chiparelli H.
20-08-2023
medRxiv.

Correction: Knowledge, Attitudes and Practices About Zika Virus Infection Among Women of Reproductive Age in Central Brooklyn, New York City, USA.

Dowling R, Thompson AB, Kolokotronis SO.
29-08-2023
J Community Health.

Early transcriptomic host response signatures in the serum of dengue patients provides insights into clinical pathogenesis and disease severity.

Yadav A, Shamim U, Ravi V, Devi P, Kumari P, Maurya R, Das P, Somani M, Budhiraja S, Tarai B, Pandey R.
29-08-2023
Sci Rep.

Technical comparison of MinIon and Illumina technologies for genotyping Chikungunya virus in clinical samples.

de Souza LM, de Oliveira ID, Sales FCS, da Costa AC, Campos KR, Abbud A, Guerra JM, Dos Santos Cirqueira Borges C, Takahashi CPFJ, de Araújo LJT.
29-08-2023
J Genet Eng Biotechnol.

Aedes aegypti container preference for oviposition and its possible implications for dengue vector surveillance in Delhi, India.

Prasad P, Lata S, Gupta SK, Kumar P, Saxena R, Arya DK, Singh H.
23-08-2023
Epidemiol Health.

Objectives: Dengue is a mosquito-borne viral disease globally transmitted by Aedes aegypti. The most effective method to prevent the transmission of the disease is proficient vector control. Understanding the breeding behaviour of the responsible vectors is very pertinent in this regard; therefore, the present study was conducted to understand Ae. aegypti behaviour regarding the selection of containers for oviposition in the megacity of Delhi. **Methods:** A household survey in different localities within Delhi was carried out during 2018-2019. All available containers were inspected for the presence of immature Ae. aegypti. In entomological surveillance, the ovipositional preference of Aedes was computed using the breeding preference ratio, container index in the field, and laboratory settings, and associations of dengue cases with monthly variation in environmental factors and container type were also calculated. **Results:** The household larval survey in 40 localities showed that 40% of 27,776 water-holding containers in 3,400 houses were plastic, followed by overhead tanks (26.2%), and coolers (12.1%). The most preferred breeding habitat was clay pots (9.3%), followed by metallic containers (8.5%) and solid waste (7.1%). A laboratory-based study showed that Aedes preferred clay containers (81.8%) over 4 other types of containers (plastic, paper, metal, and glass). **Conclusion:** The present study provides a rationale for using clay containers as a possible surveillance tool (ovitraps) or as a vector control tool. This information might aid researchers in developing novel traps and targeting preferred containers for larval control activities during transmission and non-transmission seasons.

Predictive Score for Dengue Infection with Complete Blood Count Parameters, Including the Monocyte Distribution Width: A Retrospective Single-Center Derivation and Validation Study.

Poottasane N, Phornprasitsaeng P, Onthong Y, Sinthana T, Limvorapitak W.
28-08-2023
Am J Trop Med Hyg.

Early detection of dengue virus infection will lead to proper management and reduction in morbidity/mortality. Monocyte distribution width (MDW) was recently approved for use in the early detection of sepsis. Because monocytes are involved in the innate immune system against viral infection, we sought to determine changes in MDW to develop and validate a new predictive score for dengue viral infection. This study

included patients who presented with symptoms or signs related to dengue infection and who had a complete blood count and dengue investigation performed during September 2019 to May 2020. The proportion of dengue infection was 29.5% in the current study. The MDW was significantly higher in dengue infection (median, 29.7 versus 24.2; P < 0.001). We then randomly separated patients into training and validation cohorts. Independent predictive factors of dengue infection were white blood cells < 4 × 109/L (score 1), platelets < 100 × 109/L (score 1), and MDW > 24 (score 1). Clinical features were not significantly predictive of dengue infection. The areas under the receiver operating characteristic curve (95% CI) of the prognostic score were 0.839 (0.779-0.899) in the training cohort and 0.742 (0.674-0.811) in the validation cohort. With a cutoff score ≥ 1, the sensitivity and specificity of the scores were 92.2% and 40.8% in the training cohort and 88.9% and 44.1% in the validation cohort, respectively. We concluded that MDW increases with dengue infection and MDW could easily be incorporated in the predictive scores for dengue infection.

Dried Serum Samples for Antibody Detection in Arthropod-Borne Virus Infections Are an Effective Alternative to Serum Samples.

Würsch D, Rojas-Montes O, Maldonado-Rodríguez A, Sevilla-Reyes E, Cevallos AM, Sánchez-Burgos G, Chávez-Negrete A, Lira R.
28-08-2023
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/37640289/

DENV-specific IgA contributes protective and non-pathologic function during antibody-dependent enhancement of DENV infection.

Wegman AD, Waldran MJ, Bahr LE, Lu JQ, Baxter KE, Thomas SJ, Waickman AT.
28-08-2023
PLoS Pathog.
https://pubmed.ncbi.nlm.nih.gov/37639455/

Dengue represents a growing public health burden worldwide, accounting for approximately 100 million symptomatic cases and tens of thousands of fatalities yearly. Prior infection with one serotype of dengue virus (DENV) is the greatest known risk factor for severe disease upon secondary infection with a heterologous serotype, a risk which increases as serotypes co-circulate in endemic regions. This disease risk is thought to be mediated by IgG-isotype antibodies raised during a primary infection, which poorly neutralize heterologous DENV serotypes and instead opsonize virions for uptake by FcγR-bearing cells. This antibody-dependent enhancement (ADE) of infection leads to a larger proportion of susceptible cells infected, higher viremia and greater immunopathology. We have previously characterized the induction of a serum IgA response, along with the typical IgM and IgG responses, during dengue infection, and have shown that DENV-reactive IgA can neutralize DENV and competitively antagonize IgG-mediated ADE. Here, we evaluate the

potential for IgA itself to cause ADE. We show that IgG, but not IgA, mediated ADE of infection in cells expressing both FcαR and FcγRs. IgG-mediated ADE stimulated significantly higher pro-inflammatory cytokine production by primary human macrophages, while IgA did not affect, or slightly suppressed, this production. Mechanistically, we show that DENV/IgG immune complexes bind susceptible cells significantly more efficiently than DENV/IgA complexes or virus alone. Finally, we show that over the course of primary dengue infection, the expression of FcγRI (CD64) increases during the period of acute viremia, while FcγRIIa (CD32) and FcαR (CD89) expression decreases, thereby further limiting the ability of IgA to facilitate ADE in the presence of DENV. Overall, these data illustrate the distinct protective role of IgA during ADE of dengue infection and highlight the potential therapeutic and prognostic value of DENV-specific IgA.

Observational study of clinical, epidemiological, and laboratory characteristics of pediatric patients with dengue in the city of Córdoba.

Fiora MB, Gonzalvez ML, Aguirre JP, Bacigalupo A, Garnero A, Rosa AM, Obrador MD, Grecco C.
31-08-2023
Arch Argent Pediatr.
https://pubmed.ncbi.nlm.nih.gov/37639337/

National dengue surveillance, Cambodia 2002-2020.

Yek C, Li Y, Pacheco AR, Lon C, Duong V, Dussart P, Young KI, Chea S, Lay S, Man S, Kimsan S, Huch C, Leang R, Huy R, Brook CE, Manning JE.
01-09-2023
Bull World Health Organ.
https://pubmed.ncbi.nlm.nih.gov/37638355/

The expansion of chikungunya in Brazil.

Ferreira de Almeida I, Codeço CT, Lana RM, Bastos LS, de Souza Oliveira S, Andreza da Cruz Ferreira D, Godinho VB, Souza Riback TI, Cruz OG, Coelho FC.
11-08-2023
Lancet Reg Health Am.
https://pubmed.ncbi.nlm.nih.gov/37638140/

Interferome signature dynamics during the anti-dengue immune response: a systems biology characterization.

Usuda JN, Plaça DR, Fonseca DLM, Marques AHC, Filgueiras IS, Chaves VGB, Adri AS, Torrentes-Carvalho A, Hirata MH, Freire PP, Catar R, Cabral-Miranda G, Schimke LF, Moll G, Cabral-Marques O.
10-08-2023
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/37638052/

Dengue virus (DENV) infection manifests as a febrile illness with three distinct phases: early acute, late acute, and convalescent. Dengue can result in clinical manifestations with different degrees of severity, dengue fever, dengue hemorrhagic fever, and dengue shock syndrome.

Interferons (IFNs) are antiviral cytokines central to the anti-DENV immune response. Notably, the distinct global signature of type I, II, and III interferon-regulated genes (the interferome) remains uncharacterized in dengue patients to date. Therefore, we performed an in-depth cross-study for the integrative analysis of transcriptome data related to DENV infection. Our systems biology analysis shows that the anti-dengue immune response is characterized by the modulation of numerous interferon-regulated genes (IRGs) enriching, for instance, cytokine-mediated signaling (e.g., type I and II IFNs) and chemotaxis, which is then followed by a transcriptional wave of genes associated with cell cycle, also regulated by the IFN cascade. The adjunct analysis of disease stratification potential, followed by a transcriptional meta-analysis of the interferome, indicated genes such as *IFI27*, *ISG15*, and *CYBRD1* as potential suitable biomarkers of disease severity. Thus, this study characterizes the landscape of the interferome signature in DENV infection, indicating that interferome dynamics are a crucial and central part of the anti-dengue immune response.

The Janus face of proliferating plasmablasts in dengue and COVID-19 infections.

Nayak P, Mukund K, Subramaniam S.

Introduction: B cells play an integral role in the immune response to both dengue fever and COVID-19. Prior scRNAseq analyses of peripheral plasmablasts in COVID-19 have revealed a heterogeneous population with distinct cell subsets associated with proliferation; prior studies in patients with dengue fever have likewise shown the presence of proliferative pre-plasmablasts in the circulation. These findings may have implications for disease severity. In this study, we sought to gain a mechanistic understanding of the intracellular processes in naive and memory B cells that are associated with and may lead to an expanded proliferative plasmablast population in the circulation. **Methods:** We analyzed age-controlled (pediatric and adult), peripheral blood mononuclear cell scRNAseq datasets from patients infected with either dengue (primary or secondary) or COVID-19 (non-severe or severe) from previously published studies. Our preliminary analysis showed that pediatric patients with dengue and adults with COVID-19 had an expanded proliferative plasmablast (p-PB) population. By contrast, neither the adults with dengue nor the children with COVID-19 in our dataset had p-PBs. We used this distinctive preliminary signature to guide our analyses design and expanded our analyses to naive and memory B cells. **Results:** In age/disease conditions with and without p-PBs, we found differences in cell sensing and activation, including via the B cell receptor and downstream signal transduction. Likewise, inflammation was mediated differently: relative to groups without p-PBs, those with p-PBs had increased expression of interferon response and S100 genes (particularly severe COVID-19). Furthermore, several transcription factors at the nexus of activation, inflammation, and cell fate decisions were expressed differently in groups with and without p-PBs. **Discussion:** We used dengue and COVID-19 infections in adult and pediatric patients (focusing on naive B, memory B, and plasmablast cells) as a model to better understand the mechanisms that may give rise to p-PB populations in the circulation. Our results indicate that a more pro-inflammatory state in naive and memory B cells correlated with - and could influence the generation of- proliferating plasmablasts. Further exploration of these mechanisms will have implications for immune memory, vaccine development, and post-viral autoimmune syndromes.

The virome of the invasive Asian bush mosquito Aedes japonicus in Europe.

Abbo SR, de Almeida JPP, Olmo RP, Balvers C, Griep JS, Linthout C, Koenraadt CJM, Silva BM, Fros JJ, Aguiar ERGR, Marois E, Pijlman GP, Marques JT.

Resistance development to bioinsecticides in Aedes aegypti (Culicidae: Diptera), the vector of dengue fever in Saudi Arabia.

Mahyoub JA, Algamdi AG, Aljameeli MM.

Diffusion Restriction in Bilateral Thalami: Beyond Artery of Percheron Infarct.

Shaik RS, Manorenj S, Marupaka SK, Ara T.

Background: Bilateral thalamic infarction, especially the medial thalamus, has been characteristically described in the artery of Percheron (AOP) affection. However, bilateral thalamic restriction has been described in many entities beyond the AOP infarction. **Objective:** Here we describe a case series (three cases) with infection as an etiology for bilateral thalamic lesions in the topographic distribution of the AOP from a tertiary care center in tropical India. **Materials and methods:** : Case series during a 1-year period collecting cases with bilateral thalamic diffusion restriction on MRI who did not have thalamic infarcts and their outcomes. **Results:** : Bilateral thalamic lesion can occur in both bacterial and viral infections such as tuberculosis, dengue, and SARS-COV-2. Thus, we intend to add infections as one of the etiologies in the ever-expanding list of conditions that produce bilateral thalamic restriction. **Conclusions:** All the acute symmetric thalamic lesions are not always secondary to vascular insult. Accurate assessment and prompt diagnosis can prevent unnecessary delays in treatment. To our knowledge, this is the first case series in the literature that throws light on the bilateral thalamic lesions in the topographic

distribution of the AOP secondary to infections in a tropical country like India.

Distribution areas and monthly dynamic distribution changes of three Aedes species in China: Aedes aegypti, Aedes albopictus and Aedes vexans.

Li Y, An Q, Sun Z, Gao X, Wang H.
26-08-2023
Parasit Vectors.
https://pubmed.ncbi.nlm.nih.gov/37633953/

Background: Mosquitoes play an absolute role in the spread of epidemic arbovirus diseases. Worldwide, Aedes aegypti and Aedes albopictus are the main vectors responsible for the spread of these mosquito-borne diseases. Aedes vexans, a mosquito species native to China, also carries mosquito-borne viruses, such as dengue fever virus and Japanese encephalitis virus, but research on this mosquito has been inadequate. Mapping the potential distribution range of and monthly change in the distribution of these three Aedes species is of particular importance for mosquito surveillance, eradication and disease control. Methods: Monitoring data were collected for the three Aedes species in China. Long-term temperature and precipitation data (2001-2021) and land cover data were used to represent various climate and environmental conditions. An ecological niche model was developed using a maximum entropy modeling method to predict the current optimum habitat areas for the three Aedes species and to obtain important variables influencing their monthly distribution. Results: The distribution model for the three Aedes species performed well, with an area under the receiver operating characteristic curve value of 0.991 for Ae. aegypti, 0.928 for Ae. albopictus and 0.940 for Ae. vexans. Analysis of the distribution change and mapping of the optimum habitat range for each Aedes species for each month demonstrated that temperature, precipitation and construction land were important factors influencing the distribution of these three Aedes species. Conclusions: In China, Aedes aegypti is mainly concentrated in a few tropical regions and along the Yunnan border; Aedes albopictus is widely distributed throughout most of the country, except for the arid and semi-arid regions of northwest China; and Aedes vexans is mainly found in the northern regions. Our results provide a basis for the timing and location of surveillance efforts for high-priority mosquitoes.

Dengue outbreak in Peru affects adults and children.

Sanjeet Bagcchi.
Sept-2023
Lancet Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37633296/

Repurposing of approved antivirals against dengue virus serotypes: an in silico and in vitro mechanistic study.

Rashmi SH, Disha KS, Sudheesh N, Karunakaran J, Joseph A, Jagadesh A, Mudgal PP.

26-08-2023
Mol Divers.
https://pubmed.ncbi.nlm.nih.gov/37632595/

Dengue is an emerging, mosquito-borne viral disease of international public health concern. Dengue is endemic in more than 100 countries across the world. However, there are no clinically approved antivirals for its cure. Drug repurposing proves to be an efficient alternative to conventional drug discovery approaches in this regard, as approved drugs with an established safety profile are tested for new indications, which circumvents several time-consuming experiments. In the present study, eight approved RNA-dependent RNA polymerase inhibitors of Hepatitis C virus were virtually screened against the Dengue virus polymerase protein, and their antiviral activity was assessed in vitro. Schrödinger software was used for in silico screening, where the compounds were passed through several hierarchical filters. Among the eight compounds, dasabuvir was finally selected for in vitro cytotoxicity and antiviral screening. Cytotoxicity profiling of dasabuvir in Vero cells revealed changes in cellular morphology, cell aggregation, and detachment at 50 μM. Based on these results, four noncytotoxic concentrations of dasabuvir (0.1, 0.25, 0.5, and 1 μM) were selected for antiviral screening against DENV-2 under three experimental conditions: pre-infection, co-infection, and post-infection treatment, by plaque reduction assay. Viral plaques were reduced significantly (p < 0.05) in the co-infection and post-infection treatment regimens; however, no reduction was observed in the pretreatment group. This indicated a possible interference of dasabuvir with NS5 RdRp, as seen from in silico interaction studies, translating into a reduction in virus plaques. Such studies reiterate the usefulness of drug repurposing as a viable strategy in antiviral drug discovery. In this drug repurposing study, dasabuvir, a known anti-hepatitis C drug, was selected through virtual screening and assessed for its anti-dengue activity.

Computational evaluation of quinones of Nigella sativa L. as potential inhibitor of dengue virus NS5 methyltransferase.

Roney M, Dubey A, Nasir MH, Huq AM, Tufail A, Tajuddin SN, Zamri NB, Mohd Aluwi MFF.
26-08-2023
J Biomol Struct Dyn.
https://pubmed.ncbi.nlm.nih.gov/37632317/

Aedes aegypti is the primary vector for the transmission of the dengue virus, which causes dengue fever, dengue hemorrhagic illness and dengue shock syndrome. There is now no antiviral medication available to treat DENV, which kills thousands of people each year and infects millions of individuals. A possible target for the creation of fresh and efficient dengue treatments is the DENV-3 NS5 MTase. So, *Nigella sativa* quinones were examined using *in silico* methods to find natural anti-DENV compounds. The *in silico* docking was conducted utilising the Discovery Studio software on the quinones of *N. sativa* and the active site of the target protein DENV-3 NS5 MTase. In addition, the druggability and pharmacokinetics of the lead compound were assessed. Dithymoquinone was comparable to the reference compound in terms of its ability to bind to the

active site of target protein. Dithymoquinone met the requirements for drug likeness and Lipinski's principles, as demonstrated by the ADMET analysis and drug likeness results. The current study indicated that the dithymoquinone from *N. sativa* had anti-DENV activity, suggesting further drug development and dengue treatment optimisation.Communicated by Ramaswamy H. Sarma.

Antiviral Activities of Streptomyces KSF 103 Methanolic Extracts against Dengue Virus Type-2.

Zulkifli N, Khairat JE, Azman AS, Baharudin NM, Malek NA, Zainal Abidin SA, AbuBakar S, Hassandarvish P.
20-08-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632115/

Special Issue "Chikungunya Virus and Emerging Alphaviruses".

Pereira MR, Franca RFO.
19-08-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632110/

Development of Zika Virus Mini-Replicon Based Single-Round Infectious Particles as Gene Delivery Vehicles.

Wu JS, Kan JY, Lai HC, Lin CW.
18-08-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632104/

Zika virus (ZIKV) is a type of RNA virus that belongs to the Flaviviridae family. We have reported the construction of a DNA-launched replicon of the Asian-lineage Natal RGN strain and the production of single-round infectious particles (SRIPs) via the combination of prM/E virus-like particles with the replicon. The main objective of the study was to engineer the ZIKV replicon as mammalian expression vectors and evaluate the potential of ZIKV mini-replicon-based SRIPs as delivery vehicles for heterologous gene expression in vitro and in vivo. The mini-replicons contained various genetic elements, including NS4B, an NS5 methyltransferase (MTase) domain, and an NS5 RNA-dependent RNA polymerase (RdRp) domain. Among these mini-replicons, only ZIKV mini-replicons 2 and 3, which contained the full NS5 and NS4B-NS5 genetic elements, respectively, exhibited the expression of reporters (green fluorescent protein (GFP) and cyan fluorescent protein-yellow fluorescent fusion protein (CYP)) and generated self-replicating RNAs. When the mini-replicons were transfected into the cells expressing ZIKV prM/E, this led to the production of ZIKV mini-replicon-based SRIPs. ZIKV mini-replicon 3 SRIPs showed a significantly higher yield titer and a greater abundance of self-replicating replicon RNAs when compared to ZIKV mini-replicon 2 SRIPs. Additionally, there were disparities in the dynamics of CYP expression and cytotoxic effects observed in various infected cell types between ZIKV mini-replicon 2-CYP and 3-CYP SRIPs. In particular, ZIKV mini-replicon 3-CYP SRIPs led to a substantial decrease in the survival rates of

infected cells at a MOI of 2. An in vivo gene expression assay indicated that hACE2 expression was detected in the lung and brain tissues of mice following the intravenous administration of ZIKV mini-replicon 3-hACE2 SRIPs. Overall, this study highlights the potential of ZIKV mini-replicon-based SRIPs as promising vehicles for gene delivery applications in vitro and in vivo.

Burden of Chikungunya Virus Infection during an Outbreak in Myanmar.

Ngwe Tun MM, Kyaw AK, Nwe KM, Myaing SS, Win YT, Inoue S, Takamatsu Y, Urano T, Thu HM, Hmone SW, Thant KZ, Morita K.
14-08-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632076/

Epidemiological Characteristics and Economic Burden of Dengue in Zhejiang Province, China.

Yu Y, Liu Y, Ling F, Sun J, Jiang J.
13-08-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632073/

Dengue imposes a heavy economic burden on families and society. We used surveillance data reported in 2019 to characterize the dengue epidemic in Zhejiang Province, China, which provided guidance for dengue prevention and control. Dengue epidemics mostly occurred in July to October. People aged 30-44 years, males, and commercial service workers were more likely to suffer from dengue. The epidemic areas were mainly in Hangzhou and Wenzhou. Meanwhile, we assessed the economic cost of dengue in the province from both family and organizational perspectives. The direct economic burden of dengue patients was estimated to be USD 405,038.25, and the indirect economic burden was USD 140,364.90, for a total economic burden of USD 543,213.00. The direct economic burden of dengue patients should be reduced by increasing the coverage and reimbursement of health insurance. Additionally, the total annual cost of dengue prevention and control for the government and organizational sectors was estimated to be USD 7075,654.83. Quantifying the dengue burden is critical for developing disease control strategies, allocating public health resources, and setting health policy priorities.

Seroprevalence of IgG Antibodies Directed against Dengue, Chikungunya and West Nile Viruses and Associated Risk Factors in Madagascar, 2011 to 2013.

Broban A, Olive MM, Tantely ML, Dorsemans AC, Rakotomanana F, Ravalohery JP, Rogier C, Heraud JM, Andriamandimby SF.
08-08-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632049/

Arboviruses have been shown to circulate in Madagascar, including West Nile, dengue, and chikungunya viruses,

though the extent of their circulation remains poorly documented. We estimated the seroprevalence of these three arboviruses in Madagascar and determined risk factors associated with seropositivity. Serum samples obtained from 1680 individuals surrounding the Sentinel Health Centers network in all regions of the country were analyzed using ELISA and hemagglutination inhibition assays for dengue, chikungunya, and West Nile viruses IgG antibodies, and multivariate logistic regression models were run. Overall, 6.5% [IC 95% 3.2-9.9] were seropositive for dengue virus, predominantly of Dengue serotype 1, 13.7% [IC 95% 6.5-20.9] for chikungunya virus, and 12.7% [IC 95% 9.0-16.5] for West Nile virus. There was no association with age, showing that dengue and chikungunya viruses were likely recently introduced. Eastern and Northern parts were more affected by dengue and chikungunya viruses, while West Nile virus seemed to circulate in all parts of the country. Dengue and chikungunya seropositivity were notably associated with high levels of vegetation, as well as frequent work in the forest, and West Nile seropositivity with the presence of cultivated areas, as well as standard of living. This analysis gives a new insight into arboviruses circulation and transmission patterns in Madagascar.

Sociodemographic and Clinical Factors for Microcephaly Secondary to Teratogenic Infections in Brazil: An Ecological Study.

Ferreira AP, Santana DS, Figueiredo ERL, Simões MC, de Morais DF, Tavares VB, de Sousa JG, Silva MJA, de Campos Gomes F, de Melo Neto JS.
31-07-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632018/

Morphological and Molecular Changes in the Cortex and Cerebellum of Immunocompetent Mice Infected with Zika Virus.

Rengifo AC, Rivera J, Álvarez-Díaz DA, Naizaque J, Santamaria G, Corchuelo S, Gómez CY, Torres-Fernández O.
Viruses.
27-07-2023
https://pubmed.ncbi.nlm.nih.gov/37631975/

Zika virus (ZIKV) disease continues to be a threat to public health, and it is estimated that millions of people have been infected and that there have been more cases of serious complications than those already reported. Despite many studies on the pathogenesis of ZIKV, several of the genes involved in the malformations associated with viral infection are still unknown. In this work, the morphological and molecular changes in the cortex and cerebellum of mice infected with ZIKV were evaluated. Neonatal BALB/c mice were inoculated with ZIKV intraperitoneally, and the respective controls were inoculated with a solution devoid of the virus. At day 10 postinoculation, the mice were euthanized to measure the expression of the markers involved in cortical and cerebellar neurodevelopment. The infected mice presented morphological changes accompanied by calcifications, as well as a decrease in most of the markers evaluated in the cortex and cerebellum. The modifications found could be predictive of astrocytosis, dendritic pathology, alterations in the regulation systems of neuronal excitation and inhibition, and premature maturation, conditions previously described in other models of ZIKV infection and microcephaly.

The First Case of Zika Virus Disease in Guinea: Description, Virus Isolation, Sequencing, and Seroprevalence in Local Population.

Bayandin RB, Makenov MT, Boumbaly S, Stukolova OA, Gladysheva AV, Shipovalov AV, Skarnovich MO, Camara O, Toure AH, Svyatchenko VA, Shvalov AN, Ternovoi VA, Boiro MY, Agafonov AP, Karan LS.
25-07-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37631963/

The Adjuvant Activity of BCG Cell Wall Cytoskeleton on a Dengue Virus-2 Subunit Vaccine.

Jearanaiwitayakul T, Warit S, Lekjinda K, Seesen M, Limthongkul J, Midoeng P, Sunintaboon P, Ubol S.
09-08-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631912/

The uneven immunogenicity of the attenuated tetravalent dengue vaccine has made it difficult to achieve balanced protection against all four serotypes of the dengue virus (DENV). To overcome this problem, non-replicative vaccines have come into focus, as their immunogenicity is adjustable. This approach is excellent for multivalent vaccines but commonly faces the issue of low immunogenicity. In this present study, we developed a non-replicating dengue vaccine composed of UV-inactivated dengue virus-2 (UV-DENV-2) and DENV-2 NS_{1-279} protein encapsidated within nanoparticles. This vaccine candidate was administered in the presence of BCG cell wall cytoskeleton (BCG-CWS) as an adjuvant. We revealed, here, that encapsidated immunogens with BCG-CWS exerted potent activities on both B and T cells and elicited Th-1/Th-2 responses in mice. This was evidenced by BCG-CWS significantly augmenting antibody-mediated complement-fixing activity, strongly stimulating the antigen-specific polyfunctional T cell responses, and activating mixed Th-1/Th-2 responses specific to DENV-2- and NS_{1-279} antigens. In conclusion, BCG-CWS potently adjuvanted the inactivated DENV-2 and DENV subunit immunogens. The mechanism of adjuvanticity remains unclear. This study revealed the potential use of BCG-CWS in vaccine development.

Tracing down the Updates on Dengue Virus-Molecular Biology, Antivirals, and Vaccine Strategies.

Malik S, Ahsan O, Mumtaz H, Tahir Khan M, Sah R, Waheed Y.
05-08-2023

Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631896/

Comparative Transcriptomic Analysis of Insecticide-Resistant Aedes aegypti from Puerto Rico Reveals Insecticide-Specific Patterns of Gene Expression.

Derilus D, Impoinvil LM, Muturi EJ, McAllister J, Kenney J, Massey SE, Hemme R, Kothera L, Lenhart A.
15-08-2023
Genes (Basel).
https://pubmed.ncbi.nlm.nih.gov/37628677/

Aedes aegypti transmits major arboviruses of public health importance, including dengue, chikungunya, Zika, and yellow fever. The use of insecticides represents the cornerstone of vector control; however, insecticide resistance in *Ae. aegypti* has become widespread. Understanding the molecular basis of insecticide resistance in this species is crucial to design effective resistance management strategies. Here, we applied Illumina RNA-Seq to study the gene expression patterns associated with resistance to three widely used insecticides (malathion, alphacypermethrin, and lambda-cyhalothrin) in *Ae. aegypti* populations from two sites (Manatí and Isabela) in Puerto Rico (PR). Cytochrome P450s were the most overexpressed detoxification genes across all resistant phenotypes. Some detoxification genes (CYP6Z7, CYP28A5, CYP9J2, CYP6Z6, CYP6BB2, CYP6M9, and two CYP9F2 orthologs) were commonly overexpressed in mosquitoes that survived exposure to all three insecticides (independent of geographical origin) while others including CYP6BY1 (malathion), GSTD1 (alpha-cypermethrin), CYP4H29 and GSTE6 (lambda-cyhalothrin) were uniquely overexpressed in mosquitoes that survived exposure to specific insecticides. The gene ontology (GO) terms associated with monooxygenase, iron binding, and passive transmembrane transporter activities were significantly enriched in four out of six resistant vs. susceptible comparisons while serine protease activity was elevated in all insecticide-resistant groups relative to the susceptible strain. Interestingly, cuticular-related protein genes (chinase and chitin) were predominantly downregulated, which was also confirmed in the functional enrichment analysis. This RNA-Seq analysis presents a detailed picture of the candidate detoxification genes and other pathways that are potentially associated with pyrethroid and organophosphate resistance in *Ae. aegypti* populations from PR. These results could inform development of novel molecular tools for detection of resistance-associated gene expression in this important arbovirus vector and guide the design and implementation of resistance management strategies.

First Report of Rubber Collection Bowls & Plastic and Bamboo Water Containers as the Major Breeding Source of Ae. albopictus with the Indigenous Transmission of Dengue and Chikungunya in Rural Forested Malaria-Endemic Villages of Dhalai District, Tripura, India: The Importance of Molecular Identification.

Biswas S, Rajkonwar J, Nirmolia T, Jena SR, Sarkar U, Bhattacharyya DR, Borkakoty B, Pandey A, Subbarao SK, Majumder T, Pebam R, Gogoi P, Mahanta K, Narain K, Bhowmick IP.
03-08-2023
Biomedicines.
https://pubmed.ncbi.nlm.nih.gov/37626683/

Isothermal amplification technology (IAT) for rapid diagnosis of Rickettsioses: scope, overview, existing evidence, and the way forward.

Dixit R, Gopalan N, Behera SK.
02-08-2023
Diagn Microbiol Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37625171/

Rickettsioses, a category of zoonosis primarily caused by Rickettsia and Orientia, is a huge cause of public health concern worldwide. Diseases like murine typhus, scrub typhus, Mediterranean spotted fever and rocky mountain spotted fever are major contributors of Rickettsioses globally, with peculiar distributions in south-east Asia, Africa, Arabia and the Americas. With the innovations in molecular diagnostics, Isothermal Amplification Technology is gaining popularity for its fidelity, rapidity and cost-effectiveness. Compared to commercial assays, they are easily adaptable for point-of-care (PoC) settings. Due to nonspecific presentation as an acute undifferentiated febrile illness, diagnosis of Rickettsioses poses a great challenge. Certain isothermal amplification assays have proven to be highly efficient in diagnosing vector borne diseases like dengue, malaria, and chikungunya. The purpose of this review is to provide readers the current advancements, scope, challenges, and future prospects of isothermal amplification technologies in the detection of zoonotic pathogens like Rickettsia and Orientia.

A predictive score for severity in patients with confirmed dengue fever in a tertiary care hospital in Kerala, India.

Haridas S, M GP, Bhaskaran R.
25-08-2023
Trans R Soc Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/37625166/

Background: The study aimed to identify predictors of severe dengue during the 2017 epidemic and to develop and validate a simple predictive score for severity. **Methods:** A retrospective analytical study was conducted using clinical and laboratory data from adult dengue patients with a confirmed microbiological diagnosis. The study included patients who presented to a tertiary care centre in Kerala, India, during the febrile phase (≤4 d) between June 2017 and February 2019. Using appropriate statistical tests, we derived predictors of severe disease and computed a risk score model. **Results:** Of the 153 patients (mean age 50±17 y; 64% males), 31 (20%) had severe dengue and 4 (3%) died. Petechial lesions, hypoalbuminemia (<3.5 g/dl), elevated alanine aminotransferase (>40 IU/l) and urea >40 IU/l were significant predictors. Our scoring system (cut-off: 2)

showed excellent performance, with an area under the receiver operating characteristics curve of 0.9741, sensitivity of 100%, specificity of 96% and accuracy of 98%. The risk score was secondarily validated on 48 patients hospitalized from March 2019 to June 2019. **Conclusion:** Our scoring system is easy to implement and will help primary healthcare practitioners in promptly identifying severe dengue cases upon hospital presentation.

Chemical Ecology and Management of Dengue Vectors.

Torto B, Tchouassi DP.
25-08-2023
Annu Rev Entomol.
https://pubmed.ncbi.nlm.nih.gov/37625116/

Dengue, caused by the dengue virus, is the most widespread arboviral infectious disease of public health significance globally. This review explores the communicative function of olfactory cues that mediate host-seeking, egg-laying, plant-feeding, and mating behaviors in *Aedes aegypti* and *Aedes albopictus*, two mosquito vectors that drive dengue virus transmission. *Aedes aegypti* has adapted to live in close association with humans, preferentially feeding on them and laying eggs in human-fabricated water containers and natural habitats. In contrast, *Ae. albopictus* is considered opportunistic in its feeding habits and tends to inhabit more vegetative areas. Additionally, the ability of both mosquito species to locate suitable host plants for sugars and find mates for reproduction contributes to their survival. Advances in chemical ecology, functional genomics, and behavioral analyses have improved our understanding of the underlying neural mechanisms and reveal novel and specific olfactory semiochemicals that these species use to locate and discriminate among resources in their environment. Physiological status; learning; and host- and habitat-associated factors, including microbial infection and abundance, shape olfactory responses of these vectors. Some of these semiochemicals can be integrated into the toolbox for dengue surveillance and control. Expected final online publication date for the *Annual Review of Entomology*, Volume 69 is January 2024.

Bionomics and population dynamics of anopheline larvae from an area dominated by fish farming tanks in northern Brazilian Amazon.

Barbosa LMC, Scarpassa VM.
25-08-2023
PLoS One.
https://pubmed.ncbi.nlm.nih.gov/37624846/

Resurgence of Dengue Virus Serotype 4 in Malaysia: A Comprehensive Clinicodemographic and Genomic Analysis.

Suppiah J, Ali EZ, Mohd Khalid MKN, Mohd Ghazali S, Tee KK, Zulkifli MMS, Ramli N, Adiee AH, Ramly MN, Robert F, Lakha Singh SS, Mohd Zain R, Thayan R.
11-08-2023
Trop Med Infect Dis.

https://pubmed.ncbi.nlm.nih.gov/37624348/

Mechanisms of Infection in Zika Virus.

Blázquez AB.
14-08-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37623995/

Suppression Trial through an Integrated Vector Management of Aedes albopictus (Skuse) Based on the Sterile Insect Technique in a Non-Isolated Area in Spain.

Tur C, Almenar D, Zacarés M, Benlloch-Navarro S, Pla I, Dalmau V.
03-08-2023
Insects.
https://pubmed.ncbi.nlm.nih.gov/37623398/

Microparticle-Based Detection of Viruses.

Khanthaphixay B, Wu L, Yoon JY
15-08-2023
Biosensors (Basel).
https://pubmed.ncbi.nlm.nih.gov/37622906/

The dengue virus NS1 protein; new roles in pathogenesis due to similarities with and affinity for the high-density lipoprotein (HDL)?

Alcalá AC, Ludert JE.
24-08-2023
PLoS Pathog.
https://pubmed.ncbi.nlm.nih.gov/37616216/

West Nile Virus and Other Nationally Notifiable Arboviral Diseases - United States, 2021.

Fagre AC, Lyons S, Staples JE, Lindsey N.
25-08-2023
MMWR Morb Mortal Wkly Rep.
https://pubmed.ncbi.nlm.nih.gov/37616182/

Chikungunya virus cell-to-cell transmission is mediated by intercellular extensions in vitro and in vivo.

Yin P, Davenport BJ, Wan JJ, Kim AS, Diamond MS, Ware BC, Tong K, Couderc T, Lecuit M, Lai JR, Morrison TE, Kielian M.
Sept-2023
Nat Microbiol.
https://pubmed.ncbi.nlm.nih.gov/37591996/

Chikungunya virus (CHIKV) has recently emerged to cause millions of human infections worldwide. Infection can induce the formation of long intercellular extensions that project from infected cells and form stable non-continuous membrane bridges with neighbouring cells.

The mechanistic role of these intercellular extensions in CHIKV infection was unclear. Here we developed a co-culture system and flow cytometry methods to quantitatively evaluate transmission of CHIKV from infected to uninfected cells in the presence of neutralizing antibody. Endocytosis and endosomal acidification were critical for virus cell-to-cell transmission, while the CHIKV receptor MXRA8 was not. By using distinct antibodies to block formation of extensions and by evaluation of transmission in HeLa cells that did not form extensions, we showed that intercellular extensions mediate CHIKV cell-to-cell transmission. In vivo, pre-treatment of mice with a neutralizing antibody blocked infection by direct virus inoculation, while adoptive transfer of infected cells produced antibody-resistant host infection. Together our data suggest a model in which the contact sites of intercellular extensions on target cells shield CHIKV from neutralizing antibodies and promote efficient intercellular virus transmission both in vitro and in vivo.

How habitat factors affect an Aedes mosquitoes driven outbreak at temperate latitudes: The case of the Chikungunya virus in Italy.

Solimini A, Virgillito C, Manica M, Poletti P, Guzzetta G, Marini G, Rosà R, Filipponi F, Scognamiglio P, Vairo F, Caputo B.
17-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37590255/

Background: Outbreaks of Aedes-borne diseases in temperate areas are not frequent, and limited in number of cases. We investigate the associations between habitat factors and temperature on individuals' risk of chikungunya (CHIKV) in a non-endemic area by spatially analyzing the data from the 2017 Italian outbreak.
Methodology/principal findings: We adopted a case-control study design to analyze the association between land-cover variables, temperature, and human population density with CHIKV cases. The observational unit was the area, at different scales, surrounding the residence of each CHIKV notified case. The statistical analysis was conducted considering the whole dataset and separately for the resort town of Anzio and the metropolitan city of Rome, which were the two main foci of the outbreak. In Rome, a higher probability for the occurrence of CHIKV cases is associated with lower temperature (OR = 0.72; 95% CI: 0.61-0.85) and with cells with higher vegetation coverage and human population density (OR = 1.03; 95% CI: 1.00-1.05). In Anzio, CHIKV case occurrence was positively associated with human population density (OR = 1.03; 95% CI: 1.00-1.06) but not with habitat factors or temperature.
Conclusion/significance: Using temperature, human population density and vegetation coverage data as drives for CHIKV transmission, our estimates could be instrumental in assessing spatial heterogeneity in the risk of experiencing arboviral diseases in non-endemic temperate areas.

Towards the invasion of wild and rural forested areas in Gabon (Central Africa) by the Asian tiger mosquito Aedes albopictus: Potential risks from the one health perspective.

Obame-Nkoghe J, Roiz D, Ngangue MF, Costantini C, Rahola N, Jiolle D, Lehmann D, Makaga L, Ayala D, Kengne P, Paupy C.
16-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37585443/

The La Crosse virus class II fusion glycoprotein ij loop contributes to infectivity and replication in vitro and in vivo.

Thannickal SA, Spector SN, Stapleford KA.
31-08-2023
J Virol.
https://pubmed.ncbi.nlm.nih.gov/37578236/

A low-background, fluorescent assay to evaluate inhibitors of diverse viral proteases.

Leonard RA, Rao VN, Bartlett A, Froggatt HM, Luftig MA, Heaton BE, Heaton NS.
31-08-2023
J Virol.
https://pubmed.ncbi.nlm.nih.gov/37578235/

Multiple coronaviruses (CoVs) can cause respiratory diseases in humans. While prophylactic vaccines designed to prevent infection are available for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), incomplete vaccine efficacy, vaccine hesitancy, and the threat of other pathogenic CoVs for which vaccines do not exist have highlighted the need for effective antiviral therapies. While antiviral compounds targeting the viral polymerase and protease are already in clinical use, their sensitivity to potential resistance mutations as well as their breadth against the full range of human and preemergent CoVs remain incompletely defined. To begin to fill that gap in knowledge, we report here the development of an improved, noninfectious, cell-based fluorescent assay with high sensitivity and low background that reports on the activity of viral proteases, which are key drug targets. We demonstrate that the assay is compatible with not only the SARS-CoV-2 M^{pro} protein but also orthologues from a range of human and nonhuman CoVs as well as clinically reported SARS-CoV-2 drug-resistant M^{pro} variants. We then use this assay to define the breadth of activity of two clinically used protease inhibitors, nirmatrelvir and ensitrelvir. Continued use of this assay will help define the strengths and limitations of current therapies and may also facilitate the development of next-generation protease inhibitors that are broadly active against both currently circulating and preemergent CoVs. IMPORTANCE Coronaviruses (CoVs) are important human pathogens with the ability to cause global pandemics. Working in concert with vaccines, antivirals specifically limit viral disease in people who are actively infected. Antiviral compounds that target CoV proteases are already in clinical use; their efficacy against variant proteases and preemergent zoonotic CoVs, however, remains incompletely defined. Here, we report an improved,

noninfectious, and highly sensitive fluorescent method of defining the sensitivity of CoV proteases to small molecule inhibitors. We use this approach to assay the activity of current antiviral therapies against clinically reported SARS-CoV-2 protease mutants and a panel of highly diverse CoV proteases. Additionally, we show this system is adaptable to other structurally nonrelated viral proteases. In the future, this assay can be used to not only better define the strengths and limitations of current therapies but also help develop new, broadly acting inhibitors that more broadly target viral families.

A Phase 1, double-blind, randomized, placebo-controlled study to evaluate the safety and immunogenicity of a tetravalent live attenuated dengue vaccine in adults.

Gunale B, Farinola N, Yeolekar L, Shrivastava S, Girgis H, Poonawalla CS, Dhere RM, Arankalle V, Chandra Mishra A, Mehla R, Kulkarni PS.

Tarsal exposure to atovaquone inhibits chikungunya virus transmission by Aedes aegypti mosquitoes, but not the transmission of Zika virus.

Wang L, Sanon A, Khoiriyah Z, Verwimp S, Abdelnabi R, Delang L.

Liang-Ge-San inhibits dengue virus serotype 2 infection by reducing caveolin1-induced cytoplasmic heat shock protein 70 translocation into the plasma membrane.

Chen X, Yang JB, Cao HH, Fang XC, Liu SH, Zou LF, Yu JH, Zuo JP, Zhao W, Lu ZB, Liu JS, Yu LZ.

Background: Dengue virus (DENV) is a major public health threat. However, there are no specific therapeutic drugs for DENV. Many Chinese heat-cleaning formulas, such as Liang-Ge-San (LGS), have been frequently used in the virus-induced diseases. The antiviral effect of LGS has not been reported yet. Purpose: In this study, the effect of LGS on the inhibition of dengue virus serotype 2 (DENV-2) was investigated and the relevant mechanism was explored. Methods: High-performance liquid chromatography was applied to analyze the chemical characterization of LGS. The in vitro antiviral activities of LGS against DENV-2 were evaluated by time-of-drug-addition assay. The binding of heat shock protein 70 (Hsp70) and envelope (E) protein or caveolin1 (Cav1) were analyzed by immunofluorescence and immunoprecipitation assays. Then the role of Cav1 in the anti-DENV-2 effects of LGS was further examined.

DENV-2 infected Institute of Cancer Research suckling mice (n = 10) and AG129 mice (n = 8) were used to examine the protective effects of LGS. Results: It was found that geniposide, liquiritin, forsythenside A, forsythin, baicalin, baicalein, rhein, and emodin maybe the characteristic components of LGS. LGS inhibited the early stage of DENV-2 infection, decreased the expression levels of viral E and non-structural protein 1 (NS1) proteins. LGS also reduced E protein and Hsp70 binding and attenuated the translocation of Hsp70 from cytoplasm to the cell membrane. Moreover, LGS decreased the binding of Hsp70 to Cav1. Further study showed that the overexpression of Cav1 reversed LGS-mediated E protein and Hsp70 inhibition in the plasma membrane. In the in vivo study, LGS was highly effective in prolonging the survival time, reducing viral loads. Conclusion: This work demonstrates for the first time that LGS exerts anti-DENV-2 activity in vitro and in vivo. LGS decreases DENV-2-stimulated cytoplasmic Hsp70 translocation into the plasma membrane by Cav1 inhibition, thereby inhibiting the early stage of virus infection. These findings indicate that LGS may be a candidate for the treatment of DENV.

Setting Dengue Fever Epidemic Thresholds Between 2016 and 2021 in the Central Health Region, Burkina Faso: An Ecological Study.

Ouédraogo JCRP, Ilboudo S, Ouédraogo E, Ouédraogo WT, Ouédraogo S, Samadoulougou BC, Kaboré M, Savadogo LGB.

Background: Dengue fever (DF) is endemic in Burkina Faso, with 70% of its burden supported by the Central Health Region. Then, a single confirmed case can no longer mean an epidemic. This study aimed at describing trends and setting epidemic thresholds of DF in the Central Health Region. Data and methods: An ecological study was conducted using monthly data from DF surveillance between 2016 and 2021. Three methods were applied to set alert and intervention thresholds of DF monthly incidence rate: mean [mean + 2 SD], median [3rd quartile] and cumulative sum (C-sum) [C-sum + 1.96 SD]. These thresholds were plotted with the monthly incidence rates for 2021. Results: In total, 54,429 cases were reported between 2016 and 2021. Dengue cases increased biannually. The median annual incidence rate did not vary significantly across years [Kruskal-Wallis: $\chi^2(5) = 9.825$; p = 0.0803]. Within a year, the monthly incidence rate fell under 48.91 cases per 100,000 inhabitants between January and September and peaked in October or November. With the mean and C-sum methods, the 2021 monthly incidence rate remained below the intervention thresholds (Mean + 2 SD and C-sum + 1.96 SD). With the median method, the incidence rate exceeded the alert and intervention thresholds in July-September 2021. Conclusions: If the DF incidence varied within a year due to the seasons, it was relatively stable between 2016 and 2021. The mean and C-sum methods based on the mean were subject to extreme values, giving high thresholds.

The median method seemed better for capturing the abnormal increase in dengue incidence.

Management of Hemorrhagic Fever Viruses: Intervention of Natural and Synthetic Products.

Lashgari NA, Roudsari NM, Khayatan D, Samani N, Eskandari Rad N, Mortazavi M, Abdolghaffari AH, Momtaz S.

Background: Viral hemorrhagic fevers (VHFs) are a group of clinical syndromes caused by several different RNA virus families, including several members of the arenavirus, bunyavirus, filovirus, and flavivirus families. VHFs have high mortality rates, and they have been associated with vascular permeability, malaise, fever, variable degrees of hemorrhage, reduced plasma volume, and coagulation abnormalities. To treat such conditions, antigen-presenting cells target dysregulated immune reactions and productive infections. Monocytes and macrophages produce inflammatory cytokines that damage adaptive immunity, while infected dendritic cells fail to mature correctly, compromising adaptive immunity. Inflammation and uncontrolled virus replication are associated with vascular leakage and coagulopathy. **Objective:** VHF infects both humans and animals and if not treated, causes hemorrhagic manifestations and lethal platelet dysfunction. Besides pharmacological and immunological solutions, the intervention of natural products for VHF management is of great interest. In this review, we gathered current data about the effectiveness of natural products for VHF management. **Methods:** Data were extracted from Scopus, Google Scholar, PubMed, and Cochrane library in terms of clinical and animal studies published in English between 1981 to February 2022. **Results:** Several plants from diverse families and species were identified with antiviral activity against VHF. The combination of botanical therapeutics and multitarget synergistic therapeutic effects is now the widely accepted explanation for the treatment of VHF. Most of these herbal therapeutics have shown promising immunomodulatory effects in vivo and in vitro VHF models. They can probably modulate the immune system in VHF-infected subjects mainly by interfering with certain inflammatory mediators involved in various infectious diseases. **Conclusion:** Natural, in particular, herbal sources can be valuable for the management of various VHFs and their related complications.

Promising Marine Natural Products for Tackling Viral Outbreaks: A Focus on Possible Targets and Structure-activity Relationship.

Salampe M, Mamada SS, Evary YM, Mitra S, Bin Emran T, Harapan H, Nainu F, Simal-Gandara J.

Dengue virus serotypic replacement of NS3 protease or helicase domain causes chimeric viral attenuation but can be recovered by a compensated mutation at helicase domain or NS2B, respectively.

Teramoto T.

Modified vaccinia Ankara-Bavarian Nordic vaccine against mpox in children.

Turtle L, Subramaniam K.

Dracunculose

Water lettuce (Pistia stratiotes L.) increases biogas effluent pollutant removal efficacy and proves a positive substrate for renewable energy production.

Nguyen Vo Chau N, Huynh Van T, Nguyen Cong T, Kim L, Pham DV.

Background: Aquatic plants play a crucial role in nature-based wastewater treatment and provide a promising substrate for renewable energy production using anaerobic digestion (AD) technology. This study aimed to examine the contaminant removal from AD effluent by water lettuce (WL) and produce biogas from WL biomass co-digested with pig dung (PD) in a farm-scale biogas digester. **Methods:** The first experiment used styrofoam boxes containing husbandry AD effluent. WLs were initially arranged in 50%, 25%, 12.5%, and 0% surface coverage. Each treatment was conducted in five replicates under natural conditions. In the second experiment, WL biomass was co-digested with PD into an existing anaerobic digester to examine biogas production on a farm scale. **Results:** Over 30 days, the treatment efficiency of TSS, BOD5, COD, TKN, and TP in the effluent was 93.75-97.66%, 76.63-82.56%, 76.78-82.89%, 61.75-63.75%, and 89.00-89.57%, respectively. Higher WL coverage increased the pollutant elimination potential. The WL biomass doubled after 12 days for all treatments. In the farm-scale biogas production, the biogas yield varied between 190.6 and 292.9 L kg VS_{added}^{-1}. The methane content reached over 54%. **Conclusions:** WL removed AD effluent nutrients effectively through a phytoremediation system and generated significant biomass for renewable energy production in a farm-scale model.

First Report of Colleters in Araceae: A Case Study in Anthurium andraeanum Reveals Diverse Mucilage Glands Associated with the Developing Shoot.

Pereira-Silva CG, Ballego-Campos I, Sakuragui CM, Gonçalves EG, Paiva EAS.
10-08-2023
Plants (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631124/

Ecotoxicity of Diazinon and Atrazine Mixtures after Ozonation Catalyzed by Na$^+$ and Fe^{2+} Exchanged Montmorillonites on Lemna minor.

Benghaffour A, Azzouz A, Dewez D.
17-08-2023
Molecules.
https://pubmed.ncbi.nlm.nih.gov/37630359/

Selection and Evaluation of Reference Genes for RT-qPCR Analysis in Amorphophallus Konjac Based on Transcriptome Data.

Liu Y, Zhang C, Harijati N, Diao Y, Liu E, Hu Z.
25-07-2023
Genes (Basel).
https://pubmed.ncbi.nlm.nih.gov/37628565/

Combined with the Konjac transcriptome database of our laboratory and internal reference genes commonly used in plants, the eight candidate internal reference genes were screened and detected. They are the 25S ribosomal RNA gene (*25S rRNA*), 18S ribosomal RNA gene (*18S rRNA*), actin gene (*ACT*), glyceraldehyde-3-phosphate dehydrogenase gene (*GAPDH*), ubiquitin gene (*UBQ*), β-tubulin gene (*β-TUB*), eukaryotic elongation factor 1-αgene(*eEF-1α*), and eukaryotic translation initiation factor 4α-1 gene (*eIF-4α*). The results of GeNorm, Normfinder, and BestKeeper were analyzed comprehensively. The data showed that the expression levels of *25S rRNA*, *18S rRNA*, and *ACT* at the reproductive periods, *eEF-1α* and *eIF-4α* at the nutritional periods, and *eEF-1α*, *UBQ*, and *ACT* at different leaf developmental periods were stable. These identified and stable internal reference genes will provide the basis for the subsequent molecular biology-related studies of Konjac.

Establishment of protoplasts transient expression system in Pinellia ternata (Thunb.) Breit.

Tian YH, Liu M, Tang L, Zhang YJ, Hang Y, Shangguan LY, Zhang YQ, Zhang MS.
Oct-2023
Biotechnol Lett.
https://pubmed.ncbi.nlm.nih.gov/37589824/

Integrated bioprocess for Se(VI) remediation using duckweed: Coupling selenate removal to biogas production.

Kotamraju A, Logan M, Lens PNL.
05-10-2023
J Hazard Mater.
https://pubmed.ncbi.nlm.nih.gov/37544177/

The use of phytoremediation as a method for wastewater treatment or removal of pollutants is garnering significant interest and duckweed (DW), a free floating macrophyte, depicts significant potential for the removal of nutrients and toxic compounds from contaminated waters. The present work aimed to develop an integrated process for remediating selenate (Se(VI)) using DW biomass and subsequent use of Se(VI) enriched DW for biogas production. The main objective is to extend the application of selenium (Se) enriched DW biomass for biogas production. Se(VI) enriched DW biomass (Se-DW) gave higher methane production (48.38 ± 3.6 mL gCOD^{-1}) than control DW biomass (C-DW) (24.46 ± 3.6 mL gCOD^{-1}). To further enhance methane production, three pre-treatment approaches (acid, alkali and hydrothermal) were assessed and the solid and liquid fractions obtained after pre-treatment were used as a substrate. Pre-treatments increased biogas production in both Se-DW and C-DW than untreated conditions. Liquid fractions gave higher biogas production than solid fractions. In Se-DW, highest biogas production was observed in hydrothermal pre-treated Se-DW, while in C-DW, acid pre-treatment gave higher biogas production. Methane production was shown to be enhanced up to a Se(VI) concentration of 1.7 mg L^{-1}, whereas a concentration beyond this lowered biogas production.

Two residues determine nicotinic acetylcholine receptor requirement for RIC-3.

Noonan JD, Beech RN.
Sept-2023
Protein Sci.
https://pubmed.ncbi.nlm.nih.gov/37417463/

Nicotinic acetylcholine receptors (N-AChRs) mediate fast synaptic signaling and are members of the pentameric ligand-gated ion channel (pLGIC) family. They rely on a network of accessory proteins in vivo for correct formation and transport to the cell surface. Resistance to cholinesterase 3 (RIC-3) is an endoplasmic reticulum protein that physically interacts with nascent pLGIC subunits and promotes their oligomerization. It is not known why some N-AChRs require RIC-3 in heterologous expression systems, whereas others do not. Previously we reported that the ACR-16 N-AChR from the parasitic nematode Dracunculus medinensis does not require RIC-3 in Xenopus laevis oocytes. This is unusual because all other nematode ACR-16, like the closely related Ascaris suum ACR-16, require RIC-3. Their high sequence similarity limits the number of amino acids that may be responsible, and the goal of this study was to identify them. A series of chimeras and point mutations between A. suum and D. medinensis ACR-16, followed by functional characterization with electrophysiology, identified two residues that account for a majority of the receptor requirement for RIC-3. ACR-16 with R/K159 in the cys-loop and I504 in the C-terminal tail did not require RIC-3 for functional expression. Mutating either of these to R/K159E or I504T, residues found in other nematode ACR-16, conferred a RIC-3 requirement. Our results agree with previous studies showing that these regions interact and are involved in receptor synthesis. Although it is currently

unclear what precise mechanism they regulate, these residues may be critical during specific subunit folding and/or assembly cascades that RIC-3 may promote.

Heating or ginger extract reduces the content of Pinellia ternata lectin in the raphides of Pinellia tuber.

Liu Y, Nose I, Terasaka K, Fueki T, Makino T.

Pinellia tuber, the dried tuber of Pinellia ternata, causes a very strong acridity sensation in the oral and laryngopharynx mucosa when taken orally in its unprocessed form. In traditional Chinese medicine (TCM), this sensation has been called "toxicity", and Pinellia tuber must be processed using ginger extract, licorice, or alum. In Japanese traditional Kampo medicine, since "toxicity" can be eliminated by decocting, it should not be processed. However, little is known about the mechanism underlying the "detoxification" of Pinellia tubers. In this study, we produced murine antiserum using recombinant P. ternata lectin (PTL), developed an immuno-fluorescence staining method for PTL in the needle-shaped crystals (raphides) that were prepared by petroleum ether extraction (PEX) from Pinellia tuber, and elucidated the mechanism of the processing of Pinellia tuber using heat or ginger extract. After heating the raphides in water, the amount of PTL contained in the raphides was significantly reduced by the immunostaining, although the shape of the raphides was not changed. Incubating raphides with dried ginger extract also significantly reduced the amount of PTL in the raphides in a concentration-dependent manner. By the activity-guided fractionation of ginger extract, the active ingredients in the ginger extract were oxalic acid, tartaric acid, malic acid, and citric acid. Among these four organic acids, oxalic acid mainly contributed to the effect of dried ginger extract by its content in ginger extract and its activity. These results exhibit scientific evidences for the traditional theories of processing to "detoxify" Pinellia tuber in TCM and Kampo medicine.

A non-cell-autonomous circadian rhythm of bioluminescence reporter activities in individual duckweed cells.

Watanabe E, Muranaka T, Nakamura S, Isoda M, Horikawa Y, Aiso T, Ito S, Oyama T.

Echinococcose

Evaluation of Hydatid Cyst Antigen for Serological Diagnosis.

Maleki F, Akhlaghi L, Tabatabaie F.

Background: Hydatidosis, a chronic zoonotic disease, has a distribution worldwide and is caused by the larval stage of the Echinococcus helminth. The Dot-ELISA test can diagnose hydatidosis quickly and accurately. Additionally, unlike other hydatid disease tests now used, this quick and affordable enzyme immunoassay is very serum-conservative and antigen-conservative, needing just nanogram levels of parasite antigen. **Methods:** In the present cross-sectional study, crude and B antigens of hydatid cyst fluid were obtained to diagnose human hydatidosis using CIEP (Counter Immunoelectrophoresis), ELISA (Enzyme-linked Immuno Sorbent assay), and Dot-ELISA (Dot Enzyme linked Immuno Sorbent Assay) methods. Infected liver with a hydatid cyst was collected from Tehran's slaughterhouses to prepare cyst fluid in different stages. After extracting and purifying the Cyst fluid, it is centrifuged at 4ºc, then prepared to concentrate. The study also included sera from hydatidosis (n=60), samples of helminth parasites (n=55), fascioliasis (n=35), toxocariasis (n=20) and negative control (n=35) were tested by CIEP (Counter Immunoelectrophoresis), ELISA (Enzyme-linked Immune Sorbent assay), and Dot-ELISA (Dot Enzyme linked Immuno Sorbent Assay) methods. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) for Windows release 25.0 (SPSS Inc., Chicago, IL, USA). **Results:** Crude antigen of hydatid cyst showed a specificity of 76.7%, a sensitivity of 93.3% using the ELISA method, and B antigen showed a specificity of 96.7% and sensitivity of 88.3% using the same method. The crude antigen of the hydatid cyst exhibited a specificity of 68.9% and a sensitivity of 86.7% using CIEP. The B antigen showed a specificity of 87.8% and sensitivity of 83.3% using the same method. The crude antigen of hydatid cyst having serum dilution at 1:800 exhibited a specificity of 83.3% and sensitivity of 100% using the Dot-ELISA method and B antigen having serum dilution at 1:800 serum showed a specificity of 100% and sensitivity of 98.3% using the same method. The results of this finding showed that B antigen has the maximum specificity to diagnose hydatid test using the Dot- ELISA method. **Conclusion:** Hydatid cysts present with varied symptomatology. History of exposure to infected animals may not be present. A high degree of clinical suspicion combined with meticulous history and clinical examination supported by laboratory investigations are required for its diagnosis. The Dot-ELISA system with native antigen B is a viable approach for the immunodiagnosis of human hydatidosis that is preferred to infection.

Presence of Echinococcus granulosussensulato in the endoparasitic fauna of feral dogs in Tierra del Fuego, Argentina.

Zanini F, Di Salvo V, Pierangeli N, Lazzarini L, Curto E.

The regulatory role of differential microRNA expressions on cellular inflammatory factors IL-6 and IL-10 in

Echinococcus granulosus-induced anaphylaxis.

Wang CS, Yu T, Kulaixi X, Zhou JR, Abulajiang X, Wang JL, Wang SJ, Ye JR.

Objective: To determine the pathogenesis and molecular targets of anaphylaxis caused by hydatid cyst fluid leakage.
Methods: First, Balb/c mice were infected with Echinococcus granulosus, and then the anaphylaxis model was developed. The mice were separated into: anaphylaxis caused by the cystic echinococcosis group (ANPC), the cystic echinococcosis without anaphylaxis group (CE group), and the normal control group (CTRL). Following this, the spleen tissue was collected for microRNA (miRNA) sequencing. Using bioinformatics analysis, differentially expressed miRNAs (DEMs) were identified. Then, through the use of protein-protein interaction (PPI) networks, the key target genes for miRNA regulation associated with echinococcosis-induced anaphylaxis were identified.
Results: ANPC and CE groups have 29 and 39 DEMs compared to the CTRL group, respectively. Based on these 25 DEMs, interactions between miRNA and mRNA were screened, and 174 potential target genes were identified. We performed gene ontology (GO) function and Kyoto Encyclopedia of Genes and Genomes pathway enrichment analysis on these 174 target genes, and the results revealed that the three pathways with the highest enrichment were the PI3K-Akt signaling pathway, FoxO signaling pathway, and Focal adhesion. The interaction analysis of PPI and miRNA-hub gene networks revealed that interleukin 6 (IL-6) was regulated by miR-146a-5p and miR-149-5p, while IL-10 was regulated by miR-29b-3p and miR-29c-3. Using reverse transcription polymerase chain reaction, we found that the miRNAs regulating IL-6 and IL-10 were significantly upregulated in the ANPC group, and there are three pathways involved in that process: Pathways of PI3K-Akt signaling, FoxO signaling, and Focal adhesion. IL-6 and IL-10 play an important role in cellular pyroptosis and apoptosis. Therefore, the aforementioned results provide significant reference value for elucidating the mechanism of cellular pyroptosis and apoptosis in echinococcosis-induced anaphylaxis, and for formulating tissue and organ protection strategies for patients with cystic echinococcosis when anaphylaxis is triggered by hydatid cyst rupture.

The role of memory T cells in Echinococcus granulosus-induced sensitization.

Zhou JR, Du XX, Abulajiang X, Geli W, Pu XL, Tailaiti S, Lin JY, Li YQ, Ye JR.

Age-dependent relationships among diet, body condition, and Echinococcus multilocularis infection in urban coyotes.

Sugden S, Steckler DK, Sanderson D, Abercrombie B, Abercrombie D, Seguin MA, Ford K, St Clair CC.

Urban coyotes (Canis latrans) in North America increasingly exhibit a high prevalence of Echinococcus multilocularis, a cestode of recent and rising public health concern that uses rodents as intermediate hosts and canids as definitive hosts. However, little is known about the factors that drive the high urban prevalence of this parasite. We hypothesized that the diet of urban coyotes may contribute to their higher E. multilocularis infection prevalence via either (a) greater exposure to the parasite from increased rodent consumption or (b) increased susceptibility to infection due to the negative health effects of consuming anthropogenic food. We tested these hypotheses by comparing the presence and intensity of E. multilocularis infection to physiological data (age, sex, body condition, and spleen mass), short-term diet (stomach contents), and long-term diet (δ13C and δ15N stable isotopes) in 112 coyote carcasses collected for reasons other than this study from Edmonton, Alberta and the surrounding area. Overall, the best predictor of infection status in this population was young age, where the likelihood of infection decreased with age in rural coyotes but not urban ones. Neither short- nor long-term measures of diet could predict infection across our entire sample, but we found support for our initial hypotheses in young, urban coyotes: both rodent and anthropogenic food consumption effectively predicted E. multilocularis infection in this population. The effects of these predictors were more variable in rural coyotes and older coyotes. We suggest that limiting coyote access to areas in which anthropogenic food and rodent habitat overlap (e.g., compost piles or garbage sites) may effectively reduce the risk of infection, deposition, and transmission of this emerging zoonotic parasite in urban areas.

[Giant left ventricle cardiac hydatid cyst : report of a challenging case].

Lachhab F, Leghlimi H, Mahfoudi L, Tribak M, Soufiani A, Benbagha N, Maghraoui A, Filal J, Bensouda A, Marmade L, Moughil S.

In vitro and in vivo Efficacies of Novel Harmine Derivatives in the Treatment of Cystic Echinococcosis.

Chen B, Yan M, Gao H, Ma Q, Li L, Lü G, Gong Y, Wen L, Xu S, Wang J, Zhao J.

A Novel Designed Sandwich ELISA for the Detection of Echinococcus granulosus Antigen in Camels for Diagnosis of Cystic Echinococcosis.

Toaleb NI, Aboelsoued D, Abdel Megeed KN, Hekal SHA.
06-08-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624338/

¹⁸FDG-PET/CT-Scans and Biomarker Levels Predicting Clinical Outcome in Patients with Alveolar Echinococcosis-A Single-Center Cohort Study with 179 Patients.

Peters L, Jiang W, Eberhardt N, Hagemann JB, Grüner B, Tappe D.
14-08-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37624001/

Background: Alveolar echinococcosis (AE) is a severe larval tapeworm infection with a variable clinical course of the disease. Reliable imaging techniques and biomarkers are needed to predict the course of the disease. **Methods:** 179 AE patients that received PET/CT scans between 2008 and 2012 were retrospectively included. From stored blood samples taken on the day of the scan, levels of IgE, parasite-specific serology, amyloid A, C-reactive protein, soluble interleukin 2 receptor, cytokeratin fragments, eosinophilic cell count, and eosinophil cationic protein were measured. Additionally, the current clinical outcome (cured, stable, or progressive disease) after a median duration of 8 years after baseline examination was assessed. Ultimately, an ordinal logistic regression was conducted to evaluate which imaging parameters and biomarkers independently influence the clinical outcome. **Results:** In general, patients in need of medical treatment or with progressive disease, advanced PNM stages, and positive PET/CT scans exhibited higher levels of the respective biomarkers. However, only the parasite-specific serological markers and total IgE levels differed significantly between clinical groups, WHO PNM stages, and the results of the PET/CT scan. In the multivariate analysis, PET/CT results were a strong predictor of the clinical outcome (OR 8.908, 95%CI 3.019-26.285; $p < 0.001$), and age at baseline was a moderate predictor (OR 1.031, 95%CI 1.003-1.060; $p = 0.029$). **Conclusions:** The PET/CT scan is, preferably in combination with parasite-specific serology and IgE levels, a valuable tool in the clinical management of AE and is able to predict the course of the disease.

Characterisation of extracellular vesicles isolated from hydatid cyst fluid and evaluation of immunomodulatory effects on human monocytes.

Khosravi M, Mohammad Rahimi H, Nazari A, Baghaei K, Asadzadeh Aghdaei H, Shahrokh S, Sharifdini M, Torrecilhas AC, Mehryab F, Mirjalali H, Shekari F, Zali MR.
Sept-2023
J Cell Mol Med.
https://pubmed.ncbi.nlm.nih.gov/37530547/

Hydatidosis is a disease caused by the larval stage of Echinococcus granulosus, which involves several organs of intermediate hosts. Evidence suggests a communication between hydatid cyst (HC) and hosts via extracellular vesicles. However, a little is known about the communication between EVs derived from HC fluid (HCF) and host cells. In the current study, EVs were isolated using differential centrifugation from sheep HCF and characterized by western blot, electron microscope and size distribution analysis. The uptake of EVs by human monocyte cell line (THP-1) was evaluated. The effects of EVs on the expression levels of pro- and anti-inflammatory cytokines were investigated using quantitative real-time PCR (RT-PCR), 3 and 24 h after incubation. Moreover, the cytokine level of IL-10 was evaluated in supernatant of THP-1 cell line at 3 and 24 h. EVs were successfully isolated and showed spherical shape with size distribution at 130.6 nm. After 3 h, the expression levels of pro-inflammatory cytokine genes (IL1B, IL15 and IL8) were upregulated, while after 24 h, the expression levels of pro-inflammatory cytokines were decreased and IL13 gene expression showed upregulation. A statistically significant increase was seen in the levels of IL-10 after 24 h. The main mechanism of the communication between EVs derived from HCF and their host remains unclear; however, time-dependent anti-inflammatory effects in our study suggest that HC may modulate the immune responses via EVs.

Filariose lymphatique

Current status of infectious diseases among migrants and non-citizens in Malaysia.

Mohd Putera NWS, Azman AS, Mohd Zain SN, Yahaya H, Lewis JW, Sahimin N.
01-06-2023
Trop Biomed.
https://pubmed.ncbi.nlm.nih.gov/37650399/

The mass movement of migrants to Malaysia for employment is one of the factors contributing to the emergence and re-emergence of infectious diseases in this country. Despite mandatory health screening for migrants seeking employment, prevalence records of infectious diseases amongst migrant populations in Malaysia are still within negligible proportions. Therefore, the present review highlights the incidence, mortality and overall status of infectious diseases amongst migrants' populations in Malaysia, which maybe be useful for impeding exacerbation of inequalities among them and improving our national health system thru robust and effective emergency responses in controlling the prevalent diseases found among these populations and maybe, Malaysian citizens too. Peer-reviewed articles from January 2016 to December 2020 were searched through online platform including SCOPUS, PubMed, Science Direct, and Google Scholar. Non-peer-reviewed reports and publications from ministry and government websites including data from related agencies were also scoured from in order to ensure that there are no cases being overlooked, as most published articles did not have migrants as the research subjects. A total of 29 studies had been selected in the final analysis. Migrants in Malaysia were at higher risk for tuberculosis, malaria, lymphatic filariasis, cholera, leprosy and leptospirosis. Lymphatic

filariasis was still endemic among this population while thousand cases of TB and cholera had been reported among them due to cramp living conditions and poor sanitation in their settlements respectively. While malaria had gradually decreased and become sporadic, the influx of migrant workers had led to the rising of imported malaria cases. Low cases of leprosy had been recorded in Malaysia but a significant proportion of it was contributed by migrant workers. As for leptospirosis, studies found that there are prominent cases among migrant workers, which particularly highest within workers with lower educational attainment. Infectious diseases are still prevalent among migrants in Malaysia due to various interplay factors including their working sectors, country of origin, immunization status, type of settlement, impoverished living conditions, and language and cultural barriers that impeding access to health facilities.

Factors Influencing Drug Compliance Among Adult with Lymphatic Filariasis in Indonesia: Findings From Nationwide Population-Based Health Survey.

Ipa M, Astuti EP, Wahono T, Laksono AD, Cahyati Y, Dhewantara PW.
30-08-2023
Asia Pac J Public Health.
https://pubmed.ncbi.nlm.nih.gov/37649276/

Determinants of Podoconiosis in Bensa District, Sidama Region, Ethiopia: A case control study.

Hailu M, Chea N, Ali MM, Hailu M.
29-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37643189/

Population pharmacokinetics of ivermectin after mass drug administration in lymphatic filariasis endemic communities of Tanzania.

Fimbo AM, Mlugu EM, Kitabi EN, Kulwa GS, Iwodyah MA, Mnkugwe RH, Kunambi PP, Malishee A, Kamuhabwa AAR, Minzi OM, Aklillu E.
28-08-2023
CPT Pharmacometrics Syst Pharmacol.
https://pubmed.ncbi.nlm.nih.gov/37638539/

Ivermectin (IVM) is a drug of choice used with albendazole for mass drug administration (MDA) to halt transmission of lymphatic filariasis. We investigated IVM pharmacokinetic (PK) variability for its dose optimization during MDA. PK samples were collected at 0, 2, 4, and 6 h from individuals weighing greater than 15 kg (n = 468) receiving IVM (3-, 6-, 9-, or 12 mg) and ALB (400 mg) during an MDA campaign in Tanzania. Individual characteristics, including demographics, laboratory/clinical parameters, and pharmacogenetic variations were assessed. IVM plasma concentrations were quantified by liquid-chromatography tandem mass spectrometry and analyzed using population-(PopPK) modeling. A two-compartment model with transit absorption kinetics, and allometrically scaled oral clearance (CL/F) and central volume (V_c /F) was

adapted. Fitting of the model to the data identified 48% higher bioavailability for the 3 mg dose compared to higher doses and identified a subpopulation with 97% higher mean transit time (MTT). The final estimates for CL/F, V_c /F, intercompartment clearance, peripheral volume, MTT, and absorption rate constant for a 70 kg person (on dose other than 3 mg) were 7.7 L/h, 147 L, 20.4 L/h, 207 L, 1.5 h, and 0.71/h, respectively. Monte-Carlo simulations indicated that weight-based dosing provides comparable exposure across weight bands, but height-based dosing with capping IVM dose at 12 mg for individuals with height greater than 160 cm underdoses those weighing greater than 70 kg. Variability in IVM PKs is partly explained by body weight and dose. The established PopPK model can be used for IVM dose optimization. Height-based pole dosing results in varying IVM exposure in different weight bands, hence using weighing scales for IVM dosing during MDA is recommended.

An mHealth App (eSkinHealth) for Detecting and Managing Skin Diseases in Resource-Limited Settings: Mixed Methods Pilot Study.

Yotsu RR, Almamy D, Vagamon B, Ugai K, Itoh S, Koffi YD, Kaloga M, Dizoé LAS, Kouadio K, Aka N, Yeboue LKG, Yao KA, Blanton RE.
14-06-2023
JMIR Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37632977/

Gale

Recalcitrant nodular scabies showing excellent response to tofacitinib: five case reports.

Zhao YK, Lu JF, Liu JH, Wu HH, Song LL, Wan CL, Luo DQ.
29-08-2023
Ther Adv Chronic Dis.
https://pubmed.ncbi.nlm.nih.gov/37655266/

Scabies is a contagious skin condition caused by *Sarcoptes scabiei*, and it is always associated with an intense, unbearable, nocturnal deteriorating itch. Its presentations include classic burrows, erythema, pruritic papules, pustules, vesicles, and inflammatory nodules, with diffuse or localized distribution on the finger webs, wrist flexors, elbows, axillae, buttocks, genitalia, and breasts. Nodular scabies is an uncommon clinical variant of scabies. Its management is still challenging for some patients up to date, although topical, intralesional or systemic corticosteroids, topical calcineurin inhibitors, and crotamiton as well as cryotherapy alone or in different combinations are used. We here report five male patients of nodular scabies, aged between 14 and 25 years, who had classical scabies that had been cured by sulfur ointment for at least 4 weeks except for their itching nodules, and their residual pruritic nodules also failed in previous treatments including antihistamines, topical applying and intralesional injection of steroids as well as topical tacrolimus in different combinations before being recruited to this study. The patients were administered tofacitinib 5 mg, twice a day, which led to excellent and

rapid improvement for both lesions and symptoms after 1-4 weeks of treatment, respectively, without any associations. During 6 months of follow-up, only one had re-infection of scabies associated with nodules that were cured by sulfur ointment and tofacitinib again. No adverse reaction was observed. The present results suggested that tofacitinib might be a potential agent for nodular scabies with excellent response.

Egyptian mandarin peel oil's anti-scabies potential via downregulation-of-inflammatory/immune-cross-talk: GC-MS and PPI network studies.

Elmaidomy AH, Abdel-Maqsoud NMR, Tammam OY, Abdel-Rahman IM, Elrehany MA, Bakhsh HT, Altemani FH, Algehainy NA, Alzubaidi MA, Alsenani F, Sayed AM, Abdelmohsen UR, Zahran EM.
30-08-2023
Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/37648727/

The current study investigated the scabicidal potential of Egyptian mandarin peel oil (Citrus reticulata Blanco, F. Rutaceae) against sarcoptic mange-in-rabbits. Analysis of the oil's GC-MS identified a total of 20 compounds, accounting for 98.91% of all compounds found. Mandarin peel oil topical application improved all signs of infection, causing a scabicidal effect three days later, whereas in vitro application caused complete mite mortality one day later. In comparison to ivermectin, histopathological analysis showed that the epidermis' inflammatory-infiltration/hyperkeratosis-had disappeared. In addition to TIMP-1, the results of the mRNA gene expression analysis showed upregulation of I-CAM-1-and-KGF and downregulation of ILs-1, 6, 10, VEGF, MMP-9, and MCP-1. The scabies network was constructed and subjected to a comprehensive bioinformatic evaluation. TNF-, IL-1B, and IL-6, the top three hub protein-coding genes, have been identified as key therapeutic targets for scabies. From molecular docking data, compounds 15 and 16 acquired sufficient affinity towards the three screened proteins, particularly both possessing higher affinity towards the IL-6 receptor. Interestingly, it achieved a higher binding energy score than the ligand of the docked protein rather than displaying proper binding interactions like those of the ligand. Meanwhile, geraniol (15) showed the highest affinity towards the GST protein, suggesting its contribution to the acaricidal effect of the extract. The subsequent, MD simulations revealed that geraniol can achieve stable binding inside the binding site of both GST and IL-6. Our findings collectively revealed the scabicidal ability of mandarin peel extract for the first time, paving the way for an efficient, economical, and environmentally friendly herbal alternative for treating rabbits with Sarcoptes mange.

Crusted scabies.

Lyons D, Duff E, Kilgallen C, O Brien O, Collins S, Eustace K.
14-08-2023
IDCases.
https://pubmed.ncbi.nlm.nih.gov/37645534/

[Eczema and its treatment in older adults].

Harries L, Traidl S, Klespe KC, Werfel T.
28-08-2023
Dermatologie (Heidelb).
https://pubmed.ncbi.nlm.nih.gov/37638989/

An mHealth App (eSkinHealth) for Detecting and Managing Skin Diseases in Resource-Limited Settings: Mixed Methods Pilot Study.

Yotsu RR, Almamy D, Vagamon B, Ugai K, Itoh S, Koffi YD, Kaloga M, Dizoé LAS, Kouadio K, Aka N, Yeboue LKG, Yao KA, Blanton RE.
14-06-2023
JMIR Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37632977/

Failure of scabies treatment: a systematic review and meta-analysis.

Mbuagbaw L, Sadeghirad B, Morgan RL, Mertz D, Motaghi S, Ghadimi M, Babatunde I, Zani B, Pasumarthi T, Derby M, Kothapudi VN, Palmer NR, Harder T, Aebischer A, Reichert F.
25-08-2023
Br J Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37625798/

Smartphone app to screen individuals with scabies symptoms.

Ali Z, Bourlioux M, Thomsen SF.
23-08-2023
Dan Med J.
https://pubmed.ncbi.nlm.nih.gov/37622645/

Introduction: Patients with scabies are often misdiagnosed before being attended by a dermatologist. The aim of this study was to use a smartphone app to screen individuals from the general population with scabies symptoms. Methods: Subjects who suspected that they had scabies were recruited online and downloaded a app tailored for this study. A questionnaire on symptoms was completed and photos of the skin were uploaded from within the app. Two physicians, a board-certified dermatologist and a resident dermatologist, evaluated the requests by categorising the scabies risk of each case, and categorisation triggered an auto-generated response describing the level of scabies and letting the participant know whether to contact a general practitioner or not. Results: Within 15 days of advertisement, 228 requests were sent (71% women); mean age 24 years (standard deviation: ± 10.0). Itch was experienced by 90% (n = 208) and rash by 76% (n = 174). The rash was distributed bilaterally in 79% (n = 138). The areas of rash localisation were: arms (63%), hands (56%), legs (55%), abdomen (52%), inner thigh (45%), chest (26%), genitals (24%), head and neck (17%) and axilla (16%). 5% of all cases evaluated by either the senior or junior physician were evaluated as having a high risk of scabies. Conclusion: In a very short time, the app received a high number of requests from individuals worrying about scabies; 5% of the incoming

requests were categorised as carrying a high risk of having scabies. Mobile apps are a helpful tool to screen for scabies in primary care settings. **Funding:** Omhu A/S.

Worldwide prevalence of scabies: Some knowns but still many unknowns.

Micallef D, Boffa MJ.
Sept-2023
J Eur Acad Dermatol Venereol.
https://pubmed.ncbi.nlm.nih.gov/37622220/

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

Yotsu RR, Ding Z, Hamm J, Blanton RE.
14-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37578966/

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

Prevalence of scabies worldwide-An updated systematic literature review in 2022.

Schneider S, Wu J, Tizek L, Ziehfreund S, Zink A.
Sept-2023
J Eur Acad Dermatol Venereol.
https://pubmed.ncbi.nlm.nih.gov/37147907/

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

Intestinal parasitic infections among children aged 12-59 months in Nyamasheke District, Rwanda.

Hakizimana E, Kim JY, Oh S, Yoon M, Yong TS.
Août-2023
Parasites Hosts Dis.
https://pubmed.ncbi.nlm.nih.gov/37648236/

High diversity and sharing of strongylid nematodes in humans and great apes co-habiting an unprotected area in Cameroon.

Ilík V, Kreisinger J, Modrý D, Schwarz EM, Tagg N, Mbohli D, Nkombou IC, Petrželková KJ, Pafčo B.
25-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37624869/

Rapid increases in human populations and environmental changes of past decades have led to changes in rates of contact and spatial overlap with wildlife. Together with other historical, social and environmental processes, this has significantly contributed to pathogen transmission in both directions, especially between humans and non-human primates, whose close phylogenetic relationship facilitates cross-infections. Using high-throughput amplicon sequencing, we studied strongylid communities in sympatric western lowland gorillas, central chimpanzees and humans co-occurring in an unprotected area in the northern periphery of the Dja Faunal Reserve, Cameroon. At the genus level, we classified 65 strongylid ITS-2 amplicon sequencing variants (ASVs) in humans and great apes. Great apes exhibited higher strongylid diversity than humans. Necator and Oesophagostomum were the most prevalent genera, and we commonly observed mixed infections of more than one strongylid species. Human strongylid communities were dominated by the human hookworm N. americanus, while great apes were mainly infected with N. gorillae, O. stephanostomum and trichostrongylids. We were also able to detect rare

strongylid taxa (such as Ancylostoma and Ternidens). We detected eight ASVs shared between humans and great apes (four N. americanus variants, two N. gorillae variants, one O. stephanostomum type I and one Trichostrongylus sp. type II variant). Our results show that knowledge of strongylid communities in primates, including humans, is still limited. Sharing the same habitat, especially outside protected areas (where access to the forest is not restricted), can enable mutual parasite exchange and can even override host phylogeny or conserved patterns. Such studies are critical for assessing the threats posed to all hosts by increasing human-wildlife spatial overlap. In this study, the term "contact" refers to physical contact, while "spatial overlap" refers to environmental contact.

Prevalence of Intestinal Parasitic Infections, Genotypes, and Drug Susceptibility of Giardia lamblia among Preschool and School-Aged Children: A Cross-Sectional Study in Thailand.

Wongstitwilairoong B, Anothaisintawee T, Ruamsap N, Lertsethtakarn P, Kietsiri P, Oransathid W, Oransathid W, Gonwong S, Silapong S, Suksawad U, Sornsakrin S, Bodhidatta L, Boudreaux DM, Livezey JR.
01-08-2023

This study aimed to estimate the prevalence of intestinal parasitic infections in children and assess the drug susceptibility and genotypes/assemblages of *Giardia lamblia* in Thailand. This cross-sectional study was conducted among children aged 3-12 years in Sangkhlaburi District, Kanchanaburi Province, Thailand, between 25 September 2017 and 12 January 2018. Parasites were identified by stool microscopic examination, cultivation of intestinal parasitic protozoa, and enzyme-linked immunosorbent assay (ELISA). Drug susceptibility and genotype of *G. lamblia* were performed, respectively, by a resazurin assay and Triosephosphate Isomerase A and B genes using modified primers and probes. Among the 661 participants, 445 had an intestinal parasitic infection, resulting in a prevalence of 67.32% (95% CI: 63.60-70.89%). *Blastocystis hominis* was the most prevalent protozoa infection (49.32%; 95% CI: 45.44-53.22%), while *Ascaris lumbricoides* was the most prevalent helminth infection (0.91%; 95% CI: 0.33-1.97%). The prevalence of *G. lamblia* was 17.40%, with genotype B being the most common. According to our study, intestinal parasitic infections were commonly found in Thai children. *G. lamblia* was the most common pathogenic protozoa infection identified and exhibited less susceptibility to metronidazole compared to furazolidone and mebendazole.

Prevalence of Intestinal Parasites, Risk Factors and Zoonotic Aspects in Dog and Cat Populations from Goiás, Brazil.

Souza JBB, Silva ZMA, Alves-Ribeiro BS, Moraes IS, Alves-Sobrinho AV, Saturnino KC, Ferraz HT, Machado MRF, Braga ÍA, Ramos DGS.
31-07-2023

Factors Associated with Carriage of Enteropathogenic and Non-Enteropathogenic Viruses: A Reanalysis of Matched Case-Control Data from the AFRIBIOTA Site in Antananarivo, Madagascar.

Razanajatovo IM, Andrianomiadana L, Habib A, Randrianarisoa MM, Razafimanjato H, Rakotondrainipiana M, Andriantsalama P, Randriamparany R, Andriamandimby SF, Vonaesch P, Sansonetti PJ, Lacoste V, Randremanana RV, Collard JM, Heraud JM, On Behalf Of The Afribiota Investigators.
02-08-2023

Environmental Enteric Dysfunction (EED) is an associate driver of stunting in poor settings, and intestinal infections indirectly contribute to the pathophysiology underlying EED. Our work aimed at assessing whether enteric viral carriage is determinant to stunting. A total of 464 healthy and asymptomatic children, aged 2 to 5 years, were recruited, and classified as non-stunted, moderately stunted, or severely stunted. Among the recruited children, 329 stool samples were obtained and screened for enteric and non-enteric viruses by real-time polymerase chain reaction. We statistically tested for the associations between enteric viral and potential risk factors. Approximately 51.7% of the stool samples were positive for at least one virus and 40.7% were positive for non-enteric adenoviruses. No statistical difference was observed between virus prevalence and the growth status of the children. We did not find any statistically significant association between viral infection and most of the socio-demographic risk factors studied, except for having an inadequate food quality score or an over-nourished mother. In addition, being positive for *Ascaris lumbricoides* was identified as a protective factor against viral infection. In conclusion, we did not find evidence of a direct link between stunting and enteropathogenic viral carriage in our population.

Negative association between ascaris lumbricoides seropositivity and Covid-19 severity: insights from a study in Benin.

Adjobimey T, Meyer J, Hennenfent A, Bara AJ, Lagnika L, Kocou B, Adjagba M, Laleye A, Hoerauf A, Parcina M.
09-08-2023

Introduction: The COVID-19 pandemic has had devastating effects worldwide, but the trajectory of the pandemic has been milder in Low-and-Middle-Income Countries (LMICs), including those in Africa. Co-infection with helminths, such as Ascaris lumbricoides, has been suggested as a possible factor contributing to the reduced severity observed in these regions. **Methods:** The present study investigated the association between Ascaris-specific antibody levels and COVID-19 severity in 276 SARS-CoV-2-infected

individuals in Benin. Participants were categorized into asymptomatic (n=100), mild (n=150), and severe (n=26) groups based on clinical disease severity. Sera were collected and analyzed using ELISA to measure Ascaris and SARS-CoV-2-specific antibodies, while Luminex was used to assess cytokines and SARS-CoV-2-specific neutralizing antibody expression. **Results and discussion:** The results demonstrated that asymptomatic SARS-CoV-2 seropositive individuals expressed, on average, 1.7 and 2.2-times higher levels of Ascaris antibodies compared to individuals with mild and severe COVID-19, respectively. This finding suggests an inverse correlation between Ascaris antibody levels and COVID-19 severity. Notably, logistic regression analysis showed that Ascaris seropositivity was significantly associated with a reduced risk of severe COVID-19 (OR = 0.277, p = 0.021). Interestingly, COVID-19 patients with comorbidities such as type 2 diabetes and high blood pressure showed lower expression of Ascaris antibodies. Strikingly, no correlation was observed between Ascaris antibody levels and SARS-CoV-2-specific neutralizing antibodies. On the other hand, individuals seronegative for Ascaris displayed significantly higher levels of systemic pro-inflammatory markers compared to seropositive individuals. These findings suggest that higher expression of Ascaris antibodies is associated with asymptomatic SARS-CoV-2 infections and may contribute to the reduction of the risk to develop severe COVID-19. The beneficial effect of Ascaris seropositivity on COVID-19 outcomes in Benin may be attributed to a decrease in comorbidities and pro-inflammatory markers. These observations provide valuable insights into the milder COVID-19 trajectory observed in Africa and may have implications for future therapeutic strategies.

Leishmaniose

Prevalence and incidence of canine visceral leishmaniasis and its clinical-immunological features in an endemic area of the Brazilian Amazon.

Carneiro LA, Lima LV, Campos MB, Vasconcelos Dos Santos T, Ramos PK, Laurenti MD, Silveira FT.

Background: A cohort study for 2 years period analysed the prevalence, incidence and clinical-immunological features of canine Leishmania (L.) chagasi-infection in 316 mongrel dogs in a visceral leishmaniasis-endemic area in Pará State, Brazil. **Objective/methods:** Diagnosis of infection was performed by the indirect fluorescent antibody test (IFAT-IgG), the leishmanin skin test (LST) and a parasite search (from the popliteal lymph node aspiration) at the beginning of the study and at 6, 12 and 24 months intervals. **Results:** IFAT/LST revealed three immune profiles of infection: (I) IFAT$^{(+)}$/LST$^{(-)}$ (81), (II) IFAT$^{(-)}$/LST$^{(+)}$ (17) and (III) IFAT$^{(+)}$/LST$^{(+)}$ (13). Prevalence of profiles I, II and III were 25.6, 5.4 and 4.1%, and an overall prevalence 35.1%. Incidence of profiles I, II and III were 5.4, 0.3 and 0.0%, and an overall incidence 5.7% dogs per month. Incidence at the

age ranges <1 year, ≥1 year, <7 years and ≥7 years evidenced a highest rate in the age range <1 year (6.6% dogs per month). Parasitological diagnosis was positive in 19% dogs at the prevalence (85.7% profile I), and in 11% at the incidence (100% profile I). The clinical picture of 179 infected dogs showed 145 (81%) of profile I (82% subclinical); 21 (11.7%) of profile II (100% subclinical); and 13 (7.3%) of profile III (84.6% subclinical). Conversion from subclinical to sick dogs was higher (p < 0.05) in profile I (40.2%) than in profiles II (5.8%) and III (9%). Immunological conversion showed that only 3.2% of profile I dogs (prevalence) converted to LST$^{(+)}$ (two at the end of the first 6 months and 1 after 24 months), while 82.3% of profile II dogs converted to IFAT$^{(+)}$ (11 in the first 6 months, whereas three after 12 months). A 100% death rate was observed in dogs from profile I alone. **Conclusion:** These results reinforce the need of adopting preventive strategies against CVL as early as in the first semester of the dog's life.

Effects of host species on microbiota composition in Phlebotomus and Lutzomyia sand flies.

Tabbabi A, Mizushima D, Yamamoto DS, Kato H.

Exposure to Trypanosoma cruzi and Leishmania parasites in dogs from a rural locality of Yucatan, Mexico. A serological survey.

Reyes-Novelo E, Sauri-Arceo C, Panti-May A, Marín D, Canché-Pool EB, Chan-Espinoza DE, Marín C, Bolio-González M, Rodríguez-Vivas RI, Torres-Castro M, Escobedo-Ortegón FJ.

Canine Leishmania spp. infection in two distinct foci of visceral and cutaneous leishmaniasis in Tunisia.

Zribi L, El Houda Ben-Fayala N, Aissi W, Ben-Abid M, Souissi O, Hamdi N, Boulehmi N, Ghrab J, Jemni A, Jamel A, Handous M, Bouratbine A, Oliva G, Aoun K.

Visceral leishmaniasis (VL) and zoonotic cutaneous leishmaniasis (ZCL) caused by Leishmania (L.) infantum and L. major, respectively, are endemic in Tunisia. The aim of the study was to assess canine Leishmania spp. infection prevalence as well as to identify the Leishmania species involved in two well-documented and geographically distinct VL and ZCL foci. One hundred seventy-six dogs were randomly recruited in the VL focus of Sbikha-Zaghouan (n = 100) and the ZCL focus of Echrarda-Nasrallah (n = 76). Physical examination and blood collection were systemically performed. Needle aspiration was done in case of lymph node (LN) enlargement. All sera

were tested by ELISA. kDNA RT-PCR was performed on DNA extracts from (i) buffy coats of seropositive dogs and (ii) LN aspirates. Leishmania species identification was done by ITS1 PCR-sequencing. Thirty-three dogs (18.8%) were infected by Leishmania; 30 having anti-Leishmania antibodies and 3 were seronegative dogs with Leishmania DNA in LN aspirates. Prevalence of infection was significantly higher in VL foci than in ZCL foci (27% versus 7.9%, p = 0.002). Leishmania species was identified in 11 dogs and corresponded to L. infantum. Combination of serology and qPCR on LN aspirates seems to be the best option for canine leishmaniasis diagnosis. Infection is more frequent in VL foci and L. infantum is the only identified species.

Characterisation of TcFUT1, a mitochondrial fucosyltransferase from Trypanosoma cruzi.

Franco JCP, Guther MLS, Lima ML, Ferguson MAJ.

Previous work has shown that the TbFUT1 and LmjFUT1 genes encode essential fucosyltransferases located inside the single mitochondria of the protozoan parasites Trypanosoma brucei and Leishmania major, respectively. However, nothing was known about the orthologous gene TcFUT1 or its gene product in Trypanosoma cruzi, aetiological agent of Chagas disease. In this study, we describe the overexpression of TcFUT1 with a C-terminal 6xMyc epitope tag in T. cruzi epimastigote cells. Overexpressed and immunoprecipitated TcFUT1-6xMyc was used to demonstrate enzymatic activity and to explore substrate specificity. This defined TcFUT1 as a GDP-Fuc : βGal α1-2 fucosyltransferase with a strict requirement for acceptor glycans with non-reducing terminal Galβ1-3GlcNAc structures. This differs from the specificity of the T. brucei orthologue TbFUT1, which can also tolerate non-reducing terminal Galβ1-4GlcNAc and Galβ1-4Glc acceptor sites. Immunofluorescence microscopy using α-Myc tag antibodies also showed a mitochondrial location for TcFUT1 in T. cruzi epimastigote cells. Collectively, these results are like those described for TbFUT1 and LmjFUT1 from T. brucei and L. major, suggesting that FUT1 gene products have conserved function for across the trypanosomatids and may share therapeutic target potential.

PD-1 negatively tunes macrophage immune activation by turning off JNK and STAT1 signaling: Exploited by Leishmania for its intra-macrophage survival.

Roy S, Gupta AK, Banerjee M, Das PK, Ukil A.

Antileishmanial effects, cellular mechanisms, and cytotoxicity of

Elettaria cardamomum essential oil against Leishmania major infection.

Majeed QA, Alshammari A, Alanazi AD.

Leishmaniasis is an infectious disease with various clinical manifestations. We studied the therapeutic effects of Elettaria cardamomum essential oil (ECEO) against Leishmania major infection. In vitro effects of ECEO against L. major were examined by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) and macrophage assays. Nitric oxide (NO) production, infection inhibition in macrophages, and the apoptotic activity of ECEO in treated parasites were also measured. By calculating the 50% cytotoxic concentrations (CC_{50}), we studied the cytotoxicity effects of ECEO on human macrophage cells (THP-1). The efficacy of ECEO for improving cutaneous leishmaniasis (CL) lesions in mice (BALB/c) was determined by evaluating the size of lesions and the number of amastigotes before and after four weeks of treatment. The effects of ECEO on liver and kidney function in the tested mice were also evaluated. ECEO dose-dependently (p<0.001) inhibited the viability and the mean number of promastigotes and amastigote forms of L. tropica. Four weeks of treatment with ECEO at the doses of 2.5 and 5 mg/kg/ day significantly (p<0.001) improved the CL lesions and reduced the number of parasites in the infected mice. ECEO significantly increased NO production, apoptosis induction, and infection rate in parasites. The CC_{50} value for ECEO and MA was 303.4 μg/mL and 835.2 μg/mL, respectively. In the mice receiving ECEO at the doses of 2.5 and 5 mg/kg/day for 28 days, no significant change was reported between the serum level of liver enzymes and kidney factors when compared with the control group. ECEO displayed promising efficacy in parasite reduction in vitro and in the animal model. ECEO can thus be used as an alternative medicine to treat CL.

A case report of an uncommon presentation of cutaneous leishmaniasis: A nose lesion.

Alamin AA, Gebreyesus MW, Mohamed I.

Species diversity and detection of pathogens in phlebotomine sand flies collected from forest management areas of Quintana Roo, Mexico.

Martínez-Burgos M, Lozano-Sardaneta YN, Rodríguez-Rojas JJ, Gómez-Rivera ÁS, Canto-Mis KL, Flores-Escobar E, Mis-Ávila PC, Correa-Morales F, Becker I.

Sand flies have expanded their areas of distribution, thereby increasing the risk of pathogen transmission in non-endemic areas. To establish efficient prevention and

control strategies for the transmission of vector-borne pathogens, it is important to understand seasonal dynamics of their vectors. In Mexico, there are several areas where the contact between sand flies, hosts and reservoirs favours the transmission of the pathogen. We compared sand fly communities in a forest management area and a conserved area in Noh-Bec, Quintana Roo, Mexico. The analysis included species diversity, activity peaks and molecular detection of pathogens. Sand flies were collected from November to December 2021 and April to May 2022, during 84 night-traps. The conserved area showed higher numbers and greater species heterogeneity of sand flies as compared with the other sites. The β-diversity analysis revealed that sites disturbed by logging (S1, S2, S3) had greater similarity (90%) in their sand fly species composition than a conserved area (S4) (similarity = 36%). Although none of the specimens were infected with Leishmania, we detected Wolbachia (19.4%) in all four sites, as well as Bartonella (3.25%) only in the disturbed sites. Further studies on the dynamics of sand fly populations and their association with pathogens are necessary.

Metabolomics analysis of visceral leishmaniasis based on urine of golden hamsters.

Yuan D, Chen J, Zhao Z, Qin H.
30-08-2023
Parasit Vectors.
https://pubmed.ncbi.nlm.nih.gov/37649093/

Increased Risk of American Tegumentary Leishmaniasis in an Urban and Rural Area of Caratinga, Brazil between 2016 and 2021.

Neves RL, Ker FTO, Dutra-Rêgo F, Rugani JMN, Andrade Filho JD, Soares RP, Gontijo CMF.
28-08-2023
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/37640295/

Evaluation of farnesol orally and topically against experimental cutaneous leishmaniasis: In -vivo analysis.

Sharma H, Sehgal R, Jhacak S, Deshmukh K, Nada R.
28-08-2023
PLoS One.
https://pubmed.ncbi.nlm.nih.gov/37639393/

Leishmaniasis is a zoonotic disease transmitted by an obligate intra-macrophage protozoan of the genus Leishmania through the infective bite of a vector sandfly. This study investigated the therapeutic efficacy of farnesol, a sesquiterpene compound, for the treatment of cutaneous leishmaniasis (CL) using in vivo BALB/c mouse model. In this study, farnesol's efficacy was compared with the standard drug, paromomycin. It was observed that farnesol significantly reduced lesion sizes and footpad thickness compared to the control group (paromomycin). Lymph node size was also significantly reduced in farnesol-treated mice, indicating its ability to control infection spread. Combination therapy with farnesol and Paromomycin did not demonstrate synergistic effects. These results highlight the potential of farnesol as an alternative therapeutic agent for CL. Further investigations are required to elucidate its mechanism of action and assess potential off-target effects. Optimization of oral delivery methods should be explored to enhance bioavailability. Overall, our findings support farnesol's efficacy in CL treatment, offering promising prospects for improved disease management.

Post kala-azar dermal leishmaniasis in the Indian sub-continent: challenges and strategies for elimination.

Kumar A, Singh VK, Tiwari R, Madhukar P, Rajneesh, Kumar S, Gautam V, Engwerda C, Sundar S, Kumar R.
11-08-2023
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/37638047/

Visceral leishmaniasis (VL) is a severe and often fatal form of leishmaniasis caused by *Leishmania donovani* in the Indian sub-continent. Post Kala-azar Dermal Leishmaniasis (PKDL) is a late cutaneous manifestation of VL, typically occurring after apparent cure of VL, but sometimes even without a prior history of VL in India. PKDL serves as a significant yet neglected reservoir of infection and plays a crucial role in the transmission of the disease, posing a serious threat to the VL elimination program in the Indian sub-continent. Therefore, the eradication of PKDL should be a priority within the current VL elimination program aimed at achieving a goal of less than 1 case per 10,000 in the population at the district or sub-district levels of VL endemic areas. To accomplish this, a comprehensive understanding of the pathogenesis of PKDL is essential, as well as developing strategies for disease management. This review provides an overview of the current status of diagnosis and treatment options for PKDL, highlighting our current knowledge of the immune responses underlying disease development and progression. Additionally, the review discusses the impact of PKDL on elimination programs and propose strategies to overcome this challenge and achieve the goal of elimination. By addressing the diagnostic and therapeutic gaps, optimizing surveillance and control measures, and implementing effective intervention strategies, it is possible to mitigate the burden of PKDL and facilitate the successful elimination of VL in the Indian sub-continent.

Intramacrophage lipid accumulation compromises T cell responses and is associated with impaired drug therapy against visceral leishmaniasis.

Araújo M, Moreira D, Mesquita I, Ferreira C, Mendes-Frias A, Barros-Carvalho S, Dinis-Oliveira RJ, Duarte-Oliveira C, Cunha C, Carvalho A, Saha B, Cordeiro-da-Silva A, Estaquier J, Silvestre R.
27-08-2023
Immunology.
https://pubmed.ncbi.nlm.nih.gov/37635289/

Under perturbing conditions such as infection with Leishmania, a protozoan parasite living within the phagosomes in mammalian macrophages, cellular and

organellar structures, and metabolism are dynamically regulated for neutralizing the pressure of parasitism. However, how modulations of the host cell metabolic pathways support Leishmania infection remains unknown. Herein, we report that lipid accumulation heightens the susceptibility of mice to L. donovani infection and promotes resistance to first-line anti-leishmanial drugs. Despite being pro-inflammatory, the in vitro generated uninfected lipid-laden macrophages (LLMs) or adipose-tissue macrophages (ATMs) display lower levels of reactive oxygen and nitrogen species. Upon infection, LLMs secrete higher IL-10 and lower IL-12p70 cytokines, inhibiting CD4^{+} T cell activation and Th1 response suggesting a key modulatory role for intramacrophage lipid accumulation in anti-leishmanial host defence. We, therefore, examined this causal relationship between lipids and immunomodulation using an in vivo high-fat diet (HFD) mouse model. HFD increased the susceptibility to L. donovani infection accompanied by a defective CD4^{+} Th1 and CD8^{+} T cell response. The white adipose tissue of HFD mice displays increased susceptibility to L. donovani infection with the preferential infection of F4/80^{+} CD11b^{+} CD11c^{+} macrophages with higher levels of neutral lipids reserve. The HFD increased resistance to a first-line anti-leishmanial drug associated with a defective adaptive immune response. These data demonstrate that the accumulation of neutral lipids contributes to susceptibility to visceral leishmaniasis hindering host-protective immune response and reducing the efficacy of antiparasitic drug therapies.

Clinical findings and prognostic factors for mortality in hospitalized dogs with leishmaniosis: aretrospective study.

Molina CC, Dias MJ, Domingues TD, Englar RE, Leal RO.
23-08-2023
Comp Immunol Microbiol Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37634471/

Intramuscular Immunization with a Liposomal Multi-Epitope Chimeric Protein Induces Strong Cellular Immune Responses against Visceral Leishmaniasis.

Agallou M, Margaroni M, Karagouni E.
19-08-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631952/

Polymeric Delivery Systems as a Potential Vaccine against Visceral Leishmaniasis: Formulation Development and Immunogenicity.

Silva JGLD, Gonçalves AAM, Oliveira LT, Garcia GM, Batista MA, Mendonça LZ, Viana KF, Sant'Ana RCO, Melo Júnior OAO, Silveira-Lemos D, Dutra WO, Martins-Filho OA, Galdino AS, de Moura SAL, Mosqueira VCF, Giunchetti RC.
31-07-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631877/

Recent studies suggest that the association of antigens in microparticles increases the anti-*Leishmania* vaccine immunogenicity. This study aims to investigate the in situ effect of the adjuvant performance consisting of chitosan-coated poly(*D,L*-lactic) acid submicrometric particles (SMP) and analyze the inflammatory profile and toxicity. Two formulations were selected, SMP[1], containing poly(*D,L*-lactide) (PLA) 1% *wt/v* and chitosan 1% *wt/v*; and SMP[2], containing PLA 5% *wt/v* and chitosan 5% *wt/v*. After a single dose of the unloaded SMP[1] or SMP[2] in mice, the SMPs promoted cell recruitment without tissue damage. In addition, besides the myeloperoxidase (MPO) activity having demonstrated similar results among the analyzed groups, a progressive reduction in the levels of N-acetyl-β-$_D$-glucosaminidase (NAG) until 72 h was observed for SMPs. While IL-6 levels were similar among all the analyzed groups along the kinetics, only the SMPs groups had detectable levels of TNF-α. Additionally, the *Leishmania braziliensis* antigen was encapsulated in SMPs (SMP[1]Ag and SMP[2]Ag), and mice were vaccinated with three doses. The immunogenicity analysis by flow cytometry demonstrated a reduction in NK (CD3^{-}CD49^{+}) cells in all the SMPs groups, in addition to impairment in the T cells subsets (CD3^{+}CD4^{+}) and CD3^{+}CD8^{+}) and B cells (CD19^{+}) of the SMP[2] group. The resulting data demonstrate that the chitosan-coated SMP formulations stimulate the early events of an innate immune response, suggesting their ability to increase the immunogenicity of co-administered *Leishmania* antigens.

Development of Environmentally Responsive Self-Emulsifying System Containing Copaiba Oil-Resin for Leishmaniasis Oral Treatment.

de Oliveira MC, Balbinot RB, Villa Nova M, Gonçalves RS, Bidóia DL, Caetano W, Nakamura CV, Bruschi ML.
12-08-2023
Pharmaceutics.
https://pubmed.ncbi.nlm.nih.gov/37631341/

Triose Phosphate Isomerase Structure-Based Virtual Screening and In Vitro Biological Activity of Natural Products as Leishmania mexicana Inhibitors.

González-Morales LD, Moreno-Rodríguez A, Vázquez-Jiménez LK, Delgado-Maldonado T, Juárez-Saldivar A, Ortiz-Pérez E, Paz-Gonzalez AD, Lara-Ramírez EE, Yépez-Mulia L, Meza P, Rivera G.
29-07-2023
Pharmaceutics.
https://pubmed.ncbi.nlm.nih.gov/37631260/

Cutaneous leishmaniasis (CL) is a public health problem affecting more than 98 countries worldwide. No vaccine is available to prevent the disease, and available medical treatments cause serious side effects. Additionally, treatment failure and parasite resistance have made the development of new drugs against CL necessary. In this work, a virtual screening of natural products from the BIOFACQUIM and Selleckchem databases was performed using the method of molecular docking at the triosephosphate isomerase (TIM) enzyme interface of

Leishmania mexicana (*L. mexicana*). Finally, the in vitro leishmanicidal activity of selected compounds against two strains of *L. mexicana*, their cytotoxicity, and selectivity index were determined. The top ten compounds were obtained based on the docking results. Four were selected for further in silico analysis. The ADME-Tox analysis of the selected compounds predicted favorable physicochemical and toxicological properties. Among these four compounds, **S-8** (IC_{50} = 55 µM) demonstrated a two-fold higher activity against the promastigote of both *L. mexicana* strains than the reference drug glucantime (IC_{50} = 133 µM). This finding encourages the screening of natural products as new anti-leishmania agents.

Design and Synthesis of New Anthranyl Phenylhydrazides: Antileishmanial Activity and Structure-Activity Relationship.

do Carmo Maquiaveli C, da Silva ER, Hild de Jesus B, Oliveira Monteiro CE, Rodrigues Navarro T, Pereira Branco LO, Souza Dos Santos I, Figueiredo Reis N, Portugal AB, Mendes Wanderley JL, Borges Farias A, Correia Romeiro N, de Lima EC.
09-08-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631035/

Leishmaniasis is a neglected tropical disease affecting millions of people worldwide. A centenary approach to antimonial-based drugs was first initiated with the synthesis of urea stibamine by Upendranath Brahmachari in 1922. The need for new drug development led to resistance toward antimoniates. New drug development to treat leishmaniasis is urgently needed. In this way, searching for new substances with antileishmanial activity, we synthesized ten anthranyl phenylhydrazide and three quinazolinone derivatives and evaluated them against promastigotes and the intracellular amastigotes of *Leishmania amazonensis*. Three compounds showed good activity against promastigotes 1b, 1d, and 1g, with IC_{50} between 1 and 5 µM. These new phenylhydrazides were tested against *Leishmania* arginase, but they all failed to inhibit this parasite enzyme, as we have shown in a previous study. To explain the possible mechanism of action, we proposed the enzyme PTR1 as a new target for these compounds based on in silico analysis. In conclusion, the new anthranyl hydrazide derivatives can be a promising scaffold for developing new substances against the protozoa parasite.

Synthesis of 1,2,3-Triazole-Containing Methoxylated Cinnamides and Their Antileishmanial Activity against the Leishmania braziliensis Species.

Santos FSD, Freitas RP, Freitas CS, Mendonça DVC, Lage DP, Tavares GSV, Machado AS, Martins VT, Costa AV, Queiroz VT, de Oliveira MB, Oliveira FM, Antinarelli LMR, Coimbra ES, Pilau EJ, da Silva GP, Coelho EAF, Teixeira RR.
07-08-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631028/

Transcriptome Analysis Identifies the Crosstalk between Dendritic and Natural Killer Cells in Human Cutaneous Leishmaniasis.

Nunes S, Tibúrcio R, Bonyek-Silva I, Oliveira PR, Khouri R, Boaventura V, Barral A, Brodskyn C, Tavares NM.
29-07-2023
Microorganisms.
https://pubmed.ncbi.nlm.nih.gov/37630497/

Refinement of Leishmania donovani Genome Annotations in the Light of Ribosome-Protected mRNAs Fragments (Ribo-Seq Data).

Sánchez-Salvador A, González-de la Fuente S, Aguado B, Yates PA, Requena JM.
17-08-2023
Genes (Basel).
https://pubmed.ncbi.nlm.nih.gov/37628688/

Biomolecular Minerals and Volcanic Glass Bio-Mimics to Control Adult Sand Flies, the Vector of Human Leishmania Protozoan Parasites.

Chen K, Deguenon JM, Lawrie RD, Roe RM.
10-08-2023
Biomolecules.
https://pubmed.ncbi.nlm.nih.gov/37627300/

Treatment of Cutaneous Leishmaniasis with Sodium Stibogluconate and Allopurinol in a Routine Setting in Ethiopia: Clinical and Patient-Reported Outcomes and Operational Challenges.

van Henten S, Bialfew F, Hassen S, Tilahun F, van Griensven J, Abdela SG.
14-08-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624352/

Cutaneous leishmaniasis (CL) is common in Ethiopia, but the national guideline does not offer specific treatment recommendations. Consequently, different treatment regimens are used in the country, without quality evidence. In Boru Meda Hospital, sodium stibogluconate (SSG) is routinely used in combination with allopurinol for systemic CL treatment, although evidence on its effectiveness is limited. An observational cohort study was carried out to document clinical treatment outcomes in patients receiving SSG/allopurinol at the end of each 28-day treatment cycle and after 180 days. Patient-reported outcomes were assessed by asking patients to rate lesion severity, and by the dermatological life quality index. A total of 104 patients were included. After one treatment cycle, only four patients were clinically cured, although patient-reported outcomes significantly improved. The majority (88) of patients were appointed for a second treatment cycle, of whom only 37 (42%) attended. Among the 36 patients who came for final outcome assessment, 50% were cured. Follow-up and treatment were severely affected by conflict; drug stock-outs and insufficient ward

capacity for treatment were additional challenges. The treatment outcomes of SSG/allopurinol were relatively poor, and most patients required more than one cycle of treatment. Shortages of drugs and beds indicate the existing gaps in providing CL treatment in Ethiopia.

Rectal Administration of Leishmania Cells Elicits a Specific, Th1-Associated IgG2a Response in Mice: New Perspectives for Mucosal Vaccination against Leishmaniasis, after the Repurposing of a Study on an Anti-Viral Vaccine Candidate.

Varotto-Boccazzi I, Epis S, Cattaneo GM, Guerrini N, Manenti A, Rubolini D, Gabrieli P, Otranto D, Zuccotti G, Montomoli E, Bandi C.
09-08-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624344/

The mucosal immune system plays a pivotal role in the control of infections, as it represents the first line of defense against most pathogens, from respiratory viruses to intestinal parasites. Mucosal vaccination is thus regarded as a promising strategy to protect animals, including humans, from infections that are acquired by ingestion, inhalation or through the urogenital system. In addition, antigens delivered at the mucosal level can also elicit systemic immune responses. Therefore, mucosal vaccination is potentially effective also against systemic infections acquired through non-mucosal routes, for example, through the bite of hematophagous insects, as in the case of leishmaniasis, a widespread disease that affects humans and dogs. Here, we explored the potential of antigen rectal administration for the generation of anti-*Leishmania* immunity. Mice were immunized through rectal administration of whole cells of the model parasite *Leishmania tarentolae* (using a clone engineered to express the spike protein of the SARS-CoV-2 virus generated in a previous study). A specific anti-*Leishmania* IgG antibody response was detected. In addition, the recorded IgG2a/IgG1 ratio was higher than that of animals injected subcutaneously; therefore, suggesting a shift to a Th1-biased immune response. Considering the importance of a Th1 polarization as a protective response against *Leishmania* infections, we suggest that further investigation should be focused on the development of novel types of vaccines against these parasites based on rectal immunization.

Parasite Detection in Visceral Leishmaniasis Samples by Dye-Based qPCR Using New Gene Targets of Leishmania infantum and Crithidia.

Takamiya NT, Rogerio LA, Torres C, Leonel JAF, Vioti G, de Sousa Oliveira TMF, Valeriano KC, Porcino GN, de Miranda Santos IKF, Costa CHN, Costa DL, Ferreira TS, Gurgel-Gonçalves R, da Silva JS, Teixeira FR, De Almeida RP, Ribeiro JMC, Maruyama SR.
08-08-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624343/

Kinetoplast Genome of Leishmania spp. Is under Strong Purifying Selection.

Gerasimov ES, Novozhilova TS, Zimmer SL, Yurchenko V.
27-07-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624322/

Instability is an intriguing characteristic of many protist genomes, and trypanosomatids are not an exception in this respect. Some regions of trypanosomatid genomes evolve fast. For instance, the trypanosomatid mitochondrial (kinetoplast) genome consists of fairly conserved maxicircle and minicircle molecules that can, nevertheless, possess high nucleotide substitution rates between closely related strains. Recent experiments have demonstrated that rapid laboratory evolution can result in the non-functionality of multiple genes of kinetoplast genomes due to the accumulation of mutations or loss of critical genomic components. An example of a loss of critical components is the reported loss of entire minicircle classes in *Leishmania tarentolae* during laboratory cultivation, which results in an inability to generate some correctly encoded genes. In the current work, we estimated the evolutionary rates of mitochondrial and nuclear genome regions of multiple natural *Leishmania* spp. We analyzed synonymous and non-synonymous substitutions and, rather unexpectedly, found that the coding regions of kinetoplast maxicircles are among the most variable regions of both genomes. In addition, we demonstrate that synonymous substitutions greatly predominate among maxicircle coding regions and that most maxicircle genes show signs of purifying selection. These results imply that maxicircles in natural *Leishmania* populations remain functional despite their high mutation rate.

Schistosoma and Leishmania: An Untold Story of Coinfection.

Camelo GMA, Silva JKAO, Geiger SM, Melo MN, Negrão-Corrêa DA.
27-07-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624321/

The Program for the Control of Visceral Leishmaniasis in Brazil: The Effect of the Systematic Euthanasia of Seropositive Dogs as a Single Control Action in Porteirinha, a Brazilian City with an Intense Transmission of Visceral Leishmaniasis.

França-Silva JC, Giunchetti RC, Mariano RMDS, Machado-Coelho GLL, Teixeira LAS, Barata RA, Michalsky ÉM, Rocha MF, Fortes-Dias CL, Dias ES.
18-08-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37624020/

Occurrence of Leishmania infantum in Wild Mammals Admitted to Recovery Centers in Spain.

Azami-Conesa I, Pérez-Moreno P, Matas Méndez P, Sansano-Maestre J, González F, Mateo Barrientos M, Gómez-Muñoz MT.
16-08-2023
Pathogens.

Zoonotic leishmaniasis caused by *Leishmania infantum* is distributed worldwide and affects humans and domestic and wild mammals. In Europe, specifically in the Mediterranean basin, leishmaniasis is endemic due to the concurrence of the phlebotomine vectors and reservoir mammals, including carnivorous wildlife species and other less studied wild species. In this article, spleen, skin, and eye or oral swabs taken from 134 wild mammals admitted to five wildlife recovery centers in Spain were used. PCR employing fragments of the Repeat region, ITS1, and SSUrRNA were used for detection, and positive samples were processed for sequencing. *L. infantum* was detected in three out of the nine species analyzed, including European hedgehog, European badger, and red squirrel, with percentages ranging from 11.53 to 35.71%, depending on the species. Most of the species showed higher percentages of positivity in spleen samples than in skin samples. A small number of animals from the remaining six species tested negative, including Algerian hedgehog, stone marten, least weasel, garden dormouse, western polecat, and Egyptian mongoose. Hedgehogs and badgers are good candidates for consideration as epidemiological sentinels and pose a higher risk as potential reservoirs of leishmaniasis based on their percentage of infection and wide distribution.

Dogs Harbor Leishmania braziliensis and Participate in the Transmission Cycle of Human Tegumentary Leishmaniasis.

Lago J, Fraga D, Coelho L, Jesus MS, Leite B, Werneck GL, Arruda S, Lago E, Carvalho EM, Bacellar O.
27-07-2023
Pathogens.

Rapid and Highly Sensitive Detection of Leishmania by Combining Recombinase Polymerase Amplification and Solution-Processed Oxide Thin-Film Transistor Technology.

Wu W, Biyani M, Hirose D, Takamura Y.
28-07-2023
Biosensors (Basel).
,

Niosome as an Effective Nanoscale Solution for the Treatment of Microbial Infections.

Barani M, Paknia F, Roostaee M, Kavyani B, Kalantar-Neyestanaki D, Ajalli N, Amirbeigi A.
16-08-2023
Biomed Res Int.

Numerous disorders go untreated owing to a lack of a suitable drug delivery technology or an appropriate therapeutic moiety, particularly when toxicities and side effects are a major concern. Treatment options for microbiological infections are not fulfilled owing to significant adverse effects or extended therapeutic options. Advanced therapy options, such as active targeting, may be preferable to traditional ways of treating infectious diseases. Niosomes can be defined as microscopic lamellar molecules formed by a mixture of cholesterol, nonionic surfactants (alkyl or dialkyl polyglycerol ethers), and sometimes charge-inducing agents. These molecules comprise both hydrophilic and hydrophobic moieties of varying solubilities. In this review, several pathogenic microbes such as *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, Plasmodium, Leishmania,* and *Candida* spp. have been evaluated. Also, the development of a proper niosomal formulation for the required application was discussed. This review also reviews that an optimal formulation is dependent on several aspects, including the choice of nonionic surfactant, fabrication process, and fabrication parameters. Finally, this review will give information on the effectiveness of niosomes in treating acute microbial infections, the mechanism of action of niosomes in combating microbial pathogens, and the advantages of using niosomes over other treatment modalities.

TLR-2 agonist Pam3CSK4 has no therapeutic effect on visceral leishmaniasis in BALB/c mice and may enhance the pathogenesis of the disease.

Liao X, He J, Wang R, Zhang J, Wei S, Xiao Y, Zhou Q, Zheng X, Zhu Z, Zheng Z, Li J, Zeng Z, Chen D, Chen J.
Sept-2023
Immunobiology.

Most of the existing Leishmania-related research about TLR-2 agonists was focusing on their role as adjuvants in the vaccine, few studied its therapeutic effect. This paper aims to explore the therapeutic effect of TLR-2 agonist Pam3CSK4 on Leishmania-infected mice and the underlying immune molecular mechanisms. In L. donovani-infected BALB/c mice, one group was treated with Pam3CSK4 after infection and the other group was not treated. Normal uninfected mice treated with Pam3CSK4 or untreated were used as controls. Parasite load, hepatic pathology and serum antibodies were detected to assess the severity of the infection. The expression of immune-related genes, spleen lymphocyte subsets and liver RNA-seq were employed to reveal possible molecular mechanisms. The results showed that the liver and spleen parasite load of infected mice in Pam3CSK4 treated and untreated groups had no statistical difference, indicating Pam3CSK4 might have no therapeutic effect on visceral leishmaniasis. Infected mice treated with Pam3CSK4 possessed more hepatic inflammation focus, lower IgG and IgG2a antibody titers, and a lower proportion of spleen $CD3^+CD4^+$ T cells. Transcriptome analysis revealed that Th1/Th2 differentiation, NK cells, Th17 cell, complement system and calcium signaling pathways were down-regulated

post-treatment of Pam3CSK4. In this study, TLR-2 agonist Pam3CSK4 showed no therapeutic effect on visceral leishmaniasis in BALB/c mice and might enhance the pathogenesis of the disease possibly due to the down-regulation of several immune-related pathways, which can improve our understanding of the role of TLR-2 in both treatment and vaccine development.

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

Banerjee S, Datta R.
Août-2023
J Biol Chem.

Visceral Leishmaniasis Caused by Leishmania Tropica.

Özbilgin A, Tunalı V, Çavuş İ, Tetik AV, Dinç M, Yalçın T, Gündüz C, Beyaz M, Köse Ş.
Sept-2023
Acta Parasitol.

Purpose: In Turkey, the main causative agent of visceral leishmaniasis (VL) is Leishmania. infantum and the main causative agent of cutaneous leishmaniasis (CL) is Leishmania tropica. In this study, we aimed to discuss the possible mechanisms, clinical aspects, and threat of visceralizing L. tropica. **Methods:** This study includes seven cases of VL caused by L. tropica.Five patients were male (71%) and four were adults (57%). **Results:** All the VL patients complained of fever and splenomegaly. Fatigue, pancytopenia, and hepatomegaly were present in six patients each (86%), while weight loss and gastrointestinal system (GIS) symptoms were present in 5 patients (71%). **Conclusions:** In this study, we have evaluated seven cases of visceralized L. tropica (VLT) in the context of the changing leishmaniasis epidemiology in Turkey. We have evaluated the possible mechanisms of visceralization; inter- and intraspecies genetic exchange with all the old world leishmaniasis agents present in the region, stress induced by inappropriate use of drugs, and possible ongoing adaptation mechanisms of Leishmania spp. The threat posed by VLT is significant as L. tropica is the most widespread and most common cause of leishmaniasis in Turkey. We do not know the vectorial capacity of the sand flies for the transmission of VLT strains or if these strains are in circulation in Turkey. Future studies should be carried out to investigate these issues as the transition of L. tropica from a mild disease-causing agent to a mortal one poses a significant public health concern for Turkey and Europe.

Molecular Detection of Leishmania in Wild Caught Sand Flies of Larroussius Subgenus in Iran: Combined Use of Internal and External Morphological Characters as a Mean to Differentiate Morphologically Similar Females.

Vaziri VM, Behniafar H, Spotin A, Absavarand A, Badakhshan M.

Sept-2023
Acta Parasitol.

Molecular Targets for Chalcones in Antileishmanial Drug Discovery.

de Santiago-Silva KM, da Silva Gomes GF, Perez CC, da Silva Lima CH, de Lima Ferreira Bispo M.
2023
Mini Rev Med Chem.

Lèpre

Improving measurement of tuberculosis care cascades to enhance people-centred care.

Faust L, Naidoo P, Caceres-Cardenas G, Ugarte-Gil C, Muyoyeta M, Kerkhoff AD, Nagarajan K, Satyanarayana S, Rakotosamimanana N, Grandjean Lapierre S, Adejumo OA, Kuye J, Oga-Omenka C, Pai M, Subbaraman R.
28-08-2023
Lancet Infect Dis.

Care cascades represent the proportion of people reaching milestones in care for a disease and are widely used to track progress towards global targets for HIV and other diseases. Despite recent progress in estimating care cascades for tuberculosis (TB) disease, they have not been routinely applied at national and subnational levels, representing a lost opportunity for public health impact. As researchers who have estimated TB care cascades in high-incidence countries (India, Madagascar, Nigeria, Peru, South Africa, and Zambia), we describe the utility of care cascades and identify measurement challenges, including the lack of population-based disease burden data and electronic data capture, the under-reporting of people with TB navigating fragmented and privatised health systems, the heterogeneity of TB tests, and the lack of post-treatment follow-up. We outline an agenda for rectifying these gaps and argue that improving care cascade measurement is crucial to enhancing people-centred care and achieving the End TB goals.

The complex relationship between iron status and anemia in pregnant and postpartum women in India: Analysis of two Indian study cohorts of uncomplicated pregnancies.

Nair M, Choudhury SS, Rani A, Solomi C 5th, Kakoty SD, Medhi R, Rao S, Mahanta P, Zahir F, Roy I, Chhabra S, Deka G, Minz B, Deka R, Opondo C, Churchill D, Lakhal-Littleton S, Nemeth E; MaatHRI collaboration.
31-08-2023
Am J Hematol.

Current status of infectious diseases among migrants and non-citizens in Malaysia.

Mohd Putera NWS, Azman AS, Mohd Zain SN, Yahaya H, Lewis JW, Sahimin N.

The mass movement of migrants to Malaysia for employment is one of the factors contributing to the emergence and re-emergence of infectious diseases in this country. Despite mandatory health screening for migrants seeking employment, prevalence records of infectious diseases amongst migrant populations in Malaysia are still within negligible proportions. Therefore, the present review highlights the incidence, mortality and overall status of infectious diseases amongst migrants' populations in Malaysia, which maybe be useful for impeding exacerbation of inequalities among them and improving our national health system thru robust and effective emergency responses in controlling the prevalent diseases found among these populations and maybe, Malaysian citizens too. Peer-reviewed articles from January 2016 to December 2020 were searched through online platform including SCOPUS, PubMed, Science Direct, and Google Scholar. Non-peer-reviewed reports and publications from ministry and government websites including data from related agencies were also scoured from in order to ensure that there are no cases being overlooked, as most published articles did not have migrants as the research subjects. A total of 29 studies had been selected in the final analysis. Migrants in Malaysia were at higher risk for tuberculosis, malaria, lymphatic filariasis, cholera, leprosy and leptospirosis. Lymphatic filariasis was still endemic among this population while thousand cases of TB and cholera had been reported among them due to cramp living conditions and poor sanitation in their settlements respectively. While malaria had gradually decreased and become sporadic, the influx of migrant workers had led to the rising of imported malaria cases. Low cases of leprosy had been recorded in Malaysia but a significant proportion of it was contributed by migrant workers. As for leptospirosis, studies found that there are prominent cases among migrant workers, which particularly highest within workers with lower educational attainment. Infectious diseases are still prevalent among migrants in Malaysia due to various interplay factors including their working sectors, country of origin, immunization status, type of settlement, impoverished living conditions, and language and cultural barriers that impeding access to health facilities.

Use of tofacitinib in recalcitrant cases of chronic pruritus of unknown origin.

Sardana K, Sharath S, Khurana A.

Systemic treatments in Parthenium dermatitis: A systematic review and meta-analysis.

Akham R, Bhatia R, Das A, Bhadoria AS, Pathak M, Hazarika N.

The Voice of the Lost Toe: Pseudo-Ainhum Beyond Skin.

Divyalakshmi C, Dhanta A, Bhatia R, Hazarika N, Subbaih V.

An 11-year-old boy presented with serial autoamputations of the right 4th and 5th toes during the past 6 years. This was associated with sensory loss on the right leg and development of constriction bands around the right 2nd and 3rd digits for the past 5 months. For a year, the patient had been treated with paucibacillary, multi-drug therapy (PB-MDT) with a presumptive diagnosis of leprosy. He was born from a nonconsanguinous marriage and the birth was uneventful. The developmental milestones were normal, and no family history of any congenital anomalies was reported.

Automated chronic wounds medical assessment and tracking framework based on deep learning.

Monroy B, Sanchez K, Arguello P, Estupiñán J, Bacca J, Correa CV, Valencia L, Castillo JC, Mieles O, Arguello H, Castillo S, Rojas-Morales F.

An mHealth App (eSkinHealth) for Detecting and Managing Skin Diseases in Resource-Limited Settings: Mixed Methods Pilot Study.

Yotsu RR, Almamy D, Vagamon B, Ugai K, Itoh S, Koffi YD, Kaloga M, Dizoé LAS, Kouadio K, Aka N, Yeboue LKG, Yao KA, Blanton RE.

Stevens-Johnson Syndrome in Adult Patient Secondary to COVID-19 Infection: Case Report.

Khade P, Shah A, Kharkar V.

COVID-19 is a global pandemic caused by a novel zoonotic RNA virus named SARS-CoV-2. Various cutaneous manifestations associated with COVID-19 have been described, including urticarial rash, confluent erythematous rash, papulovesicular exanthem, chilblain-like acral pattern, livedo reticularis, and purpuric vasculitis pattern. Here, we are presenting a case of a 45-year-old male with mucocutaneous features of Stevens-Johnson syndrome.

Reverse Koebner phenomenon in erythema nodosum leprosum.

Singh S, Narang T, Dogra S.
26-08-2023
Trans R Soc Trop Med Hyg.

Dyschromatosis universalis hereditaria.

Murthy AB, Palaniappan V, Karthikeyan K, Anbarasan V.
27-08-2023
Int J Dermatol.

Analyzing the Predictability of an Artificial Intelligence App (Tibot) in the Diagnosis of Dermatological Conditions: A Cross-sectional Study.

Marri SS, Inamadar AC, Janagond AB, Albadri W.
01-03-2023
JMIR Dermatol.

Background: Artificial intelligence (AI) aims to create programs that reproduce human cognition and processes involved in interpreting complex data. Dermatology relies on morphological features and is ideal for applying AI image recognition for assisted diagnosis. Tibot is an AI app that analyzes skin conditions and works on the principle of a convolutional neural network. Appropriate research analyzing the accuracy of such apps is necessary. **Objective:** This study aims to analyze the predictability of the Tibot AI app in the identification of dermatological diseases as compared to a dermatologist. **Methods:** This is a cross-sectional study. After taking informed consent, photographs of lesions of patients with different skin conditions were uploaded to the app. In every condition, the AI predicted three diagnoses based on probability, and these were compared with that by a dermatologist. The ability of the AI app to predict the actual diagnosis in the top one and top three anticipated diagnoses (prediction accuracy) was used to evaluate the app's effectiveness. Sensitivity, specificity, and positive predictive value were also used to assess the app's performance. Chi-square test was used to contrast categorical variables. P<.05 was considered statistically significant. **Results:** A total of 600 patients were included. Clinical conditions included alopecia, acne, eczema, immunological disorders, pigmentary disorders, psoriasis, infestation, tumors, and infections. In the anticipated top three diagnoses, the app's mean prediction accuracy was 96.1% (95% CI 94.3%-97.5%), while for the exact diagnosis, it was 80.6% (95% CI 77.2%-83.7%). The prediction accuracy (top one) for alopecia, acne, pigmentary disorders, and fungal infections was 97.7%, 91.7%, 88.5%, and 82.9%, respectively. Prediction accuracy (top three) for alopecia, eczema, and tumors was 100%. The sensitivity and specificity of the app were 97% (95% CI 95%-98%) and 98% (95% CI 98%-99%), respectively. There is a statistically significant association between clinical and AI-predicted diagnoses in all conditions (P<.001). **Conclusions:** The AI app has shown promising results in diagnosing various

dermatological conditions, and there is great potential for practical applicability.

Measuring leprosy case detection delay and associated factors in Indonesia: a community-based study.

Dharmawan Y, Korfage IJ, Abqari U, Widjanarko B, Richardus JH.
25-08-2023
BMC Infect Dis.

Cultural adaption and validation of the Explanatory Model Interview Catalogue-Community Stigma Scale in the assessment of public stigma related to schistosomiasis in lakeshore areas of Mwanza region, Tanzania.

Klinker L, Boeckler A, Kreibich S, Mazigo H.
14-08-2023
PLoS Negl Trop Dis.

Background: Previous qualitative studies on attitudes towards schistosomiasis demonstrated inconclusive results on the extent of stigma towards schistosomiasis in endemic communities around the world. The Explanatory Model Interview Catalogue-Community Stigma Scale (EMIC-CSS) has been used and validated for the assessment of public stigma across numerous countries in various health conditions. This study tested the performance of the scale in the context of stigma related to schistosomiasis in twelve communities in the three districts of Magu, Nyamagana and Ilemela in Mwanza region, Tanzania. **Methodology/principal findings:** The 15-item-version of the EMC-CSS was first translated to Kiswahili language. The translation was discussed within the research team to retain the meaning of the items and implement cultural adaptations. Validation of the adapted EMIC-CSS scale was conducted following the framework of Herdman and Fox- Rushby. A pilot study with 41 participants from two communities provided the basis for testing the performance of each item and assessing the semantic and operational equivalence of the scales. In addition, eight qualitative focus group discussions (FGDs) were conducted to evaluate the conceptional equivalence of the EMIC-CSS. Finally, the performance of the adjusted scale was tested on 200 participants with a 50:50 male-female ratio from ten communities. The mean score of the EMIC-CSS M = 8.35 (SD = 6.63) shows clear indications for public stigma towards schistosomiasis. The EMIC-CSS demonstrated a good internal consistency with Cronbach's alpha α = .857 and no floor and ceiling effects. **Conclusion/significance:** The results demonstrate that the EMIC-CSS is a useful instrument in assessing public stigma towards schistosomiasis and allow a clear recommendation of the EMIC-CSS for schistosomiasis in the Tanzanian culture. However, future studies are additionally recommended to address specific aspects and forms of the disease and how they contribute to the development of stigma towards schistosomiasis.

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

Yotsu RR, Ding Z, Hamm J, Blanton RE.
14-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37578966/

Obesity and hidradenitis suppurativa: targeting meta-inflammation for therapeutic gain.

Mintoff D, Agius R, Benhadou F, Das A, Frew JW, Pace NP.
25-08-2023
Clin Exp Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37171791/

Pitted keratolysis.

Palaniappan V, Murthy AB, Karthikeyan K.
25-08-2023
Clin Exp Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37151115/

Pitted keratolysis (PK) is a common superficial bacterial skin infection confined to the stratum corneum. It is clinically characterized by multifocal, discrete, pits or crater-like punched-out lesions, commonly over the pressure-bearing aspects of the foot. It is asymptomatic and associated with malodour. The surface is often moist and macerated. The diagnosis of PK is often clinical and diagnostic procedures are usually unnecessary. Lifestyle modifications form the cornerstone of the management of PK. It responds well to topical antimicrobials.

Blue light and skin: what is the intriguing link?

Das A, Sil A, Kumar P, Khan I.
25-08-2023
Clin Exp Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37097168/

Blue light has garnered attention because of its ability to penetrate more deeply into the skin layers, and induce cellular dysfunction and DNA damage. Photoageing, hyperpigmentation and melasma are some of the cutaneous changes that develop on exposure to blue light. To date, the therapeutic roles of blue light have been evaluated in dermatological conditions like psoriasis, eczema, acne vulgaris, actinic keratosis and cutaneous malignancies, among others. In this review, we have attempted to present an evidence-based compilation of the effects of blue light on the skin.

Severity grading of dermatological emergencies based on comorbidities and systemic involvement: An observational study.

Kedia A, Ranugha PSS, Chethana GS, Kanthraj GR.
Oct-2023
Arch Dermatol Res.
https://pubmed.ncbi.nlm.nih.gov/37031345/

Morsures de serpent

Survey on sea snakebite and related morbidity and mortality among Bangladeshi fishermen in the Bay of Bengal: A pilot study.

Ghose A, Alam MS, Abu Sayeed A, Shah Jahan M, Akter F, Md Erfan Uddin RA, Sarkar S, Zahed ASM, Das KK, Rahman MH, Rashid R, Nasrin H, Dutta AK, Khan MI, Kuch U, Faiz MA.
29-08-2023
Toxicon.
https://pubmed.ncbi.nlm.nih.gov/37652104/

Around two million people are engaged in marine fishing in the Bay of Bengal. Bites by sea snakes were common hazards feared by millions fishing at sea in earlier days. Current morbidity and mortality are also not known. This study was conducted to document and describe sea snake bites among selected communities of sea-going fishermen in Bangladesh. A questionnaire-based cross-sectional survey was conducted from May to October 2019 among three communities of sea-going fishermen living along the coast of the Bay of Bengal in Cox's Bazar district. Fishermen were first asked by trained interviewers to recall any sea snakebites to themselves and among their fellows on board within the last year, then within the last 5 years and at any time before that. For any bite, related information including outcome was noted. Overall, 25.4% of respondents (62 out of 244) had been bitten by sea-snakes. Mean age was 37.6(±14) years; all males. 51.6% received some sort of treatment locally; 71% hot compress and 48% tourniquets. In 80.6% the affected limb was not immobilized. The bitten site was incised in 29%. 22.6% received treatment from traditional healers, 48.4% from local hospitals, 29% from district hospital. Six victims (9.7%) suffered from severe life-threatening consequences of the sea snakebite but none died. 32% of the fishermen had seen the offending snake. Sea snakebites are potentially dangerous; therefore, educating fishermen to avoid contact with sea snakes would dramatically reduce the incidence of sea snakebites. Most bites are treated initially by local measures which are often not scientific. Provision of proper first aid and treatment might reduce mortality and morbidity. A larger survey on sea snake bites among the fishermen in all coastal areas of Bangladesh is needed to determine the nationwide burden of morbidity and mortality related to sea snakebite.

Metabolomics analyses of serum metabolites perturbations associated with Naja atra bite.

He D, Hu S, Huang Z, Mo C, Cheng X, Song P, Li Y, Song T, Guan Z, Zhou Y, Zhang X, Liao M.
28-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37639406/

Cepharanthine Exerts Antioxidant and Anti-Inflammatory Effects in Lipopolysaccharide (LPS)-Induced Macrophages and DSS-Induced Colitis Mice.

Chen G, Wen D, Shen L, Feng Y, Xiong Q, Li P, Zhao Z.

15-08-2023
Molecules.

Cepharanthine (CEP), a biscoclaurine alkaloid extracted from *Stephania cepharantha* Hayata, has been widely used for the treatment of various acute and chronic diseases, including leukopenia, and snake bites. Here, our objective was to investigate the anti-oxidative stress and anti-inflammatory response effects of CEP in lipopolysaccharide (LPS)-induced macrophages as well as dextran sulfate sodium (DSS)-induced colitis mice. Our findings demonstrated that supplementation with CEP effectively mitigates body weight loss and elevation of disease activity index (DAI), reduces the malondialdehyde (MDA) content to 2.45 nM/mL while increasing the reduced glutathione (GSH) content to 35.53 µg/mL, inhibits inflammatory response, and maintains proper intestinal epithelium tight junctions in DSS-induced wild type (WT) mice. However, it failed to provide protective effects in DSS-induced transcription factor nuclear factor erythroid 2-related factor 2 (NRF2) knockout (NRF2$^{-/-}$) mice. GSH content decreased to 10.85 µg/10^6 cells following LPS treatment, whereas supplementation with CEP increased the GSH content to 12.26 µg/10^6 cells. Moreover, CEP effectively attenuated ROS production in LPS-induced macrophages. Additionally, CEP exhibited inhibitory effects on pro-inflammatory cytokines and mediators in LPS-induced macrophages. Furthermore, we observed that supplementation with CEP promoted the expression of NRF2/heme oxygenase 1 (HO-1)/NADPH quinone oxidoreductase-1 (NQO-1) as well as the phosphorylation of the adenosine monophosphate-activated protein kinase alpha 1 (AMPK-α1)/protein kinase B (AKT)/glycogen synthase kinase-3 beta (GSK-3β) signaling pathway in macrophages while inhibiting the phosphorylation of the extracellular signal-regulated kinase (ERK)/c-Jun N-terminal kinase (JNK), and nuclear factor-kappa B p65 (NF-κB p65) signaling pathway in LPS-induced macrophages. Although CEP did not demonstrate inhibitory effects on oxidative stress or promote the expression of HO-1/NQO-1, it effectively activated the phosphorylation of the AMPK-α1/AKT/GSK-3β signaling pathway which is an upstream regulator of NRF2 in LPS-induced primary peritoneal macrophages from NRF2$^{-/-}$ mice. In summary, our findings suggest that CEP exerts protective effects against oxidative stress and inflammatory response by activating the AMPK-α1/AKT/GSK-3β/NRF2 signaling pathway while concurrently inhibiting the activation of mitogen activated protein kinases (MAPKs) and the NF-κB p65 signaling pathway. These results not only elucidate the mechanisms underlying CEP's protective effects on colon oxidative stress and inflammation but also provide evidence supporting NRF2 as a potential therapeutic target for IBD treatment.

The Need for Next-Generation Antivenom for Snakebite Envenomation in India.

Vanuopadath M, Rajan K, Alangode A, Nair SS, Nair BG.

18-08-2023
Toxins (Basel).

The limitations posed by currently available antivenoms have emphasized the need for alternative treatments to counteract snakebite envenomation. Even though exact epidemiological data are lacking, reports have indicated that most global snakebite deaths are reported in India. Among the many problems associated with snakebite envenomation, issues related to the availability of safer and more efficient antivenoms are of primary concern. Since India has the highest number of global snakebite deaths, efforts should be made to reduce the burden associated with snakebite envenoming. Alternative methods, including aptamers, camel antivenoms, phage display techniques for generating high-affinity antibodies and antibody fragments, small-molecule inhibitors, and natural products, are currently being investigated for their effectiveness. These alternative methods have shown promise in vitro, but their in vivo effectiveness should also be evaluated. In this review, the issues associated with Indian polyvalent antivenoms in neutralizing venom components from geographically distant species are discussed in detail. In a nutshell, this review gives an overview of the current drawbacks of using animal-derived antivenoms and several alternative strategies that are currently being widely explored.

Comparative Analysis of Alpha-1 Orthosteric-Site Binding by a Clade of Central American Pit Vipers (Genera Atropoides, Cerrophidion, Metlapilcoatlus, and Porthidium).

Jones L, Waite C, Neri-Castro E, Fry BG.

02-08-2023
Toxins (Basel).

Development of a high-throughput in vitro screening method for the assessment of cell-damaging activities of snake venoms.

Bittenbinder MA, Capinha L, Da Costa Pereira D, Slagboom J, van de Velde B, Casewell NR, Jennings P, Kool J, Vonk FJ.

17-08-2023
PLoS Negl Trop Dis

Burden and risk factors of snakebite in Mopeia, Mozambique: Leveraging larger malaria trials to generate data of this neglected tropical disease.

O'Bryan E, Imputiua S, Elobolobo E, Nicolas P, Montana J, Jamisse E, Munguambe H, Casellas A, Ruiz-Castillo P, Rabinovich R, Saute F, Sacoor C, Chaccour C.

Frequency, geographical distribution and outcomes of pit viper bites in Malaysia consulted to Remote Envenomation Consultancy Services (RECS) from 2017 to 2020.

Qamruddin RM, Safferi RS, Mohamed Ismail Z, Salleh MS, Abd Hamid MNH, Frederic Ng VER, Goh WC, Ismail AK.

Not all pit viper species are present in every state of Malaysia and their distribution varies according to altitude. There is limited information on pit viper bite incidence and its geographical distribution. This was a cross-sectional study of confirmed pit viper bite cases referred to Remote Envenomation Consultancy Services (RECS) from January 2017 to December 2020. Data was collected following the approval of institutional research ethics committee. Universal sampling methods were used. Confirmed pit viper bite cases in each state, geographical location and the antivenom used were reported. A total of 523 confirmed pit viper bite injuries occurred over the 4-year study period. The majority were Malaysians, male and young adults. Most were non-occupational related (83.9%) and involved the upper limbs (46.8%). The commonest pit viper species involved was Trimeresurus purpureomaculatus (23.7%). Green pit viper antivenom (GPAV) was the most frequent antivenom used (n = 51) with the majority of patients requiring only one dose (3 vials). This study provides a better appreciation of indigenous pit viper species distribution for each state and reflects the requirement of appropriate antivenom to be stocked in each state or district hospital.

Compartment Syndrome after Crotalid Envenomation in the United States: A Review of the North American Snakebite Registry from 2013 to 2021 on Behalf of the ToxIC Snakebite Study Group.

Spyres MB, Maker G, Aldy K, Wolk BJ, Meadors KE, Christian M, Ruha AM.

Delayed Compression Paralysis Following an Iliopsoas Hematoma 30 Days After Saw-Scaled Viper (Echis carinatus sochureki) Envenoming: A Case Report.

Kachhwaha A, Kumar A, Garg P, Sharma A, Garg MK, Gopalakrishnan M.

Mycétome

Sustaining Hope amid Struggle: The Plight of Cancer Patients in Sudan's Ongoing War.

Siddig EE, Eltigani HF, Ali ET, Bongomin F, Ahmed A.

First report on mycetoma in Turkana County-North-western Kenya.

Colom MF, Ferrer C, Ekai JL, Ferrández D, Ramírez L, Gómez-Sánchez N, Leting S, Hernández C.

Mycetoma is one of the six Neglected Tropical Diseases that are prevalent in Turkana County (northwest Kenya). The aim of the study was to estimate the prevalence of mycetoma in the county, as well as to describe the main causative agents involved in the disease using methods affordable locally. Based on the data collected by the team of cooperative medicine Cirugia en Turkana (Surgery in Turkana), a specific study for mycetoma was started during the 16th humanitarian medicine campaign in February 2019. Patients with suspected mycetoma were studied at the Lodwar County Referral Hospital (LCRH). After informing the patient and getting their consent, the lesions were examined and sampled (mainly by biopsy) and clinical data were recorded. Samples were washed in sterile saline solution and cut in fragments. Some of these were inoculated on Sabouraud Dextrose Agar, Malt Extract Agar, and diluted Nutrient Agar plates. One fragment of each sample was used for DNA extraction. The DNA and the rest of the fragments of samples were kept at -20°C. All cultures were incubated at room temperature at the LCRH laboratory. The DNA obtained from clinical samples was submitted to PCR amplification of the ITS-5.8S and the V4-V5 16S rRNA gene region, for the detection and identification of fungi and bacteria respectively. From February 2019 till February 2022, 60 patients were studied. Most of them were men (43, 74,1%) between 13 and 78 y.o. (mean age 37). Half of the patients were herdsmen but, among women 40% (6) were housewives and 26.7% (4) charcoal burners. Lesions were mainly located at the feet (87.9%) and most of the patients (54; 93.1%) reported discharge of grains in the exudate, being 27 (46.6%) yellow or pale colored and 19 (32.8%) of them dark grains. Culture of clinical samples yielded 35 fungal and bacterial putative causative agents. Culture and molecular methods allowed the identification of a total of 21 causative agents of mycetoma (39.6% of cases studied). Most of them (17) corresponded to fungi causing eumycetoma (80.9%) being the most prevalent the genus Madurella (7; 41.2%), with two species involved (M. mycetomatis and M. fahalii), followed by Aspergillus (2; 11.8%). Other minority genera detected were Cladosporium, Fusarium, Acremonium, Penicillium, and Trichophyton (5.9% each of them). Actinobacteria were

detected in 19.1% of samples, but only Streptomyces somaliensis was identified as a known agent of mycetoma, the rest being actinobacteria not previously described as causative agents of the disease, such as Cellulosimicrobium cellulans detected in two of the patients. Although Kenya is geographically located in the mycetoma belt, to our knowledge this is the first report on mycetoma in this country from 1973, and the first one for Turkana County.

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

Yotsu RR, Ding Z, Hamm J, Blanton RE.

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

Onchocercose

Genome structure and population genomics of the canine heartworm Dirofilaria immitis.

Gandasegui J, Power RI, Curry E, Ching-Wai Lau D, O'Neill CM, Wolstenholme A, Prichard R, Šlapeta J, Doyle SR.

The heartworm, Dirofilaria immitis, is a filarial parasitic nematode responsible for significant morbidity and mortality in wild and domesticated canids. Resistance to macrocyclic lactone drug prevention represents a significant threat to parasite control and has prompted investigations to understand the genetic determinants of resistance. This study aimed to improve the genomic resources of D. immitis to enable a more precise understanding of how genetic variation is distributed within and between parasite populations worldwide, which will inform the likelihood and rate by which parasites, and in turn, resistant alleles, might spread. We have guided the scaffolding of a recently published genome assembly for D. immitis (ICBAS_JMDir_1.0) using the chromosomal-scale reference genomes of Brugia malayi and Onchocerca volvulus, resulting in an 89.5 Mb assembly composed of four autosomal- and one sex-linked chromosomal-scale scaffolds representing 99.7% of the genome. Publicly available and new whole-genome sequencing data from 32 D. immitis samples from Australia, Italy and the USA were assessed using principal component analysis, nucleotide diversity (Pi) and absolute genetic divergence (Dxy) to characterise the global genetic structure and measure within- and between-population diversity. These population genetic analyses revealed broad-scale genetic structure among globally diverse samples and differences in genetic diversity between populations; however, fine-scale subpopulation analysis was limited and biased by differences between sample types. Finally, we mapped single nucleotide polymorphisms previously associated with macrocyclic lactone resistance in the new genome assembly, revealing the physical linkage of high-priority variants on chromosome 3, and determined their frequency in the studied populations. This new chromosomal assembly for D. immitis now allows for a more precise investigation of selection on genome-wide genetic variation and will enhance our understanding of parasite transmission and the spread of genetic variants responsible for resistance to treatment.

Biological implications of long-term anthelmintic treatment: what else besides resistance are we selecting for?

Nielsen MK, Kaplan RM, Abbas G, Jabbar A.

Trends Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37633759/

In Vitro Filaricidal Properties of Hydro-Methanolic Extracts of Powdery Fractions of Khaya senegalensis (Meliaceae) on Onchocerca ochengi.

Galani Tietcheu BR, Betrosse T, Ayiseh RB, Yuunoeoene EI, Mfotie Njoya E, Nveikoueng F, Njintang NY, Ndjonka D.
Sept-2023
Acta Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37336863/

Pian

An mHealth App (eSkinHealth) for Detecting and Managing Skin Diseases in Resource-Limited Settings: Mixed Methods Pilot Study.

Yotsu RR, Almamy D, Vagamon B, Ugai K, Itoh S, Koffi YD, Kaloga M, Dizoé LAS, Kouadio K, Aka N, Yeboue LKG, Yao KA, Blanton RE.
14-06-2023
JMIR Dermatol.
https://pubmed.ncbi.nlm.nih.gov/37632977/

Background: In sub-Saharan Africa, the disease burden from skin diseases, including skin-related neglected tropical diseases (skin NTDs), is extremely high. These diseases often are overlooked due to limited access to health care stemming from, for example, remote geographical locations and a lack of experts. To address these gaps, we developed a mobile health app, eSkinHealth, which is a field-adapted platform to serve as a portable electronic patient chart and for teledermatology. **Objective:** The purpose of the study is to evaluate the usability and effectiveness of the app in rural Côte d'Ivoire for diagnosing and managing skin NTDs and other skin diseases. **Methods:** A 2-arm trial with local health care providers and patients with skin diseases was implemented over a 3-month period. The providers were assigned to an intervention receiving the eSkinHealth app or control with usual care. Four nurses and 8 community health care workers participated in each arm. The training was provided on the use of the app to the intervention arm only, while both arms were trained on skin diseases. For the usability study, we evaluated our approach with the System Usability Scale (SUS) and in-depth interviews. For the effectiveness study, our primary outcome was to evaluate the detection and management of 5 skin NTDs as our targeted diseases, namely, Buruli ulcer, leprosy, lymphatic filariasis, scabies, and yaws, using the eSkinHealth app. Procedures of our methods were reviewed and approved by the institutional review board of the Ministry of Health and by Tulane University. **Results:** The mean age of our participants (providers) was 40.5 and 42.5 years for the intervention and control arms, respectively, and all were male (n=24). The average SUS scores taken from the intervention arm at baseline, the midpoint (6 weeks), and the end of study (12 weeks) were 72.3 (SD 11.5), 72.3 (SD 12.4), and 86.3 (SD 10.8), respectively. All participants interviewed, including 4 dermatologists and program managers, were satisfied with the app. Especially community health care workers felt empowered by being equipped with the tool. A total of 79 cases of skin NTDs were reported in the intervention arm as compared to 17 cases in the control arm (P=.002). Besides the skin NTDs, more skin diseases and conditions were reported from the control than from the intervention arm (P<.001). However, 100 cases (66%) were not given any particular diagnosis in the control arm and were documented only as a "dermatosis." In the intervention arm, 151 cases (72.9%) were diagnosed within the eSkinHealth platform, and the remaining were diagnosed on-site by dermatologists. **Conclusions:** The study provided evidence for the usability and effectiveness of the eSkinHealth app embedded into our surveillance approach to improve the detection and management of skin NTDs and other skin diseases in Côte d'Ivoire and, furthermore, is expected to contribute to knowledge on mobile health approaches in the control of skin diseases in resource-limited settings.

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

Yotsu RR, Ding Z, Hamm J, Blanton RE.
14-08-2023
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/37578966/

Rage

Canine Leishmania spp. infection in two distinct foci of visceral and cutaneous leishmaniasis in Tunisia.

Zribi L, El Houda Ben-Fayala N, Aissi W, Ben-Abid M, Souissi O, Hamdi N, Boulehmi N, Ghrab J, Jemni A, Jamel A, Handous M, Bouratbine A, Oliva G, Aoun K.
2023
Vet Parasitol Reg Stud Reports.
https://pubmed.ncbi.nlm.nih.gov/37652625/

Epidemic diseases during the World War I and Dr Server Kamil Tokgöz.

Sarı M.
28-08-2023
J Med Biogr.
https://pubmed.ncbi.nlm.nih.gov/37641211/

Server Kamil became one of the most prominent doctors during the period of the Ottoman Empirey. Server Kamil, who specialized in bacteriology and sanitation, made a name for himself primarily through his fight in the memories against epidemic diseases on the Caucasus front during World War I. He was sent to the Caucasus front as chief physician of Erzurum Red Crescent (Hilâl-i Ahmer) Hospital, and made great efforts to prevent the disease typhus-which was a major problem in the region-as soon as he reached the front line. He worked long and hard to develop a vaccine to prevent typhus, which affects thousands of soldiers and civilians. He also played a

pioneering role in establishing important institutions such as the Sivas Smallpox Vaccine Laboratory and the Rabies Treatment Centre, which accomplished significant work and achieved great success both during the World War I and in the period that followed. This article attempts to clarify the activities of Server Kamil on Caucasus front during World War I based on the documents of the Turkish Red Crescent Archive, the reports of the Red Crescent Society.

Sick as a dog? The prevalence, politicization, and health policy consequences of canine vaccine hesitancy (CVH).

Motta M, Motta G, Stecula D.
26-08-2023
Vaccine.
https://pubmed.ncbi.nlm.nih.gov/37640567/

Canine vaccine hesitancy (CVH) can be thought about as dog owners' skepticism about the safety and efficacy of administering routine vaccinations to their dogs. CVH is problematic not only because it may inspire vaccine refusal - which may in turn facilitate infectious disease spread in both canine and human populations - but because it may contribute to veterinary care provider mental/physical health risks. In a nationally representative survey of US adults (N = 2200), we introduce a novel survey-based instrument for measuring CVH. We document pervasive CVH in dog owner subpopulations. Troublingly, we find that CVH is associated with rabies non-vaccination, as well as opposition to evidence-based vaccine policies. We conclude by discussing the human and animal health consequences of CVH, and outline a research agenda for future opinion-based research on this important topic.

Dynamic analysis of rabies transmission and elimination in mainland China.

Lv MM, Sun XD, Jin Z, Wu HR, Li MT, Sun GQ, Pei X, Wu YT, Liu P, Li L, Zhang J.
16-08-2023
One Health.
https://pubmed.ncbi.nlm.nih.gov/37638210/

Antiviral mechanisms of two broad-spectrum monoclonal antibodies for rabies prophylaxis and therapy.

Zorzan M, Castellan M, Gasparotto M, Dias de Melo G, Zecchin B, Leopardi S, Chen A, Rosato A, Angelini A, Bourhy H, Corti D, Cendron L, De Benedictis P.
10-08-2023
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/37638057/

Characterisation of a Live-Attenuated Rabies Virus Expressing a Secreted scFv for the Treatment of Rabies.

Smith SP, Shipley R, Drake P, Fooks AR, Ma J, Banyard AC.
31-07-2023

Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632016/

Rabies virus (RABV) causes possibly the oldest disease and is responsible for an estimated >59,000 human fatalities/year. Post exposure prophylaxis (PEP), the administration of vaccine and rabies immunoglobulin, is a highly effective tool which is frequently unavailable in RABV endemic areas. Furthermore, due to the constraints of the blood-brain barrier, current PEP regimes are ineffective after the onset of clinical symptoms which invariably result in death. To circumvent this barrier, a live-attenuated recombinant RABV expressing a highly RABV-neutralising scFv antibody (62-71-3) linked to the fluorescent marker mCherry was designed. Once rescued, the resulting construct (named RABV-62scFv) was grown to high titres, its growth and cellular dissemination kinetics characterised, and the functionality of the recombinant 62-71-3 scFv assessed. Encouraging scFv production and subsequent virus neutralisation results demonstrate the potential for development of a therapeutic live-attenuated virus-based post-infection treatment (PIT) for RABV infection.

An Oil-Based Adjuvant Improves Immune Responses Induced by Canine Adenovirus-Vectored Vaccine in Mice.

Broutin M, Costa F, Peltier S, Maye J, Versillé N, Klonjkowski B.
30-07-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632007/

Emerging Genomic Trends on Rabies Virus in Davao Region, Philippines, 2018-2021.

Capin JBG, Sanque AJC, Eng MNJ, Lagare A, Sepulveda MCB, Murao LAE.
30-07-2023
Viruses.
https://pubmed.ncbi.nlm.nih.gov/37632001/

Efficiency Comparative Approach of Plant-Produced Monoclonal Antibodies against Rabies Virus Infection.

Lumlertdacha B, Mahong B, Rattanapisit K, Bulaon CJI, Hemachudha T, Phoolcharoen W.
17-08-2023
Vaccines (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631945/

A Randomized, Double-Blind, Controlled Phase III Clinical Trial to Evaluate the Immunogenicity and Safety of a Lyophilized Human Rabies Vaccine (Vero Cells) in Healthy Participants Aged 10-60 Years Following Essen and Zagreb Vaccination Procedures.

Wu X, Li J, Zhou L, Chen J, Jin Z, Meng Q, Chai J, Gao H, Wang Y, Zhao D, Wu H, Yu J, Chen N, Wang Y, Lin Y, Huang P, Li Y, Zhang Y.

Objective: In this paper, we aim to show that the immunogenicity of the lyophilized human rabies vaccine (Vero cells) (investigational vaccine) developed by Dalian Aleph Biomedical Co., Ltd. in healthy participants aged 10-60 years old is non-inferior to the lyophilized PVRV (positive control) manufactured by Liaoning Chengda Biotechnology Co., Ltd. (Shenyang, China), and that its safety is clinically acceptable. **Method:** A total of 2776 participants were enrolled in this study and divided into four groups: a five-dose test group, a five-dose control group, a four-dose test group, and a four-dose control group. The patients in the four-dose groups (Zagreb) were vaccinated on Days 0 (two doses), 7 (one dose), and 21 (one dose), and those in the five-dose groups (Essen) were vaccinated on Days 0, 3, 7, 14, and 28 (one dose each). The rabies-virus-neutralizing antibody assay with the RFFIT was used to assess the immunogenicity, and the adverse events (AEs) and serious adverse events (SAEs) were identified and collated. **Results:** The positive seroconversion rate was up to 100% on Days 14 and 35/42 after vaccination following any procedures in pre-immunization antibody-negative participants, and the positive seroconversion rate and geometric mean concentration (GMC) of the test groups (Zagreb and Essen vaccination procedures) was not inferior to that of the control groups. On Day 7 after vaccination, the immunogenicity of the Zagreb procedure with two doses of the vaccine on Day 0 was superior to the Essen procedure with one dose of vaccine, that is, the former had a higher seroconversion rate and RVNA titer. The non-inferiority criterion of immunogenicity was met for the whole population, the population aged 10-18 years and ≥18 years, and the pre-immunization antibody-positive population. The incidences of all AEs, solicited AEs, and unsolicited AEs in both groups were not statistically significant, and no vaccination-related SAEs were observed. **Conclusion:** The investigated vaccine is safe, its immunogenicity is non-inferior to that of the control vaccine, and the efficacy of the Zagreb procedure is superior to that of the Essen procedure 7 days after the first dose.

TRIM25 Suppresses Rabies Virus Fixed HEP-Flury Strain Production by Activating RIG-1-Mediated Type I Interferons.

Zhang B, Cai T, He H, Huang X, Luo Y, Huang S, Luo J, Guo X.

Rabies remains a great threat to public health worldwide. So far, the mechanism of rabies virus (RABV) infection is not fully understood, and there is no effective treatment for rabies. Identifying more host restriction factors of RABV will spur the development of novel therapeutic interventions against rabies. Accumulating studies suggest that tripartite motif-containing (TRIM) proteins have great effects on virus replication. TRIMs control the antiviral responses through either direct interaction with viral proteins or indirect regulation of innate immune signaling molecules in the host. The role of TRIM25 in rabies virus (RABV) infection is poorly understood. Using next-generation sequencing, we found that TRIM25 is upregulated during HEP-Flury infection. Knockdown of TRIM25 enhances HEP-Flury production, while overexpression of TRIM25 suppresses HEP-Flury replication. Knockdown of interferon α and interferon β weakens the anti-RABV response induced by TRIM25 overexpression, and potentiates RABV production. Furthermore, we found that TRIM25 regulates type-I interferon response by targeting retinoic acid-inducible gene I (RIG-I) during HEP-Flury infection. Knockdown of RIG-I weakens the anti-HEP-Flury response induced by TRIM25 overexpression, indicating that TRIM25 regulates RABV production via the RIG-I-IFN axis. In addition, we observed that TRIM25 does not directly interact with HEP-Flury structural proteins, suggesting that TRIM25 regulates HEP-Flury production indirectly. Taken together, our work identifies TRIM25 as a new host factor involved in HEP-Flury infection, which may be a potential target for the development of antiviral drugs against RABV.

Investigations into SARS-CoV-2 and other coronaviruses on mink farms in France late in the first year of the COVID-19 pandemic.

Wasniewski M, Boué F, Richomme C, Simon-Lorière E, der Werf SV, Donati F, Enouf V, Blanchard Y, Beven V, Leperchois E, Leterrier B, Corbet S, Le Gouil M, Monchatre-Leroy E, Picard-Meyer E.

The Use of Dog Collars Offers Significant Benefits to Rabies Vaccination Campaigns: The Case of Zanzibar, Tanzania.

Omar KN, Coetzer A, Hamdu M, Malan AJ, Moh'd AZ, Suleiman TS, Nel LH.

Tools and resources that could increase dog vaccination coverage have become increasingly critical towards progressing the goal to eliminate dog-mediated human rabies by 2030. In this regard, dog collars that are fitted during vaccination campaigns could potentially enhance owner participation. The use of dog collars will, however, increase the cost per dog vaccinated and the impact and benefit of this practice should be elucidated. This study evaluated the impact of dog collars by testing the perception and related behavioural influences in communities in Zanzibar. In this cross-sectional investigation-conducted approximately two months after the implementation of a mass dog vaccination (MDV) where dog collars were provided to vaccinated dogs-data were collected from 600 respondents in 56 municipal wards in Zanzibar. Descriptive analyses and logistic

regressions were undertaken to determine the impact the collars had on respondents with regards to (i) engaging with the community dogs, (ii) health seeking behaviour after exposure, and (iii) overall participation during dog vaccination campaigns. From the data, it was evident that the collars had a positive impact on the community's perception of dogs, with 57% of the respondents feeling safer around a dog with a collar, while 66% of the respondents felt less safe around a dog without a collar. Furthermore, the collars had a positive impact on participation during dog vaccination campaigns. Of the 142 respondents who owned dogs, 64% reported that the collars made them more likely to take their dogs for vaccination, and 95% felt that the collar was an important sign of the dog's vaccination status. This study demonstrated that dog collars could not only improve participation during dog vaccination campaigns, but that they could also play a significant role in the community's perception of rabies vaccination campaigns and vaccinated dogs in general.

Schistosomiase

Evaluation of schistosomula lung antigen preparation and soluble egg antigen vaccines on experimental schistosomiasis mansoni.

Aly NSM, Kim HS, Eraky MA, Kholy AAE, Ali BT, Miyoshi SI, Omar RE.

Août-2023
Parasites Hosts Dis.
https://pubmed.ncbi.nlm.nih.gov/37648230/

Schistosomiasis causes significant morbidity and mortality worldwide. This study aimed to assess the effect of schistosomula lung antigen preparation (SLAP) and soluble egg antigen (SEA) on a murine schistosomiasis mansoni model. Ninety laboratory-bred male Swiss albino mice were divided into 6 groups. Two doses of the vaccine were given at 2-week intervals. All mice were subcutaneously infected with 80±10 Schistosoma mansoni cercariae 2 weeks after the last vaccination dose. They were sacrificed 7 weeks post-infection. Parasitological and histopathological studies were conducted to assess the effect of inoculated antigens (single or combined). The results showed that the combination of SLAP and SEA (combination group) led to a significant reduction in worm burden (65.56%), and liver and intestine egg count (59% and 60.59%, respectively). The oogram pattern revealed a reduction in immature and mature eggs (15±0.4 and 10±0.8, respectively) and an increased number of dead eggs in the combination group (P<0.001). In terms of histopathological changes, the combination group showed notably small compact fibrocellular egg granuloma and moderate fibrosis in the liver. A high percentage of destroyed ova was observed in the intestine of the combination group. This study demonstrates for the first time the prophylactic effect of combined SLAP and SEA vaccine. The vaccine induced a significant reduction in the parasitological and pathological impacts of schistosomiasis mansoni in hepatic and intestinal tissues, making it a promising vaccine candidate for controlling schistosomiasis.

HIV specific Th1 responses are altered in Ugandans with HIV and Schistosoma mansoni coinfection.

Obuku AE, Lugemwa JK, Abaasa A, Joloba M, Ding S, Pollara J, Ferrari G, Harari A, Pantaleo G, Kaleebu P.

29-08-2023
BMC Immunol.
https://pubmed.ncbi.nlm.nih.gov/37644394/

Background: Fishing communities surrounding Lake Victoria in Uganda have HIV prevalence of 28% and incidence rates of 5 per 100 person years. More than 50% of the local fishermen are infected with Schistosoma mansoni (S. mansoni). We investigated the role of S. mansoni coinfection as a possible modifier of immune responses against HIV. Using polychromatic flow cytometry and Gran-ToxiLux assays, HIV specific responses, T cell phenotypes, antibody-dependent cell-mediated cytotoxic (ADCC) potency and titres were compared between participants with HIV-S. mansoni coinfection and participants with HIV infection alone. Results: S. mansoni coinfection was associated with a modified pattern of anti-HIV responses, including lower frequency of bifunctional (IFNγ + IL-2 - TNF-α+) CD4 T cells, higher overall CD4 T cell activation and lower HIV ADCC antibody titres, compared to participants with HIV alone. Conclusions: These results support the hypothesis that S. mansoni infection affects T cell and antibody responses to HIV in coinfected individuals.

Bsep/Abcb11 knockout ameliorates Schistosoma mansoni liver pathology by reducing parasite fecundity.

Macháček T, Fuchs CD, Winkelmann F, Frank M, Scharnagl H, Stojakovic T, Sombetzki M, Trauner M.

29-08-2023
Liver Int.
https://pubmed.ncbi.nlm.nih.gov/37641872/

Metagenomic sequencing for identifying pathogen-specific circulating DNAs and development of diagnostic methods for schistosomiasis.

Liu J, Wang X, Sheng F, Giri BR, Li S, Xia T, Li X, Cheng G.

27-07-2023
iScience
https://pubmed.ncbi.nlm.nih.gov/37636036/

Timely diagnosis of *Schistosoma* infection, particularly in the early stage is crucial for identifying infected hosts and then taking effective control strategies. Here, metagenomic next-generation sequencing was used to identify pathogen-specific circulating DNAs (cDNAs) in the sera/plasma of New Zealand rabbits infected with *S. japonicum*, and the identified cDNAs were validated by PCR and qPCR. Loop-mediated isothermal amplification (LAMP)-based CRISPR-Cas12a and recombinase polymerase amplification-based lateral flow strip (RPA-LF) methods combined with the newly identified cDNA were

developed to evaluate the potentials for diagnosing murine and human schistosomiasis. The results indicated that twenty-two cDNAs were identified. The developed LAMP-based CRISPR/Cas12a and RPA-LF methods showed a good potential for diagnosing murine or human schistosomiasis as early as 5 days of post-infection with 5 cercariae infection. In a word, *S. japonicum* specific cDNAs in circulation of infected hosts could be effective biomarkers for detecting *Schistosoma* infection particularly for early stages.

Identification and characterization of microRNAs in Biomphalaria tenagophila and comparative analysis of their expression in Schistosoma mansoni-resistant and -susceptible snail populations.

Caixeta Alves T, Ribeiro Queiroz F, Borges de Melo Neto A, da Rocha Fernandes G, Sviatopolk-Mirsky Pais F, de Jesus Jeremias W, Hideo Baba E, de Moraes Mourão M, Rezende Morais E, Janku Cabral F, Rodrigues do Amaral L, Lima Caldeira R, Marcos Zech Coelho P, de Souza Gomes M.
25-08-2023
Gene.
https://pubmed.ncbi.nlm.nih.gov/37634882/

Molluscicidal and Cercaricidal Effects of Myrciaria floribunda Essential Oil Nanoemulsion.

Machado FP, Folly D, Esteves R, Ruppelt BM, da Silva VM, Matos APDS, Santos JAAD, Rangel LDS, Santos MG, von Ranke NL, Rodrigues CR, Ricci-Junior E, Rocha L, Faria RX.
08-08-2023
Molecules.
https://pubmed.ncbi.nlm.nih.gov/37630195/

Gynecological Fistulae-Has Anything Changed in the Diagnosis and Treatment over the Last Decade? A Narrative Literature Review.

Misiak M, Dworak M, Wyszomirska M, Kurt M, Walędziak M, Różańska-Walędziak A.
12-08-2023
Medicina (Kaunas).
https://pubmed.ncbi.nlm.nih.gov/37629745/

Gynecological fistulae are a rare but severe complication of radiation therapy, pelvic surgery, prolonged labor, cesarean deliveries, or inflammatory bowel diseases. A gynecological fistula is an abnormal pathway formed between the urinary and gynecological tract, most commonly located between the urinary bladder and vagina. Vesico-uterine and vesicovaginal fistulae are an important health issue, common in women of reproductive age in developing countries with limited access to obstetrical care. Various surgical techniques have been described for VVF repair, depending on the location, severity, and cause of the fistula and the surgeon's experience. The purpose of our review was to evaluate the present state of knowledge about the prevalence and treatment of gynecological fistulae. The PubMed scientific database was searched for original articles on the subject of gynecological fistulae that had been published between 2013 and 2023.

Review of Recent Prevalence of Urogenital Schistosomiasis in Sub-Saharan Africa and Diagnostic Challenges in the Field Setting.

Hong ST.
31-07-2023
Life (Basel).
https://pubmed.ncbi.nlm.nih.gov/37629527/

Schistosoma and Leishmania: An Untold Story of Coinfection.

Camelo GMA, Silva JKAO, Geiger SM, Melo MN, Negrão-Corrêa DA.
27-07-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624321/

Screening for Resistant Bacteria, Antimicrobial Resistance Genes, Sexually Transmitted Infections and Schistosoma spp. in Tissue Samples from Predominantly Vaginally Delivered Placentae in Ivory Coast and Ghana.

Franz R, Hahn A, Hagen RM, Rohde H, Eberhardt KA, Ehrhardt S, Baum J, Claussen L, Feldt T, Hinz R, Barthel D, Bindt C, Tagbor H, Nguah SB, Koffi M, Köller T, Warnke P, Pankok F, Taudien S, Frickmann H, Schoppen S.
30-07-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37623959/

Medical complications during pregnancy have been frequently reported from Western Africa with a particular importance of infectious complications. Placental tissue can either become the target of infectious agents itself, such as, e.g., in the case of urogenital schistosomiasis, or be subjected to contamination with colonizing or infection-associated microorganisms of the cervix or the vagina during vaginal delivery. In the retrospective cross-sectional assessment presented here, the quantitative dimension of infection or colonization with selected resistant or pathogenic bacteria and parasites was regionally assessed. To do so, 274 collected placental tissues from Ivory Coastal and Ghanaian women were subjected to selective growth of resistant bacteria, as well as to molecular screening for beta-lactamase genes, *Schistosoma* spp. and selected bacterial causative agents of sexually transmitted infections (STI). Panton-Valentine-negative methicillin-resistant *Staphylococcus aureus* (MRSA) was grown from 1.8% of the tissue samples, comprising the *spa* types t008 and t688, as well as the newly detected ones, t12101 (n = 2) and t12102. While the culture-based recovery of resistant Enterobacterales and nonfermentative rod-shaped Gram-negative bacteria failed, molecular assessments confirmed beta-lactamase genes in 31.0% of the samples with multiple detections of up to four resistance genes per sample and bla_{CTX-M}, bla_{IMP},

bla_{GES}, bla_{VIM}, bla_{OXA-58}-like, bla_{NDM}, bla_{OXA-23}-like, bla_{OXA-48}-like and bla_{KPC} occurring in descending order of frequency. The beta-lactamase genes $bla_{OXA-40/24}$-like, $bla_{NMC\_A/IMI}$, bla_{BIC}, bla_{SME}, bla_{GIM} and bla_{DIM} were not detected. DNA of the urogenital schistosomiasis-associated *Schistosoma haematobium* complex was recorded in 18.6% of the samples, but only a single positive signal for *S. mansoni* with a high cycle-threshold value in real-time PCR was found. Of note, higher rates of schistosomiasis were observed in Ghana (54.9% vs. 10.3% in Ivory Coast) and Cesarean section was much more frequent in schistosomiasis patients (61.9% vs. 14.8% in women without *Schistosoma* spp. DNA in the placenta). Nucleic acid sequences of nonlymphogranuloma-venereum-associated *Chlamydia trachomatis* and of *Neisseria gonorrhoeae* were recorded in 1.1% and 1.9% of the samples, respectively, while molecular attempts to diagnose *Treponema pallidum* and *Mycoplasma genitalium* did not lead to positive results. Molecular detection of *Schistosoma* spp. or STI-associated pathogens was only exceptionally associated with multiple resistance gene detections in the same sample, suggesting epidemiological distinctness. In conclusion, the assessment confirmed considerable prevalence of urogenital schistosomiasis and resistant bacterial colonization, as well as a regionally expected abundance of STI-associated pathogens. Continuous screening offers seem advisable to minimize the risks for the pregnant women and their newborns.

A Miniature Biomedical Sensor for Rapid Detection of Schistosoma japonicum Antibodies.

Hu S, Jiang X, Yang L, Tang X, Yang G, Hu Y, Wang J, Lu N.
20-08-2023
Biosensors (Basel).
https://pubmed.ncbi.nlm.nih.gov/37622917/

Schistosomiasis, typically characterized by chronic infection in endemic regions, has the potential to affect liver tissue and pose a serious threat to human health. Detecting and screening for this disease early on is crucial for its prevention and control. However, existing methods encounter challenges such as low sensitivity, time-consuming processes, and complex sample handling. To address these challenges, we report a soluble egg antigen (SEA)-based functionalized gridless and meander-type AlGaN/GaN high electron mobility transistors (HEMT) sensor for the highly sensitive detection of antibodies to *Schistosoma japonicum*. Immobilization of the self-assembled membrane on the gate surface was verified using a semiconductor parameter analyzer, scanning electron microscope (SEM), and atomic force microscopy (AFM). The developed biosensor demonstrates remarkable performance in detecting anti-SEA, exhibiting a linear concentration range of 10 ng/mL to 100 µg/mL and a sensitivity of 0.058 mA/log (ng/mL). It also exhibits similar excellent performance in serum systems. With advantages such as rapid detection, high sensitivity, miniaturization, and label-free operation, this biosensor can fulfill the requirements for blood defense.

Accuracy of Diagnostic Tests for Detecting Schistosoma mansoni and S. haematobium in Sub-Saharan Africa: A Systematic Review and Meta-Analysis.

Feleke DG, Alemu Y, Bisetegn H, Debash H.
16-08-2023
Biomed Res Int.
https://pubmed.ncbi.nlm.nih.gov/37621699/

Trachome

Understanding the Role of Gender in Trichiasis Case Finding in Tanzania.

Kishiki E, Kabona G, Mwangi G, Mkocha H, Shija F, Courtright P, Geneau R.
25-08-2023
Ophthalmic Epidemiol.
https://pubmed.ncbi.nlm.nih.gov/37622668/

Purpose: Despite the importance of trachomatous trichiasis (TT) case-finding activities in national trachoma elimination campaigns, the scientific literature on the determinants of good outcomes - finding and managing all TT cases - is still sparse. In Tanzania, we studied differences in case finding activities and outcomes between male and female case finders. Methods: This case study was conducted in two districts in Tanzania in 2021-2022. Quantitative data were extracted from case finder forms and outreach registers, and qualitative data were collected through direct observation, interviews, and focus group discussions. Results: Across both districts, more males were trained as case finders (68%). Productivity differences were minor, not statistically significant, between male and female case finders regarding the number of households visited and the number of adults examined. Whether identified by a male or female case finder, similar proportions of men and women suspected to have TT were subsequently managed. There is evidence that suggests that female case finders were more active in supporting suspected and confirmed TT cases to access follow-up services. Conclusion: The findings do not suggest that gender balance in the recruitment of TT case finders would have led to better TT campaign outcomes in the study districts. Programmes may benefit from integrating gender considerations in the design and implementation of case finding activities - e.g. in monitoring gender differences among case finders and the relationship with key outcomes. This study also highlights how women with TT face greater barriers to care.

Prevalence and associated factors of active trachoma among 1-9 years of age children in Andabet district, northwest Ethiopia, 2023: A multi-level mixed-effect analysis.

Asmare ZA, Seifu BL, Mare KU, Asgedom YS, Kase BF, Shibeshi AH, Tebeje TM, Lombebo AA, Sabo KG, Fente BM, Teshale AB, Asebe HA.
17-08-2023
PLoS Negl Trop Dis.

Background: Trachoma is the chief cause of preventable blindness worldwide and has been earmarked for elimination as a public health problem by 2030. Despite the five-year Surgery, Antibiotics, Facial cleanliness, and Environmental improvement (SAFE)-based interventions in the Andabet district, the prevalence of trachomatous follicular (TF) was 37%. With such a high prevalence of TF, the determinant factors were not revealed. Besides, there were no reports on the overall prevalence of active trachoma (i.e.TF and or trachomatous intense (TI)). **Objective:** To determine the prevalence and associated factors of active trachoma among 1-9 years of age children in the Andabet district. **Method:** A community-based cross-sectional study was conducted among children aged under nine years from March 1-30, 2023 in Andabet district, Northwest Ethiopia. Multi-stage systematic random sampling was employed to reach 540 children. A multilevel mixed-effect logistic regression analysis was employed to assess factors associated with active trachoma. We fitted both random effect and fixed effect analysis. Finally, variables with $p<0.05$ in the multivariable multilevel analysis were claimed to be significantly associated with active trachoma. **Result:** In this study, the overall prevalence of active trachoma was 35.37% (95% CI: 31.32%, 39.41%). The prevalence of TF and TI was 31.3% and 4.07% respectively. In the multilevel logistic regression analysis ocular discharge, fly-eye contact, latrine utilization, and source of water were significantly associated with the prevalence of active trachoma. **Conclusion:** In this study, the prevalence of active trachoma was much higher than the World Health Organization (WHO) threshold prevalence. Ocular discharge, fly-eye contact, latrine utilization, and source of water were independent determinants of active trachoma among children (1-9 years). Therefore, paying special attention to these high-risk groups could decrease the prevalence of a neglected hyperendemic disease, active trachoma.

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

Immunodiagnosis of Fascioliasis in Ruminants by ELISA Method: A Mini-Review.

Nur Hafizah S, Noor Izani NJ, Ahmad Najib M, Wan-Nor-Amilah WAW.

Genetic characterization and regional distribution of lymnaeid snails in northern Patagonia, Argentina.

Soler P, Abdala AM, Larroza M.

Gastrointestinal parasites of domestic sheep from Patagonia throughout historical times: A paleoparasitological approach.

Beltrame MO, Moviglia GS, De Tommaso D, Quintana S.

Sheep husbandry in Patagonia, Argentina, started at the beginning of the 20th century from European settlers. Sanitary management is minimal, which has serious implications for the sheep health. Sheep can be infested by diverse parasites, with well over 150 species of internal and external parasites reported worldwide. Gastrointestinal parasitism is one of the most common and important infections in sheep concerning the health status, and is the cause of significant morbidity and mortality, which generates considerable production losses. The present work is the first paleoparasitological study of sheep coprolites from Patagonia throughout historical times. Fifty-seven coprolites from the 'Cueva Peligro' archaeological site (Patagonia, Argentina) were analyzed using the Lutz spontaneous sedimentation technique and the modified Faust flotation technique. Ancient DNA (aDNA) study was carried out in order to identify the zoological origin of coprolites. The results obtained from Cytb analysis confirmed the identity of the host as Ovis aries (domestic sheep). A total of 39 coprolites examined were positive for parasites by at least one of the studied methods. Thirty eight samples were positive by spontaneous sedimentation and 10 samples were positive by the modified Faust technique. The parasitic fauna found was Trichuris sp. (Trichinellida: Trichuridae), Nematodirus sp., Nematodirus spathiger (Strongylida, Trichostrongyloidea), two unidentified Strongylida-type egg morphotypes, Fasciola hepatica (Trematoda: Digenea) and coccidia oocysts of Eimeria spp. (Apicomplexa: Eimeriidae). The modified Faust technique provided satisfactory results in terms of sensitivity for the detection of Eimeria spp. The use of this methodology as a routine procedure enables the processing of ancient samples, in order to increase recoveries. These results show the importance of integrating different diagnostic approaches in order to optimize parasitic findings. The recorded parasite diversity appears to have not changed over the last 120 years. The study displayed the presence of different parasitic species which suggests potential exposure to parasitic diseases through the historical times, both for sheep and for other domestic and wild mammals from Patagonia. Also, suggests the presence of fasciolosis, a zoonotic disease that implies a potential risk for Patagonian populations in the past.

Fasciola hepatica infection in horses in three governorates in northern Egypt: prevalence and risk factors.

Alshammari A, Gattan HS, Marzok M, Salem M, Al-Jabr OA, Selim A.

Wide variation of heterozygotic genotypes of recent fasciolid hybrids from livestock in Bangladesh assessed by rDNA internal transcribed spacer region sequencing and cloning.

Ahasan SA, De Elías-Escribano A, Artigas P, Alam MZ, Mondal MMH, Blair D, Chowdhury EH, Bargues MD, Mas-Coma S.

Fascioliasis causes high economic losses in livestock and underlies public health problems in rural areas, mainly of low-income countries. The increasing animal infection rates in Bangladesh were assessed, by focusing on host species, different parts of the country, and rDNA sequences. Fasciolid flukes were collected from buffaloes, cattle, goats and sheep from many localities to assess prevalences and intensities of infection. The nuclear rDNA internal transcribed spacer (ITS) region including ITS-1 and ITS-2 spacers was analyzed by direct sequencing and cloning, given the detection of intermediate phenotypic forms in Bangladesh. The 35.4% prevalence in goats and 55.5% in buffaloes are the highest recorded in these animals in Bangladesh. In cattle (29.3%) and sheep (26.8%) prevalences are also high for these species. These prevalences are very high when compared to lowlands at similar latitudes in neighboring India. The high prevalences and intensities appear in western Bangladesh where cross-border importation of animals from India occur. The combined haplotype CH3A of Fasciola gigantica widely found in all livestock species throughout Bangladesh fits its historical connections with the western Grand Trunk Road and the eastern Tea-Horse Road. The "pure" F. hepatica sequences only in clones from specimens showing heterozygotic positions indicate recent hybridization events with local "pure" F. gigantica, since concerted evolution did not yet have sufficient time to homogenize the rDNA operon. The detection of up to six different sequences coexisting in the cloned specimens evidences crossbreeding between hybrid parents, indicating repeated, superimposed and rapidly evolving hybridization events. The high proportion of hybrids highlights an increasing animal infection trend and human infection risk, and the need for control measures, mainly concerning goats in household farming management. ITS-1 and ITS-2 markers prove to be useful for detecting recent hybrid fasciolids. The introduction of a Fasciola species with imported livestock into a highly prevalent area of the other Fasciola species may lead to a high nucleotide variation in the species-differing positions in the extremely conserved fasciolid spacers. Results suggest that, in ancient times, frequent crossbreeding inside the same Fasciola species gave rise to the very peculiar characteristics of the present-day nuclear genome of both fasciolids.

Editorial: Trematode infection in ruminants, volume II.

Zhang H, Wang J, Mehmood K, Li K.

First morphometric and molecular characterization of Fasciola spp. in Northwest Tunisia.

Hammami I, Ciuca L, Maurelli MP, Romdhane R, Sassi L, Rjeibi MR, Farhat N, Simo AK, Rinaldi L, Rekik M, Gharbi M.

Diagnostic performance of Strongyloides-specific IgG4 detection in urine for diagnosis of human strongyloidiasis.

Wongphutorn P, Worasith C, Kopolrat KY, Homwong C, Sithithaworn J, Eamudomkarn C, Techasen A, Tippayawat P, Pitaksakurat O, Hongsrichan N, Crellen T, Sithithaworn P.

Background: Detection of parasite-specific IgG in urine is a sensitive method for diagnosis of strongyloidiasis and gives similar accuracy to serum IgG. However, there are no data concerning detection of IgG subclass in urine. To further explore the utility of diagnosis from urine samples, we evaluated the diagnostic performance of IgG4 in urine compared with parasitological and other immunological methods. **Methods:** The urine and sera included proven strongyloidiasis (group 1, n = 93), other parasitic infections (group 2, n = 40) and parasite negatives (group 3, n = 93). The performance of Strongyloides-specific IgG4 in urine for diagnosis of strongyloidiasis using fecal examinations as the reference standard was assessed. **Results:** With fecal examination as a gold standard, Strongyloides-specific IgG4 in urine had 91.4% sensitivity and 93.2% specificity while serum IgG4 had 93.6% sensitivity and 91.0% specificity. IgG4 in both urine and serum had almost perfect diagnostic agreements with fecal examination (Cohen's kappa coefficient was > 0.8). Cross-reactivity to Opisthorchis viverrini and Taenia spp. of IgG4 in urine were 7.5% and 12.5% in serum. Concurrent analyses of total IgG in urine and serum showed that the sensitivities (97.9-100%) and specificities (88.7-91.0%) were similar (P > 0.05). The sensitivity for parasitological examination by the formalin-ethyl acetate concentration technique (FECT) was 49.5% and that for agar plate culture technique (APC) it was 92.6%. **Conclusion:** Our findings showed that specific IgG4 detection in urine yielded similar diagnostic

performance to the same biomarkers in serum. This suggests that accurate diagnosis of strongyloidiasis can be performed using urine samples and IgG4 is a valid choice of diagnostic marker. Further assessment is required to assess the utility of urine IgG4 for measuring the response treatment in strongyloidiasis.

Liver fluke in a young Nepalese girl: A rare diagnostic puzzle.

Pandey A, Mishra A, Khadka S, Manandhar SR, Shrestha AL.
24-08-2023
Clin Case Rep.
https://pubmed.ncbi.nlm.nih.gov/37636892/

Key clinical message: Fascioliasis poses diagnostic challenges to clinicians for its broad spectrum of hepatobiliary symptoms and lower detection rates. Timely and precise identification avoids long-standing hepatic complications. Abstract: Fasciola hepatica, a trematode parasite, inhabits snails and sheep. Human hepatic fascioliasis is a neglected tropical disease with no specific tests. In this instance, the significance of clinical awareness, appropriate imaging, and serological investigations is demonstrated. A young Nepalese girl was diagnosed and managed successfully.

Immunol detection of cathepsin L from Fasciola hepatica infection in sheep by monoclonal antibody-based colloidal gold test strip assay.

Liu S, Zhang N, Yu Q, Li J, Wang X, Li X, Zhang X, Cheng S, Yue T, Zhang H, Gong P, Zhang X.
28-08-2023
Acta Biochim Biophys Sin (Shanghai).
https://pubmed.ncbi.nlm.nih.gov/37635410/

Parasite Diversity in a Freshwater Ecosystem.

Shafiq A, Abbas F, Hafeez-Ur-Rehman M, Khan BN, Aihetasham A, Amin I, Hmidullah, Mothana RA, Alharbi MS, Khan I, Khalil AAK, Ahmad B, Mubeen N, Akram M.
29-07-2023
Microorganisms.
https://pubmed.ncbi.nlm.nih.gov/37630500/

A Novel Designed Sandwich ELISA for the Detection of Echinococcus granulosus Antigen in Camels for Diagnosis of Cystic Echinococcosis.

Toaleb NI, Aboelsoued D, Abdel Megeed KN, Hekal SHA.
06-08-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624338/

An Unexpected Case of Opisthorchis felineus Infection Revealed during Liver Transplantation.

Mangano VD, Campani D, Cacciato Insilla A, Coco B, Gomez Morales MA, Brunetto M, La Rosa G, Ludovisi A, De Simone P, Bruschi F
31-07-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37623963/

Protein Modelling and Molecular Docking Analysis of Fasciola hepatica β-Tubulin's Interaction Sites, with Triclabendazole, Triclabendazole Sulphoxide and Triclabendazole Sulphone.

Olivares-Ferretti P, Beltrán JF, Salazar LA, Fonseca-Salamanca F.
Sept-2023
Acta Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37330945/

Purpose: Fasciola hepatica is a globally distributed trematode that causes significant economic losses. Triclabendazole is the primary pharmacological treatment for this parasite. However, the increasing resistance to triclabendazole limits its efficacy. Previous pharmacodynamics studies suggested that triclabendazole acts by interacting mainly with the β monomer of tubulin. Methods: We used a high-quality method to model the six isotypes of F. hepatica β-tubulin in the absence of three-dimensional structures. Molecular dockings were conducted to evaluate the destabilization regions in the molecule against the ligands triclabendazole, triclabendazole sulphoxide and triclabendazole sulphone. Results: The nucleotide binding site demonstrates higher affinity than the binding sites of colchicine, albendazole, the T7 loop and pβVII ($p < 0.05$). We suggest that the binding of the ligands to the polymerization site of β-tubulin can lead a microtubule disruption. Furthermore, we found that triclabendazole sulphone exhibited significantly higher binding affinity than other ligands ($p < 0.05$) across all isotypes of β-tubulin. Conclusions: Our investigation has yielded new insight on the mechanism of action of triclabendazole and its sulphometabolites on F. hepatica β-tubulin through computational tools. These findings have significant implications for ongoing scientific research ongoing towards the discovery of novel therapeutics to treat F. hepatica infections.

Trypanosomes (trypanosomiase et maladie de Chagas)

Functional annotation and comparative genomics analysis of Balamuthia mandrillaris reveals potential virulence-related genes.

Otero-Ruiz A, Rodriguez-Anaya LZ, Lares-Villa F, Lozano Aguirre Beltrán LF, Lares-Jiménez LF, Gonzalez-Galaviz JR, Cruz-Mendívil A.
31-08-2023

Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/37653073/

Exposure to Trypanosoma cruzi and Leishmania parasites in dogs from a rural locality of Yucatan, Mexico. A serological survey.

Reyes-Novelo E, Sauri-Arceo C, Panti-May A, Marín D, Canché-Pool EB, Chan-Espinoza DE, Marín C, Bolio-González M, Rodríguez-Vivas RI, Torres-Castro M, Escobedo-Ortegón FJ.
Sept-2023
Vet Parasitol Reg Stud Reports.
https://pubmed.ncbi.nlm.nih.gov/37652628/

Trypanosoma cruzi, the causal agent of American trypanosomiasis, and Leishmania spp., the causal agents of Leishmaniasis, are prevalent in more than 20 American countries, including Mexico. Dogs have been reported as incidental hosts for both parasites and may be helpful as transmission sentinels. We surveyed the dog population in a rural locality of the Merida municipality in Yucatan, Mexico, to evaluate the seroreactivity against T. cruzi and Leishmania spp. using two antigens, parasite homogenate (H) and iron superoxide dismutase extract (FeSODe), with two serological techniques (ELISA and Western Blot). Our study found that 3.33% of the tested dogs were seroreactive to T. cruzi using ELISA-H, and 29.5% were seroreactive to FeSODe antigen, with a 94.4% consistency between the two tests. Similarly, for L. mexicana, 1.6% were seroreactive using ELISA-H, and 9.8% were seroreactive using ELISA-FeSODe, with an 83.3% consistency between tests. For L. braziliensis, no dogs were seroreactive using ELISA-H, but 16.4% were seroreactive using ELISA-FeSODe, with a 90% consistency between tests. Finally, for L. infantum, 4.9% were seropositive using ELISA-H, and 6.6% were seropositive using ELISA-FeSODe, with a 75% consistency between tests. These results show noticeable evidence of exposure of dogs to trypanosomatid parasites and highlight the potential disease risk for the people and their companion animals in the region.

Characterization of the major surface glycoconjugates of Trypanosoma theileri.

Nagar R, Hambleton I, Tinti M, Carrington M, Ferguson MAJ.
29-08-2023
Mol Biochem Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37652240/

Characterisation of TcFUT1, a mitochondrial fucosyltransferase from Trypanosoma cruzi.

Franco JCP, Guther MLS, Lima ML, Ferguson MAJ.
29-08-2023
Mol Biochem Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37652239/

Novel diamides inspired by protein kinase inhibitors as anti-Trypanosoma cruzi agents: in vitro and in vivo evaluations.

Vieira da Silva Torchelsen FK, Fernandes Pedrosa TC, Rodrigues MP, de Aguiar AR, de Oliveira FM, Amarante GW, Sales-Junior PA, Branquinho RT, Gomes da Silva SP, Talvani A, Fonseca Murta SM, Martins FT, Braun RL, Teixeira RR, Furtado Mosqueira VC, Lana M.
31-08-2023
Future Med Chem.
https://pubmed.ncbi.nlm.nih.gov/37650735/

Background: Chagas disease is a life-threatening illness caused by *Trypanosoma cruzi*. The involvement of serine-arginine-rich protein kinase in the *T. cruzi* life cycle is significant. **Aims:** To synthesize, characterize and evaluate the trypanocidal activity of diamides inspired by kinase inhibitor, SRPIN340. **Material & Methods:** Synthesis using a three-step process and characterization by infrared, nuclear magnetic resonance and high-resolution mass spectrometry were conducted. The selectivity index was obtained by the ratio of CC_{50}/IC_{50} in two *in vitro* models. The most active compound, **3j**, was evaluated using *in vitro* cytokine assays and assessing *in vivo* trypanocidal activity. **Results: 3j** activity in the macrophage J774 lineage showed an anti-inflammatory profile, and mice showed significantly reduced parasitemia and morbidity at low compound dosages. **Conclusion:** Novel diamide is active against *T. cruzi in vitro* and *in vivo*.

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

Nascimento JF, O Souza RO, Alencar MB, Marsiccobetre S, Murillo AM, Damasceno FS, M Girard RBM, Marchese L, Luévano-Martinez LA, Achjian RW, Haanstra JR, M Michels PA, Silber AM.
30-08-2023
PLoS Pathog.
https://pubmed.ncbi.nlm.nih.gov/37647328/

DOES TRYPANOSOMA EVANSI HAVE THE MAXICIRCLE GENE, OR CAN TRYPANOSOMA EQUIPERDUM BE ISOLATED FROM BOVINES?

Subekti DT, Ekawasti F, Azmi Z, Yuniarto I, Fong S, Fahrimal Y.
01-08-2023
J Parasitol.
https://pubmed.ncbi.nlm.nih.gov/37646443/

Identifying a trypanosome isolate is generally based on morphological observations and molecular identification of one of the genes, usually internal transcribed spacer 1 and 2 of ribosomal DNA (ITS1 rDNA, ITS2 rDNA), a variant surface glycoprotein of Rode Trypanozoon antigen type 1.2 (VSG RoTat 1.2), or expression site-associated genes (ESAG). However, this identification is insufficient because these genes cannot distinguish organisms in the subgenus

Trypanozoon to the species level. A molecular approach using at least 5 sets of primers is needed, namely, ITS1, ESAG6/7, MINI, RoTat 1.2, and ND5, for stratified selection to obtain more targeted and conclusive results. Using this method to analyze isolates from Indonesia provided unexpected results: 9 isolates previously identified as Trypanozoon were found to have the kDNA maxicircle gene. Nine isolates of Trypanosoma equiperdum were identified for the first time in Indonesia, isolated from bovine (cattle and buffaloes). The identification of T. equiperdum in the 9 isolates was confirmed by analysis of the nucleotide sequence identity of the nad5-kDNA maxicircle gene.

γδ T cells control murine skin inflammation and subcutaneous adipose wasting during chronic Trypanosoma brucei infection.

Quintana JF, Sinton MC, Chandrasegaran P, Lestari AN, Heslop R, Cheaib B, Ogunsola J, Ngoyi DM, Kuispond Swar NR, Cooper A, Mabbott NA, Coffelt SB, MacLeod A.
29-08-2023
Nat Commun.
https://pubmed.ncbi.nlm.nih.gov/37644007/

African trypanosomes colonise the skin to ensure parasite transmission. However, how the skin responds to trypanosome infection remains unresolved. Here, we investigate the local immune response of the skin in a murine model of infection using spatial and single cell transcriptomics. We detect expansion of dermal IL-17A-producing Vγ6+ cells during infection, which occurs in the subcutaneous adipose tissue. In silico cell-cell communication analysis suggests that subcutaneous interstitial preadipocytes trigger T cell activation via Cd40 and Tnfsf18 signalling, amongst others. In vivo, we observe that female mice deficient for IL-17A-producing Vγ6+ cells show extensive inflammation and limit subcutaneous adipose tissue wasting, independently of parasite burden. Based on these observations, we propose that subcutaneous adipocytes and Vγ6+ cells act in concert to limit skin inflammation and adipose tissue wasting. These studies provide new insights into the role of γδ T cell and subcutaneous adipocytes as homeostatic regulators of skin immunity during chronic infection.

Cell-cell communication in African trypanosomes.

McWilliam KR.
Août-2023
Microbiology (Reading).
https://pubmed.ncbi.nlm.nih.gov/37643128/

Importance of CD40/CD40 dyad in the course of infection with Trypanosoma cruzi: Impact of its inhibition.

Frank FM, Wagner DH Jr, Postan M, Petray PB.
26-08-2023
Microb Pathog.
https://pubmed.ncbi.nlm.nih.gov/37640275/

Identifying inhibitors of Trypanosoma cruzi nucleoside diphosphate kinase 1 as potential repurposed drugs for Chagas' disease.

Galceran F, Digirolamo FA, Rengifo M, Reigada C, Saye M, Maciel BJ, Estecho IG, Errasti AE, Pereira CA, Miranda MR.
25-08-2023
Biochem Pharmacol.
https://pubmed.ncbi.nlm.nih.gov/37634596/

FAP106 is an interaction hub for assembling microtubule inner proteins at the cilium inner junction.

Shimogawa MM, Wijono AS, Wang H, Zhang J, Sha J, Szombathy N, Vadakkan S, Pelayo P, Jonnalagadda K, Wohlschlegel J, Zhou ZH, Hill KL.
26-08-2023
Nat Commun.
https://pubmed.ncbi.nlm.nih.gov/37633952/

Motility of pathogenic protozoa depends on flagella (synonymous with cilia) with axonemes containing nine doublet microtubules (DMTs) and two singlet microtubules. Microtubule inner proteins (MIPs) within DMTs influence axoneme stability and motility and provide lineage-specific adaptations, but individual MIP functions and assembly mechanisms are mostly unknown. Here, we show in the sleeping sickness parasite Trypanosoma brucei, that FAP106, a conserved MIP at the DMT inner junction, is required for trypanosome motility and functions as a critical interaction hub, directing assembly of several conserved and lineage-specific MIPs. We use comparative cryogenic electron tomography (cryoET) and quantitative proteomics to identify MIP candidates. Using RNAi knockdown together with fitting of AlphaFold models into cryoET maps, we demonstrate that one of these candidates, MC8, is a trypanosome-specific MIP required for parasite motility. Our work advances understanding of MIP assembly mechanisms and identifies lineage-specific motility proteins that are attractive targets to consider for therapeutic intervention.

Legionella pneumophila macrophage infectivity potentiator protein appendage domains modulate protein dynamics and inhibitor binding.

Wiedemann C, Whittaker JJ, Carrillo VHP, Goretzki B, Dajka M, Tebbe F, Harder JM, Krajczy PR, Joseph B, Hausch F, Guskov A, Hellmich UA.
24-08-2023
Int J Biol Macromol.
https://pubmed.ncbi.nlm.nih.gov/37633566/

Macrophage infectivity potentiator (MIP) proteins are widespread in human pathogens including Legionella pneumophila, the causative agent of Legionnaires' disease and protozoans such as Trypanosoma cruzi. All MIP proteins contain a FKBP (FK506 binding protein)-like prolyl-cis/trans-isomerase domain that hence presents an attractive drug target. Some MIPs such as the Legionella pneumophila protein (LpMIP) have additional appendage

domains of mostly unknown function. In full-length, homodimeric LpMIP, the N-terminal dimerization domain is linked to the FKBP-like domain via a long, free-standing stalk helix. Combining X-ray crystallography, NMR and EPR spectroscopy and SAXS, we elucidated the importance of the stalk helix for protein dynamics and inhibitor binding to the FKBP-like domain and bidirectional crosstalk between the different protein regions. The first comparison of a microbial MIP and a human FKBP in complex with the same synthetic inhibitor was made possible by high-resolution structures of LpMIP with a [4.3.1]-aza-bicyclic sulfonamide and provides a basis for designing pathogen-selective inhibitors. Through stereospecific methylation, the affinity of inhibitors to L. pneumophila and T. cruzi MIP was greatly improved. The resulting X-ray inhibitor-complex structures of LpMIP and TcMIP at 1.49 and 1.34 Å, respectively, provide a starting point for developing potent inhibitors against MIPs from multiple pathogenic microorganisms.

Use of Nanocarriers Containing Antitrypanosomal Drugs for the Treatment of Chagas Disease.

Paiva DF, Matos APDS, Garófalo DA, do Nascimento T, Monteiro MSSB, Santos-Oliveira R, Ricci-Junior E.
15-08-2023
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/37631078/

Chagas Disease Control-Many Approaches to Prospect.

Branquinha MH, Sangenito LS, Oliveira SSC, d'Avila-Levy CM, Santos ALS.
02-08-2023
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/37624333/

The Therapeutic Potential of Angeli's Salt in Mitigating Acute Trypanosoma cruzi Infection in Mice.

Hideko Tatakihara VL, Malvezi AD, Pereira RS, Lucchetti BFC, Dos Santos LF, Cecchini R, Yamauchi LM, Yamada-Ogatta SF, Miranda KM, Verri WA, Martins-Pinge MC, Pinge-Filho P.
19-08-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37624023/

Chagas disease (CD), caused by *Trypanosoma cruzi*, is a neglected tropical disease prevalent in Latin America. Infected patients are treated to eliminate the parasite, reduce the cardiomyopathy risk, and interrupt the disease transmission cycle. The World Health Organization recognizes benznidazole (BZ) and nifurtimox as effective drugs for CD treatment. In the chronic phase, both drugs have low cure rates and serious side effects. *T. cruzi* infection causes intense tissue inflammation that controls parasite proliferation and CD evolution. Compounds that liberate nitric oxide (NO) (NO donors) have been used as anti-*T. cruzi* therapeutics. Currently, there is no evidence that nitroxyl (HNO) affects *T. cruzi* infection outcomes. This study investigated the effects of the HNO donor Angeli's

salt (AS) on C57BL/6 mice infected with *T. cruzi* (Y strain, 5 × 10³ trypomastigotes, intraperitoneally). AS reduced the number of parasites in the bloodstream and heart nests and increased the protective antioxidant capacity of erythrocytes in infected animals, reducing disease severity. Furthermore, in vitro experiments showed that AS treatment reduced parasite uptake and trypomastigote release by macrophages. Taken together, these findings from the murine model and in vitro testing suggest that AS could be a promising therapy for CD.

Antiprotozoal Activity of Benzoylthiourea Derivatives against Trypanosoma cruzi: Insights into Mechanism of Action.

Pereira PML, Fernandes BT, Dos Santos VR, Cabral WRC, Lovo-Martins MI, Alonso L, Lancheros CAC, de Paula JC, Camargo PG, Suzukawa HT, Alonso A, Macedo F Jr, Nakamura CV, Tavares ER, de Lima Ferreira Bispo M, Yamauchi LM, Pinge-Filho P, Yamada-Ogatta SF.
03-08-2023
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/37623972/

Anti-Protozoan Activities of Polar Fish-Derived Polyalanine Synthetic Peptides.

Nunes EAC, da Silva MC, Cardoso MH, Preza SLE, de Oliveira LS, Frihling BEF, Charneau SO, Grellier P, Franco OL, Migliolo L.
31-07-2023
Mar Drugs.
https://pubmed.ncbi.nlm.nih.gov/37623715/

Chagas disease, sleeping sickness and malaria are infectious diseases caused by protozoan parasites that kill millions of people worldwide. Here, we performed in vitro assays of *Pa-MAP*, *Pa-MAP1.9*, and *Pa-MAP2* synthetic polyalanine peptides derived from the polar fish *Pleuronectes americanus* toward *Trypanosoma cruzi*, *T. brucei gambiense* and *Plasmodium falciparum* activities. We demonstrated that the peptides *Pa-MAP1.9* and *Pa-MAP2* were effective to inhibit *T. brucei* growth. In addition, structural analyses using molecular dynamics (MD) studies showed that *Pa-MAP2* penetrates deeper into the membrane and interacts more with phospholipids than *Pa-MAP1.9*, corroborating the previous in vitro results showing that *Pa-MAP1.9* acts within the cell, while *Pa-MAP2* acts via membrane lysis. In conclusion, polyalanine *Pa-MAP1.9* and *Pa-MAP2* presented activity against bloodstream forms of *T. b. gambiense*, thus encouraging further studies on the application of these peptides as a treatment for sleeping sickness.

Ulcère de Buruli

An mHealth App (eSkinHealth) for Detecting and Managing Skin Diseases in Resource-Limited Settings: Mixed Methods Pilot Study.

Yotsu RR, Almamy D, Vagamon B, Ugai K, Itoh S, Koffi YD, Kaloga M, Dizoé LAS, Kouadio K, Aka N, Yeboue LKG, Yao KA, Blanton RE.

Mycolactone A vs. B: Multiscale Simulations Reveal the Roles of Localization and Association in Isomer-Specific Toxicity.

Nguyen JDM, da Hora GCA, Swanson JMJ.

Mycolactone is an exotoxin produced by *Mycobacterium ulcerans* that causes the neglected tropical skin disease Buruli ulcer. This toxin inhibits the Sec61 translocon in the endoplasmic reticulum (ER), preventing the host cell from producing several secretory and transmembrane proteins, resulting in cytotoxic and immunomodulatory effects. Interestingly, only one of the two dominant isoforms of mycolactone is cytotoxic. Here, we investigate the origin of this specificity by performing extensive molecular dynamics (MD) simulations with enhanced free energy sampling to query the association trends of the two isoforms with both the Sec61 translocon, using two distinct cryo-electron microscopy (cryo-EM) models as references, and the ER membrane, which serves as a toxin reservoir prior to association. Our results suggest that mycolactone B (the cytotoxic isoform) has a stronger association with the ER membrane than mycolactone A due to more favorable interactions with membrane lipids and water molecules. This could increase the reservoir of toxin proximal to the Sec61 translocon. In one model of Sec61 inhibited by mycolactone, we find that isomer B interacts more closely with residues thought to play a key role in signal peptide recognition and, thus, are essential for subsequent protein translocation. In the other model, we find that isomer B interacts more closely with the lumenal and lateral gates of the translocon, the dynamics of which are essential for protein translocation. These interactions induce a more closed conformation, which has been suggested to block signal peptide insertion and subsequent protein translocation. Collectively, these findings suggest that isomer B's unique cytotoxicity is a consequence of both increased localization to the ER membrane and channel-locking association with the Sec61 translocon, facets that could be targeted in the development of Buruli Ulcer diagnostics and Sec61-targeted therapeutics.

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

Yotsu RR, Ding Z, Hamm J, Blanton RE.

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