Réseau MTN Francophone

Veille scientifique
Maladies tropicales négligées

Semaine 47
21 au 27 novembre 2022

Dengue, chikungunya et maladie à virus Zika

Rage

Trachome

Is it just a cure? Re-evaluating the effects of prenatal exposure to the Great Chinese Famine on the risk of infectious diseases in adulthood.

He P, Luo Y, Ding R, Zheng X.
Dec. 2022
Soc Sci Med.
https://pubmed.ncbi.nlm.nih.gov/36335705/

Background: Very limited studies focused on the early-life adversities on infectious diseases. Taking the Great Chinese famine as a natural experiment, this study re-evaluated the long-term effect of prenatal famine exposure on infectious diseases by using nationally representative data. Methods: Using difference-in-difference (DID) models, we analyzed 215,216 adults who participated in the Second National Sample Survey on Disability in 2006 across 734 counties of China to detect the effects of prenatal exposure to the Great Chinese Famine on the risk of infectious diseases in adulthood. Infectious diseases were ascertained by using the combination of self-reports or family members' reports and on-site medical diagnosis by experienced specialists, and the severity of famine was measured by the cohort size shrinkage index (CSSI) at the county level. Results: All DID estimates of the effects of famine on the probability of infectious diseases were insignificant, with a coefficient of 0.0007 (-0.0024, 0.0026) for all participants and coefficients of 0.0001 (-0.0041, 0.0043) and -0.0002 (-0.0036, 0.0033) for males and females, respectively. That is, the famine cohort dwelling in regions with a greater intensity of famine had similar levels of infectious disease risks than the cohorts with post-famine prenatal exposure experience in less affected famine regions. Furthermore, there were no significant famine and post-famine cohort differences in the DID estimates by examining the variations in subgroups with different types of infectious diseases (trachoma, poliomyelitis, tuberculosis, maternal infections and other infectious diseases). Conclusion: No significant impact of prenatal exposure to the Chinese famine was observed on the risk of infectious diseases in adulthood. Famine survivors may be "cured" by the famine and were resilient to adverse environments in their life course because selective mortality may weaken the association between adverse prenatal exposure and later health.

Comment on: Recurrent upper eyelid trachomatous entropion repair: long-term efficacy of a five-step approach.

Kreis AJ, Nouhoum G.
Dec 2022
Eye (Lond).
https://pubmed.ncbi.nlm.nih.gov/35525859/

Ulcère de Buruli

Identification of potential candidate vaccines against Mycobacterium ulcerans based on the major facilitator superfamily transporter protein.

Ishwarlall TZ, Adeleke VT, Maharaj L, Okpeku M, Adeniyi AA, Adeleke MA.
Nov. 2022
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/36426350/

Buruli ulcer is a neglected tropical disease that is characterized by non-fatal lesion development. The causative agent is Mycobacterium ulcerans (M. ulcerans). There are no known vectors or transmission methods, preventing the development of control methods. There are effective diagnostic techniques and treatment routines; however, several socioeconomic factors may limit patients' abilities to receive these treatments. The Bacillus Calmette-Guérin vaccine developed against tuberculosis has shown limited efficacy, and no conventionally designed vaccines have passed clinical trials. This study aimed to generate a multi-epitope vaccine against M. ulcerans from the major facilitator superfamily transporter protein using an immunoinformatics approach. Twelve M. ulcerans genome assemblies were analyzed, resulting in the identification of 11 CD8+ and 7 CD4+ T-cell epitopes and 2 B-cell epitopes. These conserved epitopes were computationally predicted to be antigenic, immunogenic, non-allergenic, and non-toxic. The CD4+ T-cell epitopes were capable of inducing interferon-gamma and interleukin-4. They successfully bound to their respective human leukocyte antigens alleles in in silico docking studies. The expected global population coverage of the T-cell epitopes and their restricted human leukocyte antigens alleles was 99.90%. The population coverage of endemic regions ranged from 99.99% (Papua New Guinea) to 21.81% (Liberia). Two vaccine constructs were generated using the Toll-like receptors 2 and 4 agonists, LprG and RpfE, respectively. Both constructs were antigenic, non-allergenic, non-toxic, thermostable, basic, and hydrophilic. The DNA sequences of the vaccine constructs underwent optimization and were successfully in-silico cloned with the pET-28a(+) plasmid. The vaccine constructs were successfully docked to their respective toll-like receptors. Molecular dynamics simulations were carried out to analyze the binding interactions within the complex. The generated binding energies indicate the stability of both complexes. The constructs generated in this study display severable favorable properties, with construct one displaying a greater range of favorable

properties. However, further analysis and laboratory validation are required.

A combined effort of 11 laboratories in the WHO African region to improve quality of Buruli ulcer PCR diagnosis: The "BU-LABNET".

Marion E, Hycenth N, Vedithi SC, Robbe-Saule M, Donkeng V, Ganlonon LM, Dissou A, Ngazoa SK, Kabedi MJ, Mabika Mabika A, Phillips R, Frimpong M, Yeboah-Manu D, Walker VY, Akinwale O, Issaka M, Bretzel G, Asiedu K, Eyangoh S.
Nov. 2022
PLoS Negl Trop Dis
https://pubmed.ncbi.nlm.nih.gov/36331971/

Buruli ulcer is one of the 20 neglected tropical diseases in the world. This necrotizing hypodermitis is a chronic debilitating disease caused by an environmental Mycobacterium ulcerans. At least 33 countries with tropical, subtropical and temperate climates have reported Buruli ulcer in African countries, South America and Western Pacific regions. Majority of cases are spread across West and Central Africa. The mode of transmission is unclear, hindering the implementation of adequate prevention for the population. Currently, early diagnosis and treatment are crucial to minimizing morbidity, costs and preventing long-term disability. Biological confirmation of clinical diagnosis of Buruli ulcer is essential before starting chemotherapy. Indeed, differential diagnosis are numerous and Buruli ulcer has varying clinical presentations. Up to now, the gold standard biological confirmation is the quantitative PCR, targeting the insertion sequence IS2404 of M. ulcerans performed on cutaneous samples. Due to the low PCR confirmation rate in endemic African countries (under 30% in 2018) for numerous identified reasons within this article, 11 laboratories decided to combine their efforts to create the network "BU-LABNET" in 2019. The first step of the network was to harmonize the procedures and ship specific reagents to each laboratory. With this system in place, implementation of these procedures for testing and follow-up was easy and the laboratories were able to carry out their first quality control with a very high success rate. It is now time to integrate other neglected tropical diseases to this platform, such as yaws or leprosy.

Can membrane composition traffic toxins? Mycolactone and preferential membrane interactions.

da Hora GCA, Nguyen JDM, Swanson JMJ.
Nov.2022
Biophys J.
https://pubmed.ncbi.nlm.nih.gov/36258678/

Mycolactone is a cytotoxic and immunosuppressive macrolide produced by Mycobacterium ulcerans and the sole causative agent of the neglected tropical skin disease Buruli ulcer. The toxin acts by invading host cells and interacting with intracellular targets to disrupt multiple fundamental cellular processes. Mycolactone's amphiphilic nature enables strong interactions with lipophilic environments, including cellular membranes; however, the specificity of these interactions and the role of membranes in the toxin's pathogenicity remain unknown. It is likely that preferential interactions with lipophilic carriers play a key role in the toxin's distribution in the host, which, if understood, could provide insights to aid in the development of needed diagnostics for Buruli ulcer disease. In this work, molecular dynamics simulations were combined with enhanced free-energy sampling to characterize mycolactone's association with and permeation through models of the mammalian endoplasmic reticulum (ER) and plasma membranes (PMs). We find that increased order in the PMs not only leads to a different permeation mechanism compared with that in the ER membrane but also an energetic driving force for ER localization. Increased hydration, membrane deformation, and preferential interactions with unsaturated lipid tails stabilize the toxin in the ER membrane, while disruption of lipid packing is a destabilizing force in the PMs.

Pian

Improved rapid diagnostic tests to detect syphilis and yaws: a systematic review and meta-analysis.

Zhang Y, Goh SM, Mello MB, Baggaley RC, Wi T, Johnson CC, Asiedu KB, Marks M, Pham MD, Fairley CK, Chow EPF, Mitjà O, Toskin I, Ballard RC, Ong JJ.
Dec. 2022
Sex Transm Infect.
https://pubmed.ncbi.nlm.nih.gov/36180209/

Background: Current rapid tests for syphilis and yaws can detect treponemal and non-treponemal antibodies. We aimed to critically appraise the literature for rapid diagnostic tests (RDTs) which can better distinguish an active infection of syphilis or yaws. Methods: We conducted a systematic review and meta-analysis, searching five databases between January 2010 and October 2021 (with an update in July 2022). A generalised linear mixed model was used to conduct a bivariate meta-analysis for the pooled sensitivity and specificity. Heterogeneity was assessed using the I^2 statistic. We used the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) to assess the risk of bias and Grading of Recommendations, Assessment, Development and Evaluations (GRADE) to evaluate the certainty of evidence. Results: We included 17 studies for meta-analyses. For syphilis, the pooled sensitivity and specificity of the treponemal component were 0.93 (95% CI: 0.86 to 0.97) and 0.98 (95% CI: 0.96 to 0.99), respectively. For the non-treponemal component, the pooled sensitivity and specificity were 0.90 (95% CI: 0.82 to 0.95) and 0.97 (95% CI: 0.92 to 0.99), respectively. For yaws, the pooled sensitivity and specificity of the treponemal component were 0.86 (95% CI: 0.66 to 0.95) and 0.97 (95% CI: 0.94 to 0.99), respectively. For the non-treponemal component, the pooled sensitivity and specificity were 0.80 (95% CI: 0.55 to 0.93) and 0.96 (95% CI: 0.92 to 0.98), respectively.

Conclusions: RDTs that can differentiate between active and previously treated infections could optimise management by providing same-day treatment and reducing unnecessary treatment.

Lèpre

Implementing tuberculosis patient cost surveys in resource-constrained settings: lessons from Tanzania.

Kilale AM, Makasi C, Majaha M, Manga CD, Haule S, Hilary P, Kimbute O, Kitua S, Jani B, Range N, Ngowi B, Nkiligi E, Matechi E, Muhandiki W, Mahamba V, Mutayoba B, Ershova J.
Nov. 2022
BMC Public Health.
https://pubmed.ncbi.nlm.nih.gov/36434606/

Tuberculosis (TB) disproportionally affects persons and families who are economically and socially disadvantaged. Therefore, a patient cost survey was conducted in Tanzania to evaluate the costs incurred by patients and their households before and after the diagnosis of TB. It was the first survey in Tanzania to ascertain baseline information and experience for subsequent surveys. This paper aims to share the experience encountered during the survey to ensure a standardized approach and elimination of potential barriers for the implementation of future surveys. A total of 777 TB patients from 30 clusters selected based on probability proportional to the size were interviewed during the study period. As the sample size was calculated based on notification data from the previous year, some health facilities experienced an inadequate number of TB patients during the study to meet the allocated cluster size for the survey. Most facilities had poor recording and recordkeeping in TB registers where deaths were not registered, and some patients had not been assigned district identification numbers. Fixed days for TB drug refills in health facilities affected the routine implementation of the survey as the interviews were conducted when patients visited the facility to pick up the drugs. Tablets used to collect data failed to capture the geographic location in some areas. The households of TB patients lost to follow-up and those who had died during TB treatment were not included in the survey. When planning and preparing for patient costs surveys, it is important to consider unforeseen factors which may affect planned activities and findings. During the survey in Tanzania, the identified challenges included survey logistics, communications, patient enrollment, and data management issues. To improve the quality of the findings of future surveys, it may be reasonable to revise survey procedures to include households of TB patients who were lost to follow-up and those who died during TB treatment; the households of such patients may have incurred higher direct and indirect costs than households whose patient was cured as a result of receiving TB treatment.

Leprosy rash precipitated by immunotherapy for suspected inflammatory neuropathy.

Leung A, Arnold BJ, Hodgson TO, Cutfield NJ.
Nov. 2022
Pract Neurol.
https://pubmed.ncbi.nlm.nih.gov/36428101/

Leprosy is a chronic granulomatous infection caused by Mycobacterium leprae complex, causing skin and nerve lesions with potential for permanent disability. Leprosy can be overlooked in Western settings, as it is more prevalent in low-income and middle-income countries. We describe a 38-year-old woman with a 4-year history of progressive numbness of the left hand incorrectly diagnosed as multifocal acquired demyelinating sensory and motor neuropathy on the basis of clinical and neurophysiological findings. Treatment with empirical weekly corticosteroid followed by intravenous immunoglobulin resulted in the sudden development of a widespread rash; we then diagnosed borderline lepromatous leprosy on skin biopsy. We postulate that the immune treatments induced a temporary state of immune tolerance followed by a rebound of a T cell-mediated immune response resulting in a type 1 immunological response.

A-waves associated are with neuropathic pain in leprosy.

Garbino JA, Kirchner DR, França MC Jr.
Nov. 2022
Muscle Nerve
https://pubmed.ncbi.nlm.nih.gov/36420641/

Activated TLR2/4-positive T cells boost cell exhaustion during lepromatous leprosy infection via PD-1 upregulation.

Sadhu S, Kumar S, Mitra DK, Joshi B.
15-11-2022
Heliyon.
https://pubmed.ncbi.nlm.nih.gov/36419668/

The most important stage in activating an appropriate immune response during an infection is pathogen detection. Pattern recognition receptors (PRRs) are innate sensors used for pathogen detection that mould and link the innate and adaptive immune responses by the host. Toll Like receptors (TLRs) specifically TLR2 and TLR4, are PRRs, which have gained prominence due to their exceptional capacity to recognize unique molecular patterns from invading pathogens. They also play a critical role in maintaining the balance between Th1 and Th2 responses, which are necessary for the host's survival. Leprosy is a spectral disease with a wide range of immunological manifestations in the host. Cells of both the innate and adaptive branches play crucial roles in this polarized immune state. Here, we have analysed the proportional expression patterns of TLR2 and TLR4 on the surface of CD3+, CD4+, CD8+, CD19+ and CD161+ lymphocytes and CD14+ monocytes in different groups of leprosy patients. Further, these TLRs positive cells were

correlated with the surface markers of cell exhaustion such as Programmed Death-1 (PD-1) and its ligand (PD-L1), which indicated their role in immunosuppression. Additionally, blocking the interaction of PD-1 with PD-L1 in lymphocytes demonstrated visible improvement in their immune activation status through release of pro-inflammatory cytokines (IFN-γ and TNF-α).

Seroepidemiologic survey of the household contacts of leprosy patients.

Barbosa AM, Silva SUD, Toledo ACCG, Abreu MAMM.
21-11-2022
Rev Assoc Med Bras
https://pubmed.ncbi.nlm.nih.gov/36417641/

Objective: Leprosy is a disabling infectious disease caused by Mycobacterium leprae. This study aimed to investigate the prevalence of leprosy among household contacts of leprosy patients. Methods: This study is a serological survey in household contacts of leprosy patients who had been treated or were undergoing treatment in the city of Presidente Prudente, São Paulo, Brazil, from 2006-2016, using clinical examination and screening for anti- Phenolic glycolipid-I antibodies with Mycobacterium leprae-flow serology. Results: A total of 263 index cases of leprosy were identified during the study period. Of these, 53 were approached, and among their household contacts, 108 were examined. The ML-flow test was positive in 2 (1.85%) individuals, but clinical examination revealed no signs or symptoms of leprosy in them. Therefore, they were considered to have a subclinical infection. Leprosy was not confirmed in any household contacts. In this study, a lower percentage of household contacts, when compared to that in the literature, had a positive Mycobacterium leprae-flow test result. Conclusion: The use of Mycobacterium leprae-flow should be encouraged during the follow-up of at-risk populations, such as the household contacts of leprosy patients.

Risk areas for the occurrence of leprosy in border countries of South America - Brazil and Argentina.

Silva-Sobrinho RA, Oliveira KS, Deschutter EJ, Arcoverde MAM, Hoare I, Izurieta R, Zilly A, Topanotti ML, de Almeida AM, Meira MCR, da Luz LDP, Cicchelero LM, Zimermann F.
23-11-2022
PLoS One
https://pubmed.ncbi.nlm.nih.gov/36417347

Objective: The aim was to analyze the spatial association and relative risk (RR) of leprosy cases diagnosed in southern Brazil and in the Argentinean province of Misiones during 2010 to 2016. Methods: This ecological-type epidemiological study analyzed data from the Health Ministries of both countries. The analysis included frequency measures, spatial autocorrelation, RR cluster analysis and map construction. Results: A hyperendemic occurrence was identified in all study regions, in the state of Paraná 71.2% of the municipalities were hyperendemic and in Misiones, Argentina 41.2%. The GI* statistical analysis showed clusters of high incidence rates in the state of Paraná and low-risk clusters in much of the state of Rio Grande do Sul, both in Brazil. The analysis indicated an area with RR equal to 3.87 - ($p < .0001$) when considering the entire territory and an RR of 2.80 - ($p < .0001$) excluding the state of Paraná, with the number of departments of Misiones, Argentina included in the risk clusters increasing significantly. Conclusions: The findings indicate a high probability of similar illness in adjacent areas, according to their relative position in space, as the occurrence of the disease is influenced by neighboring clusters.

Knowledge, attitude, and practice of Nepalese residents in the prevention and control of COVID-19: A cross-sectional web-based survey.

Rajbanshi M, Bhusal S, Paudel K, Poudel B, Gaire A, Khatri E, Kalauni BR, Aryal B, Sharma G, Karki N.
Dec. 2022
Ann Med Surg (Lond)
https://pubmed.ncbi.nlm.nih.gov/36411829/

Background: Coronavirus disease 2019 (COVID-19) has caused a global public health crisis. Preventive measures to tackle the deadly virus are influenced by people's knowledge, attitude, and practice (KAP) toward COVID-19. This study aimed to assess the level of knowledge, attitude, and practice toward COVID-19 among Nepalese residents in Nepal. Methodology: A web-based cross-sectional survey was conducted among 755 Nepalese residents across all seven provinces of Nepal. The questionnaire used to determine the KAP of the participants was derived from a previous study conducted in Nepal. Descriptive analysis was done to identify the distribution of socio-economic and demographic characteristics of participants. Factors associated with residents' KAP regarding COVID-19 were examined using Chi-square tests at the significance level of 0.05. Results: The mean age of the participants was 24.6 years. At the time of data collection, 8.2% of the participants had their families in isolation or quarantine center. In this study, 76.4%, 58.0%, and 63.6% of the participants had a good knowledge level, attitude level, and practice level respectively regarding COVID-19. Occupation and marital status were significantly associated with knowledge, attitude, and practice level. Age was significantly associated with knowledge and attitude level. Those participants who had their family members in quarantine were found to have a good level of preventive practice. The knowledge-attitude ($r_{ka} = 0.184$, $p < 0.001$), attitude-practice ($r_{ap} = 0.125$, $p < 0.001$) and knowledge-practice ($r_{kp} = 0.07$, $p < 0.05$) were positively correlated in this study.Conclusion: This study showed satisfactory awareness regarding COVID-19 among Nepalese residents. Community-based health education programs should be promoted to develop a positive attitude toward healthy practices to tackle the COVID-19 pandemic or any future health crisis.

Epidemiological Characteristics and Factors Associated with Cure of Leprosy in Chongqing, China, from 1949 to 2019.

Wang Y, Xiao D, Wu M, Qing L, Yang T, Xiao P, Deng D.
Nov. 2022
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/36410327/

Chongqing is one of the focuses of leprosy control in China. Although leprosy control in Chongqing has achieved remarkable results over the years, there are also some problems, such as recurrent epidemics and insufficient early detection in some areas. The aim of this study was to analyze the epidemiological characteristics of leprosy in Chongqing, from 1949 to 2019 and explore the potential factors sociated with cure of leprosy to provide a basis for improving leprosy prevention and treatment strategies in Chongqing. Epidemiological indicators such as incidence and prevalence rates were used to evaluate the prevalence of leprosy. The epidemiological characteristics and control situation of leprosy in patients were analyzed using demographic characteristics, diagnosis, and treatment. Survival analysis was conducted to explore factors associated with the cure of leprosy. From 1949 to 2019, 3,703 cases of leprosy were registered in Chongqing. The incidence of leprosy in the city peaked at 0.853/105 in 1960 and remained below 0.100/105 after 2003. The number of high incidence areas decreased significantly, but they were mainly concentrated in the northeast and southeast regions. The early detection rate increased yearly from 1949 to 2019, and the rate of grade 2 disability ranged from 38.2% to 21.7%, with a fluctuating downward trend after 1960. Male, young age, employment as a farmer, delayed diagnosis, and multibacillary leprosy were risk factors for leprosy cure. Chongqing should continue to strengthen leprosy monitoring to improve the early detection of leprosy and focus on sociated risk factors to carry out multiple strategies.

Ross Syndrome Presenting as Heat Exhaustion: A Report of Two Cases.

Singh GK, Arora S, Bahuguna A, Das P, Bellad P.
Jul-Sep. 2022
Indian J Occup Environ Med.
https://pubmed.ncbi.nlm.nih.gov/36408429/

Treatment outcomes of tuberculosis patients in a Directly Observed Treatment Short course (DOTS) Referral Centre in Delta State, Nigeria: a five-year review (2012 - 2016).

Awunor NS, Alenoghena IO, Akpodiete A.
22-06-2022
Afr Health Sci.
https://pubmed.ncbi.nlm.nih.gov/36407334

Introduction: The objective of this study is to observe the trend in treatment outcomes and identify determinants of treatment success among patients recruited into care through the DOTS strategy. Methodology: A retrospective record review of tuberculosis patients (2012-2016) was carried out at the Tuberculosis and Leprosy Referral Centre, Eku, Delta State, Nigeria. Results: Records of four hundred and twenty five (425) tuberculosis patients under DOTS were reviewed over five years. The highest number of cases under treatment, 102 (24.0%), was recorded in 2013. The mean age (SD) of patients was 37.3 (±16.5) years, majority of the patients were male (62.4%) and 18% had TB/HIV co-infection. Treatment outcomes of patients were cured (53.4%), completed (27.8%), died (6.8%), failed (2.4%), lost to follow up (4.9%), transferred out (1.2%) and not evaluated (3.5%). Over all, treatment success rate was 81.2% with a trend of 88.7% (2012), 87.3% (2013), 85.9% (2014), 65.0% (2015) and 65.8% (2016) respectively. Patient characteristics were not associated with treatment success. Conclusion: The treatment success rate was high and in line with the national recommendation of 80% and above. The trend showed a reduction in number of new cases enrolled into the DOTS programme, reduction in success rate with a concomitant increase in loss to follow up. There was no association between patient characteristics and TB treatment success. System strengthening on patient follow up, community health education and treatment adherence is recommended.

How much has been achieved to prevent and control leprosy in Malawi since 2012?

Muula AS.
Sep. 2022
Malawi Med J.
https://pubmed.ncbi.nlm.nih.gov/36406097

A Clinico-Trichoscopic Analysis of Hair Density and Diameter Variability in Relation to Severity Grading of Female Pattern Hair Loss.

Michelle V, Shilpa K, Leelavathy B.
2022 Sep-Oct
Int J Trichology.
https://pubmed.ncbi.nlm.nih.gov/36404884/

Context: Hair loss is a common complaint among Indian women. For female pattern hair loss (FPHL), diagnosis is primarily clinical. In the early stages, it can be confused with other conditions. Histopathology is the diagnostic method of choice but requires multiple biopsies and can be disfiguring. Trichoscopy is an alternative noninvasive, rapid tool. Aim: The aim of this study is to study the hair density and hair diameter variance in relation with severity grading of FPHL. Settings and design: Cross-sectional study. Materials and methods: Ninety women aged 18 years and above were included in this cross-sectional study conducted at the dermatology department of Bangalore Medical College and Research Institute. Trichoscopic examination was done with a videodermoscope (Firefly DE300) at 20 and 70-fold magnification. Only those patients who met the trichoscopic diagnostic criteria for FPHL were included. Statistical analysis used: Descriptive statistics, ANOVA, and Spearman's correlation test for fitness of good, using Microsoft Excel data analysis tools. Results: Increase in disease severity from grade one to grade three positively correlated with a decrease in hair density over the frontal scalp ($P < 0.001$) and the occipital scalp ($P < 0.001$), decrease in average hair shaft diameter over both frontal and occipital scalp ($P < 0.001$).

Conclusion: Trichoscopic tools, particularly hair density and hair diameter variance over both frontal and occipital scalp can be useful to help determine FPHL disease severity and its progression.

Central Nervous System Mycobacterium Infection: Tuberculosis and Beyond.

Park M, Gupta RK.
Feb. 2022
Neuroimaging Clin N Am.
https://pubmed.ncbi.nlm.nih.gov/36404038

Tuberculosis is a contagious infectious disease caused by Mycobacterium tuberculosis, and is the leading cause of death from a single infectious agent worldwide. Imaging plays an important role in the early diagnosis of central nervous system tuberculosis and may prevent unnecessary morbidity and mortality. This article presents an extensive review of pathogenesis, clinical symptoms, typical and atypical imaging appearances of intracranial and spinal tuberculosis, and advanced imaging of intracranial tuberculosis. Furthermore, we explore central nervous system infection of nontuberculous mycobacteria and leprosy and their imaging findings.

The protective role of tissue-resident interleukin 17A-producing gamma delta T cells in Mycobacterium leprae infection.

Liu Y, Shi C, Ma S, Ma Y, Lu X, Zhu J, Yang D.
26-10-2022
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/36389696

Mycobacterium leprae is a kind of disease-causing bacteria and results in leprosy in human. Gamma delta (γδ) T cell is a T-cell subset that is presented in both human dermis and epidermis. These cells bridge innate and adaptive immune responses and play critical roles in regulating anti-microbial defense, wound healing, and skin inflammation. Here, we investigated skin resident γδ T cells in patients with leprosy. Our data showed that γδ T cells significantly accumulated in skin lesions of leprosy patients with tuberculoid (TT) form. IL-23 can predominantly stimulate dermal γδ T cells to produce interleukin 17 (IL-17), a cytokine which may lead to disease protection. These γδ T cells expressed a specific set of surface molecules, and majority of these cells were Vδ1⁺. Also, IL-23 can stimulate the expansion of dermal γδ T cells expansion. Moreover, our results revealed that the transcription factor RORγt was responsible for IL-17A expression in leprosy lesion. Therefore, these data indicated that IL-23-responsive dermal γδ T cells were the major resource of IL-17A production in the skin and could be a potential target in the treatment of leprosy.

microRNAs associated with the pathogenesis and their role in regulating various signaling pathways during Mycobacterium tuberculosis infection.

Davuluri KS, Chauhan DS.
27-10-2022
Front Cell Infect Microbiol.
https://pubmed.ncbi.nlm.nih.gov/36389170/

Despite more than a decade of active study, tuberculosis (TB) remains a serious health concern across the world, and it is still the biggest cause of mortality in the human population. Pathogenic bacteria recognize host-induced responses and adapt to those hostile circumstances. This high level of adaptability necessitates a strong regulation of bacterial metabolic characteristics. Furthermore, the immune reponse of the host virulence factors such as host invasion, colonization, and survival must be properly coordinated by the pathogen. This can only be accomplished by close synchronization of gene expression. Understanding the molecular characteristics of mycobacterial pathogenesis in order to discover therapies that prevent or resolve illness relies on the bacterial capacity to adjust its metabolism and replication in response to various environmental cues as necessary. An extensive literature details the transcriptional alterations of host in response to in vitro environmental stressors, macrophage infection, and human illness. Various studies have recently revealed the finding of several microRNAs (miRNAs) that are believed to play an important role in the regulatory networks responsible for adaptability and virulence in Mycobacterium tuberculosis. We highlighted the growing data on the existence and quantity of several forms of miRNAs in the pathogenesis of M. tuberculosis, considered their possible relevance to disease etiology, and discussed how the miRNA-based signaling pathways regulate bacterial virulence factors.

Microbiota in promoting liver regeneration.

Wang C, Li W.
10-11-2022
Cell Rep Med.
https://pubmed.ncbi.nlm.nih.gov/36384098/

Extensive work has revealed well-coordinated mechanisms that underlie liver regeneration, albeit with a focus on intrinsic interactions within hepatic cells. Here, Hess et al.1 demonstrate that Mycobacterium leprae infection can induce liver growth of nine-banded armadillo without obvious side effects.

Leprosy among female prisoners in Brazil.

Parente EO, Leal M, Kendall C, Mota RMS, Pires Neto RDJ, Macena RHM, Kerr L.
Dec. 2022
Cien Saude Colet.
https://pubmed.ncbi.nlm.nih.gov/36383862/

To estimate the prevalence of leprosy among Brazilian female prisoners and identify factors associated with the disease. Cross-sectional study conducted between 2014 and 2015 in 15 Brazilian female prisons. The data of 1,327 women were collected using Audio Computer-Assisted Self-Interviewing and dermatological and neurological examination to identify suspicious lesions of leprosy. The

average age was 33.4 years. Suspicion of leprosy was identified in 5.1% of women in prison, and lifetime self-reported prevalence was 7.5%. The variables that were associated with lifetime self-reported leprosy were: women in prison once being twice as likely to have leprosy; white women were 1.4 time more likely to have leprosy than non-white women; women who knew someone with leprosy was 1.9 time more likely to have leprosy; and women who shared a cell with 11 or more women were 2.5 times more likely to have leprosy than women who shared a cell with two or fewer people. The leprosy prevalence among female prisoners in Brazil were greater than that found in a Brazilian woman of the general population and show the extremely high vulnerability of this population generated through pre-incarceration poverty, as well as potential transmission in prison.

Evaluation of the influence of genetic variants in Cereblon gene on the response to the treatment of erythema nodosum leprosum with thalidomide.

Costa PDSS, Maciel-Fiuza MF, Kowalski TW, Fraga LR, Feira MF, Camargo LMA, Caldoncelli DIO, Silveira MIDS, Schuler-Faccini L, Vianna FSL
Nov 2022
Mem Inst Oswaldo Cruz.
https://pubmed.ncbi.nlm.nih.gov/36383784/

Estimation of the morbidity and mortality of congenital Chagas disease: A systematic review and meta-analysis.

Matthews S, Tannis A, Puchner KP, Bottazzi ME, Cafferata ML, Comandé D, Buekens P.
Nov. 2022
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/36342961/

Chagas disease is caused by the parasite Trypanosoma cruzi which can be transmitted from mother to baby during pregnancy. There is no consensus on the proportion of infected infants with clinical signs of congenital Chagas disease (cCD). The objective of this systematic review is to determine the burden of cCD. Articles from journal inception to 2020 reporting morbidity and mortality associated with cCD were retrieved from academic search databases. Observational studies, randomized-control trials, and studies of babies diagnosed with cCD were included. Studies were excluded if they were case reports or series, without original data, case-control without cCD incidence estimates, and/or did not report number of participants. Two reviewers screened articles for inclusion. To determine pooled proportion of infants with cCD with clinical signs, individual clinical signs, and case-fatality, random effects meta-analysis was performed. We identified 4,531 records and reviewed 4,301, including 47 articles in the narrative summary and analysis. Twenty-eight percent of cCD infants showed clinical signs (95% confidence interval (CI) = 19.0%, 38.5%) and 2.2% of infants died (95% CI = 1.3%, 3.5%). The proportion of infected infants with hepatosplenomegaly was 12.5%, preterm birth 6.0%, low birth weight 5.8%, anemia 4.9%, and jaundice 4.7%. Although most studies did not include a comparison group of non-infected infants, the proportion of infants with cCD with clinical signs at birth are comparable to those with congenital toxoplasmosis (10.0%-30.0%) and congenital cytomegalovirus (10.0%-15.0%). We conclude that cCD burden appears significant, but more studies comparing infected mother-infant dyads to non-infected ones are needed to determine an association of this burden to cCD.

Meyerozyma guilliermondii species complex: review of current epidemiology, antifungal resistance, and mechanisms.

Ghasemi R, Lotfali E, Rezaei K, Madinehzad SA, Tafti MF, Aliabadi N, Kouhsari E, Fattahi M.
Dec. 2022
Braz J Microbiol.
https://pubmed.ncbi.nlm.nih.gov/36306113/

A case of mycobacteriosis associated with Mycobacterium pseudoshottsii in aquarium-reared fish in Japan.

Komine T, Ihara H, Ono K, Yoshida M, Sugimoto Y, Inohana M, Fukano H, Kurata O, Wada S.
18-11-2022
J Vet Med Sci.
https://pubmed.ncbi.nlm.nih.gov/36273872/

In 2019, several aquarium-reared fish died at a sea life park in Japan. Necropsy revealed micronodules on the spleen in the dotted gizzard shad (Konosirus punctatus). Seven of 16 fish exhibited microscopic multifocal granulomas associated with acid-fast bacilli in the spleen, kidney, liver, alimentary tract, mesentery, gills, and/or heart. Bacterial cultures yielded isolates from the dotted gizzard shad and a Japanese sardine (Sardinops melanostictus). Microbiological and molecular biological examinations revealed the isolates as Mycobacterium pseudoshottsii. To our knowledge, this is the first isolation of M. pseudoshottsii from aquarium-reared fish.

Nights, Bites, and Cries.

Karthikeyan K, Prarthana M.
12-06-2022
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/36096411/

The anti-Trypanosoma activities of medicinal plants: A systematic review of the literature.

Nekoei S, Khamesipour F, Habtemariam S, de Souza W, Mohammadi Pour P, Hosseini SR.
Nov. 2022
Vet Med Sci.
https://pubmed.ncbi.nlm.nih.gov/36037401/

Leonine facies and madarosis in lepromatous leprosy.

Palaniappan V, Karthikeyan K.
Dec.2022

Postgrad Med J.
https://pubmed.ncbi.nlm.nih.gov/34588291/

Trypanosomes (trypanosomiase et maladie de Chagas)

Phenotypic Evaluation of Nucleoside Analogues against Trypanosoma cruzi Infection: In Vitro and In Vivo Approaches.

Fiuza LFA, Batista DGJ, Girão RD, Hulpia F, Finamore-Araújo P, Aldfer MM, Elmahallawy EK, De Koning HP, Moreira O, Van Calenbergh S, Soeiro MNC.
21-11-2022
Molecules.
https://pubmed.ncbi.nlm.nih.gov/36432189/

Chagas disease, caused by *Trypanosoma cruzi* (*T. cruzi*), is a serious public health problem. Current treatment is restricted to two drugs, benznidazole and nifurtimox, displaying serious efficacy and safety drawbacks. Nucleoside analogues represent a promising alternative as protozoans do not biosynthesize purines and rely on purine salvage from the hosts. Protozoan transporters often present different substrate specificities from mammalian transporters, justifying the exploration of nucleoside analogues as therapeutic agents. Previous reports identified nucleosides with potent trypanocidal activity; therefore, two 7-derivatized tubercidins (FH11706, FH10714) and a 3'-deoxytubercidin (FH8513) were assayed against *T. cruzi*. They were highly potent and selective, and the uptake of the tubercidin analogues appeared to be mediated by the nucleoside transporter TcrNT2. At 10 µM, the analogues reduced parasitemia >90% in 2D and 3D cardiac cultures. The washout assays showed that FH10714 sterilized the infected cultures. Given orally, the compounds did not induce noticeable mouse toxicity (50 mg/kg), suppressed the parasitemia of *T. cruzi*-infected Swiss mice (25 mg/kg, 5 days) and presented DNA amplification below the limit of detection. These findings justify further studies with longer treatment regimens, as well as evaluations in combination with nitro drugs, aiming to identify more effective and safer therapies for Chagas disease.

The Trypanosoma cruzi TcrNT2 Nucleoside Transporter Is a Conduit for the Uptake of 5-F-2'-Deoxyuridine and Tubercidin Analogues.

Aldfer MM, Alfayez IA, Elati HAA, Gayen N, Elmahallawy EK, Milena Murillo A, Marsiccobetre S, Van Calenbergh S, Silber AM, de Koning HP.
19-11-2022
Molecules
https://pubmed.ncbi.nlm.nih.gov/36432150

Among the scarce validated drug targets against Chagas disease (CD), caused by *Trypanosoma cruzi*, the parasite's nucleoside salvage system has recently attracted considerable attention. Although the trypanocidal activity of tubercidin (7-deazapurine) has long been known, the identification of a class of 7-substituted tubercidin analogs with potent in vitro and in vivo activity and much-enhanced selectivity has made nucleoside analogs among the most promising lead compounds against CD. Here, we investigate the recently identified TcrNT2 nucleoside transporter and its potential role in antimetabolite chemotherapy. TcrNT2, expressed in a *Leishmania mexicana* cell line lacking the NT1 nucleoside transporter locus, displayed very high selectivity and affinity for thymidine with a K_m of 0.26 ± 0.05 µM. The selectivity was explained by interactions of 2-oxo, 4-oxo, 5-Me, 3'-hydroxy and 5'-hydroxy with the transporter binding pocket, whereas a hydroxy group at the 2' position was deleterious to binding. This made 5-halogenated 2'-deoxyuridine analogues good substrates but 5-F-2'-deoxyuridine displayed disappointing activity against *T. cruzi* trypomastigotes. By comparing the EC_{50} values of tubercidin and its 7-substituted analogues against *L. mexicana* Cas9, Cas9$^{\Delta NT1}$ and Cas9$^{\Delta NT1+TcrNT2}$ it was shown that TcrNT2 can take up tubercidin and, at a minimum, a subset of the analogs.

Drug Combination Studies of the Dipeptide Nitrile CD24 with Curcumin: A New Strategy to Synergistically Inhibit Rhodesain of Trypanosoma brucei rhodesiense.

Di Chio C, Previti S, De Luca F, Bogacz M, Zimmer C, Wagner A, Schirmeister T, Zappalà M, Ettari R.
21-11-2022
Int J Mol Sci.
https://pubmed.ncbi.nlm.nih.gov/36430948/

Rhodesain is a cysteine protease that is crucial for the life cycle of Trypanosoma brucei rhodesiense, a parasite causing the lethal form of Human African Trypanosomiasis. CD24 is a recently developed synthetic inhibitor of rhodesain, characterized by a nanomolar affinity towards the trypanosomal protease (Ki = 16 nM), and acting as a competitive inhibitor. In the present work, we carried out a combination study of CD24 with curcumin, the multitarget nutraceutical obtained from Curcuma longa L., which we demonstrated to inhibit rhodesain in a non-competitive manner. By applying the Chou and Talalay method, we obtained an initial additive effect at IC50 (fa = 0.5, Combination Index = 1), while for the most relevant fa values, ranging from 0.6 to 1, i.e., from 60% to 100% of rhodesain inhibition, we obtained a combination index < 1, thus suggesting that an increasingly synergistic action occurred for the combination of the synthetic inhibitor CD24 and curcumin. Furthermore, the combination of the two inhibitors showed an antitrypanosomal activity better than that of CD24 alone (EC50 = 4.85 µM and 10.1 µM for the combination and CD24, respectively), thus suggesting the use of the two inhibitors in combination is desirable

Trypanosoma cruzi DNA Polymerase β Is Phosphorylated In Vivo and In Vitro by

Protein Kinase C (PKC) and Casein Kinase 2 (CK2).

Maldonado E, Rojas DA, Urbina F, Valenzuela-Pérez L, Castillo C, Solari A.
21-22-2022
Cells.
https://pubmed.ncbi.nlm.nih.gov/36429121/

DNA polymerase β plays a fundamental role in the life cycle of Trypanosoma cruzi since it participates in the kinetoplast DNA repair and replication. This enzyme can be found in two forms in cell extracts of T. cruzi epimastigotes form. The H form is a phosphorylated form of DNA polymerase β, while the L form is not phosphorylated. The protein kinases which are able to in vivo phosphorylate DNA polymerase β have not been identified yet. In this work, we purified the H form of this DNA polymerase and identified the phosphorylation sites. DNA polymerase β is in vivo phosphorylated at several amino acid residues including Tyr35, Thr123, Thr137 and Ser286. Thr123 is phosphorylated by casein kinase 2 and Thr137 and Ser286 are phosphorylated by protein kinase C-like enzymes. Protein kinase C encoding genes were identified in T. cruzi, and those genes were cloned, expressed in bacteria and the recombinant protein was purified. It was found that T. cruzi possesses three different protein kinase C-like enzymes named TcPKC1, TcPKC2, and TcPKC3. Both TcPKC1 and TcPKC2 were able to in vitro phosphorylate recombinant DNA polymerase β, and in addition, TcPKC1 gets auto phosphorylated. Those proteins contain several regulatory domains at the N-terminus, which are predicted to bind phosphoinositols, and TcPKC1 contains a lipocalin domain at the C-terminus that might be able to bind free fatty acids. Tyr35 is phosphorylated by an unidentified protein kinase and considering that the T. cruzi genome does not contain Tyr kinase encoding genes, it is probable that Tyr35 could be phosphorylated by a dual protein kinase. Wee1 is a eukaryotic dual protein kinase involved in cell cycle regulation. We identified a Wee1 homolog in T. cruzi and the recombinant kinase was assayed using DNA polymerase β as a substrate. T. cruzi Wee1 was able to in vitro phosphorylate recombinant DNA polymerase β, although we were not able to demonstrate specific phosphorylation on Tyr35. Those results indicate that there exists a cell signaling pathway involving PKC-like kinases in T. cruzi.

Silver and copper-benznidazole derivatives as potential antiparasitic metallodrugs: Synthesis, characterization, and biological evaluation.

de Souza CC, de Azevedo-França JA, Barrias E, Cavalcante SCF, Vieira EG, Ferreira AMDC, de Souza W, Navarro M.
08-11-2022
J Inorg Biochem.
https://pubmed.ncbi.nlm.nih.gov/36428157/

Currently the only drug available to treat Chagas disease in Brazil is benznidazole (BZN). Therefore, there is an urgent need to discover and develop new anti-Trypanosoma cruzi candidates. In our continuous effort to enhance clinical antiparasitic drugs using synergistic strategy, BZN was coordinated to silver and copper ions to enhance its effectiveness to treat that illness. In this work, the syntheses of four novel metal-BZN complexes, [Ag(BZN)2]NO3·H2O (1), [CuCl2(BZN)(H2O)]·1/2CH3CN (2), [Ag(PPh3)2(BZN)2]NO3·H2O (3), and [Cu(PPh3)2(BNZ)2]NO3·2H2O (4), and their characterization using multiple analytical and spectroscopic techniques such as Infrared (FTIR), Nuclear Magnetic Resonance (1H, 13C, 31P), UV-Visible (UV-Vis), Electron Paramagnetic Resonance (EPR), conductivity and elemental analysis are described. IC50 (Half-maximal inhibitory concentration) values of Ag-BZN compounds are about five to ten times lower than benznidazole itself in both proliferation stages of the parasite (epimastigotes and amastigotes). The cytotoxicity of both compounds in human cells (fibroblasts and hepatocytes) are comparable to BZN, indicating that Ag-BZN complexes can be more selective than BZN.

Design, Synthesis, and Antiprotozoal Evaluation of New Promising 2,9-Bis[(substituted-aminomethyl)]-4,7-phenyl-1,10-phenanthroline Derivatives, a Potential Alternative Scaffold to Drug Efflux.

Guillon J, Cohen A, Boudot C, Monic S, Savrimoutou S, Moreau S, Albenque-Rubio S, Lafon-Schmaltz C, Dassonville-Klimpt A, Mergny JL, Ronga L, Bernabeu de Maria M, Lamarche J, Lago CD, Largy E, Gabelica V, Moukha S, Dozolme P, Agnamey P, Azas N, Mullié C, Courtioux B, Sonnet P.
13-11-2022
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/36422591/

Trypanosoma cruzi Antigenic Proteins Shared with Acute Lymphoblastic Leukemia and Neuroblastoma.

Eligio García L, Crisóstomo Vázquez MDP, Maravelez Acosta VA, Soria Guerrero M, Cortés Campos A, Jiménez Cardoso E.
15-11-2022
Pharmaceuticals (Basel).
https://pubmed.ncbi.nlm.nih.gov/36422551/

Background. Research studies indicate that immunization with protein extracts of *Trypanosoma cruzi*, the protozoan parasite that causes Chagas disease, prevents the appearance of tumors in 60% of mice injected with the murine lung carcinoma tumor line. The molecular basis of this process is unknown, although the presence of specific antigens in tumor cells and on the surface of *T. cruzi* suggests an antiparasitic immune response, with an effective cross-reaction against cancer cells, hence the importance to identify the antigens involved and determine their potential as target cells in anticancer therapy. Aim. This study aimed to determine the presence of antigenic proteins of *T. cruzi* shared with acute lymphoblastic leukemia and neuroblastoma cells. Material and methods. To achieve this, polyclonal antibodies against *T. cruzi* were developed in rabbits, and reactivity was determined with protein extracts of acute

lymphoblastic leukemia cells and neuroblastoma. The immunodetection of five different strains of *T. cruzi* against anti-*T. cruzi* polyclonal antibodies was also performed. Conclusion. The study allows the knowledge of the immunological interactions between cancer and parasites to be expanded and, therefore, contributes to the design of more and better projects that improve the therapeutic strategies applied in oncology.

Laboratory Evaluation and Field Feasibility of Micro-Encapsulated Insecticide Effect on Rhodnius prolixus and Triatoma dimidiata Mortality in Rural Households in Boyacá, Colombia.

Gual-Gonzalez L, Medina M, Valverde-Castro C, Beltrán V, Caro R, Triana-Chávez O, Nolan MS, Cantillo-Barraza O.
17-11-2022
Insects
https://pubmed.ncbi.nlm.nih.gov/36421964/

Chagas disease is a neglected vector-borne zoonosis caused by the parasite Trypanosoma cruzi that is primarily transmitted by insects of the subfamily Triatominae. Although control efforts targeting domestic infestations of Rhodnius prolixus have been largely successful, with several regions in Boyacá department certified free of T. cruzi transmission by intradomicile R. prolixus, novel native species are emerging, increasing the risk of disease. Triatoma dimidiata is the second most important species in Colombia, and conventional control methods seem to be less effective. In this study we evaluated the efficacy and usefulness of micro-encapsulated insecticide paints in laboratory conditions and its applicability in rural communities to avoid triatomine domiciliation. Laboratory conditions measured mortality at 6 months and 12 months, with an average mortality between 93-100% for T. dimidiata and 100% for R. prolixus. Evaluation of triatomine infestation in rural households was measured after one year, with an overall perception of effectiveness in reducing household domiciliation. Although triatomines were still spotted inside and around the homes, our findings demonstrate the ability of micro-encapsulated insecticide to prevent colonization inside the households when comparing infestation rates from previous years. Current control measures suggest insecticide spraying every six months, which implies great economic cost and logistical effort. Complementary triatomine control measures with insecticide spraying and micro-encapsulated insecticide paint would make public health efforts more efficient and reduce the frequency of treatment.

Tipping the balance between erythroid cell differentiation and induction of anemia in response to the inflammatory pathology associated with chronic trypanosome infections.

Nguyen HTT, Radwanska M, Magez S.
07-11-2022
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/36420267/

Infection caused by extracellular single-celled trypanosomes triggers a lethal chronic wasting disease in livestock and game animals. Through screening of 10 Trypanosoma evansi field isolates, exhibiting different levels of virulence in mice, the current study identifies an experimental disease model in which infection can last well over 100 days, mimicking the major features of chronic animal trypanosomosis. In this model, despite the well-controlled parasitemia, infection is hallmarked by severe trypanosomosis-associated pathology. An in-depth scRNA-seq analysis of the latter revealed the complexity of the spleen macrophage activation status, highlighting the crucial role of tissue resident macrophages (TRMs) in regulating splenic extramedullary erythropoiesis. These new data show that in the field of experimental trypanosomosis, macrophage activation profiles have so far been oversimplified into a bi-polar paradigm (M1 vs M2). Interestingly, TRMs exert a double-sided effect on erythroid cells. On one hand, these cells express an erythrophagocytosis associated signature. On another hand, TRMs show high levels of Vcam1 expression, known to support their interaction with hematopoietic stem and progenitor cells (HSPCs). During chronic infection, the latter exhibit upregulated expression of Klf1, E2f8, and Gfi1b genes, involved in erythroid differentiation and extramedullary erythropoiesis. This process gives rise to differentiation of stem cells to BFU-e/CFU-e, Pro E, and Baso E subpopulations. However, infection truncates progressing differentiation at the orthochromatic erythrocytes level, as demonstrated by scRNAseq and flow cytometry. As such, these cells are unable to pass to the reticulocyte stage, resulting in reduced number of mature circulating RBCs and the occurrence of chronic anemia. The physiological consequence of these events is the prolonged poor delivery of oxygen to various tissues, triggering lactic acid acidosis and the catabolic breakdown of muscle tissue, reminiscent of the wasting syndrome that is characteristic for the lethal stage of animal trypanosomosis.

Pathogenicity and virulence of African trypanosomes: from laboratory models to clinically relevant hosts.

Morrison LJ, Steketee PC, Tettey MD, Matthews KR.
23-11-2022
Virulence.
https://pubmed.ncbi.nlm.nih.gov/36419235/

African trypanosomes are vector-borne protozoa, which cause significant human and animal disease across sub-Saharan Africa, and animal disease across Asia and South America. In humans, infection is caused by variants of Trypanosoma brucei, and is characterised by varying rate of progression to neurological disease, caused by parasites exiting the vasculature and entering the brain. Animal disease is caused by multiple species of trypanosome, primarily T. congolense, T. vivax and T. brucei. These trypanosomes also infect multiple species of mammalian host, and this complexity of trypanosome and host diversity is reflected in the spectrum of severity of disease in animal trypanosomiasis, ranging from hyperacute infections associated with mortality to long term chronic

infections, and is also a main reason why designing interventions for animal trypanosomiasis is so challenging. In this review, we will provide an overview of the current understanding of trypanosome determinants of infection progression and severity, covering laboratory models of disease, as well as human and livestock disease. We will also highlight gaps in knowledge and capabilities, which represent opportunities to both further our fundamental understanding of how trypanosomes cause disease, as well as facilitating the development of the novel interventions that are so badly needed to reduce the burden of disease caused by these important pathogens.

Increased angiogenesis parallels cardiac tissue remodelling in experimental acute Trypanosoma cruzi infection.

Nisimura LM, Ferreira RR, Coelho LL, Souza EM, Gonzaga BM, Ferrão PM, Waghabi MC, Mesquita LB, Pereira MCS, Moreira ODC, Lannes-Vieira J, Garzoni LR.
21-11-2022
Mem Inst Oswaldo Cruz.
https://pubmed.ncbi.nlm.nih.gov/36417626/

Background: Angiogenesis has been implicated in tissue injury in several noninfectious diseases, but its role in Chagas disease (CD) physiopathology is unclear. Objectives: The present study aimed to investigate the effect of Trypanosoma cruzi infection on cardiac angiogenesis during the acute phase of experimental CD. Methods: The signalling pathway involved in blood vessel formation and cardiac remodelling was evaluated in Swiss Webster mice infected with the Y strain of T. cruzi. The levels of molecules involved in the regulation of angiogenesis, such as vascular endothelial growth factor-A (VEGF-A), Flk-1, phosphorylated extracellular-signal-regulated protein kinase (pERK), hypoxia-inducible factor-1α (HIF-1α), CD31, α-smooth muscle actin (α-SMA) and also the blood vessel growth were analysed during T. cruzi infection. Hearts were analysed using conventional histopathology, immunohistochemistry and western blotting. Findings: In this study, our data demonstrate that T. cruzi acute infection in mice induces exacerbated angiogenesis in the heart and parallels cardiac remodelling. In comparison with noninfected controls, the cardiac tissue of T. cruzi-infected mice presented higher levels of (i) HIF-1α, VEGF-A, Flk-1 and pERK; (ii) angiogenesis; (iii) α-SMA+ cells in the tissue; and (iv) collagen -1 deposition around blood vessels and infiltrating throughout the myocardium. Main conclusions: We observed cardiac angiogenesis during acute experimental T. cruzi infection parallels cardiac inflammation and remodelling.

Trypanosoma cruzi infection changes the chromatin proteome profile of infected human cells.

Florentino PTV, Vitorino FNL, Mendes D, da Cunha JPC, Menck CFM.
19-11-2022
J Proteomics.
https://pubmed.ncbi.nlm.nih.gov/36414228/

Chagas disease is endemic in 22 Latin American countries, with approximately 8 million individuals infected worldwide and 10,000 deaths yearly. Trypanosoma cruzi presents an intracellular life cycle in mammalian hosts to sustain infection. Parasite infection activates host cell responses, promoting an unbalance in reactive oxygen species (ROS) in the intracellular environment inducing genomic DNA lesions in the host cell during infection. To further understand changes in host cell chromatin induced by parasite infection, we investigated alterations in chromatin caused by infection by performing quantitative proteomic analysis. DNA Damage Repair proteins, such as Poly-ADP-ribose Polymerase 1 (PARP-1) and X-Ray Repair Cross Complementing 6 (XRRC6), were recruited to the chromatin during infection. Also, changes in chromatin remodeling enzymes suggest that parasite infection may shape the epigenome of the host cells. Interestingly, the abundance of oxidative phosphorylation mitochondrial and vesicle-mediated transport proteins increased in the host chromatin at the final stages of infection. In addition, Apoptosis-inducing Factor (AIF) is translocated to the host cell nucleus upon infection, suggesting that cells enter parthanatos type of death. Altogether, this study reveals how parasites interfere with the host cells' responses at the chromatin level leading to significant crosstalk that support and disseminate infection. SIGNIFICANCE: The present study provides novel insights into the effects of Trypanosoma cruzi on the chromatin from the host cell. This manuscript investigated proteomic alterations in chromatin caused by parasite infection at early and late infection phases by performing a quantitative proteomic analysis. In this study, we revealed that parasites interfere with DNA metabolism in the early and late stages of infection. We identified that proteins related to DNA damage repair, oxidative phosphorylation, and vesicle-mediated transport have increased abundance at the host chromatin. Additionally, we have observed that Apoptosis-inducing Factor is translocated to the host cell nucleus upon infection, suggesting that the parasites could lead the cells to enter Parthanatos as a form of programmed cell death. The findings improve our understanding on how the parasites modulate the host cell chromatin to disseminate infection. In this study, we suggest a mechanistic parasite action towards host nucleus that could be used to indicate targets for future treatments.

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

Phan TN, Park KP, Benítez D, Comini MA, Shum D, No JH.
17-11-2022
Biochem Biophys Res Commun.
https://pubmed.ncbi.nlm.nih.gov/36413853/

Human Trypanosoma cruzi chronic infection leads to individual level steady-state parasitemia: Implications for drug-trial optimization in Chagas disease.

De Salazar PM, Sosa-Estani S, Salvador F, Sulleiro E, Sánchez-Montalvá A, Ribeiro I, Molina I, Buckee CO.
21-11-2022
PLoS Negl Trop Dis.

https://pubmed.ncbi.nlm.nih.gov/36409773/

Currently available drugs against Trypanosoma cruzi infection, which causes 12000 deaths annually, have limitations in their efficacy, safety and tolerability. The evaluation of therapeutic responses to available and new compounds is based on parasite detection in the bloodstream but remains challenging because a substantial proportion of infected individuals have undetectable parasitemia even when using diagnostic tools with the highest accuracy. We characterize parasite dynamics which might impact drug efficacy assessments in chronic Chagas by analyzing pre- and post-treatment quantitative-PCR data obtained from blood samples collected regularly over a year. We show that parasitemia remains at a steady-state independently of the diagnostic sensitivity. This steady-state can be probabilistically quantified and robustly predicted at an individual level. Furthermore, individuals can be assigned to categories with distinct parasitological status, allowing a more detailed evaluation of the efficacy outcomes and adjustment for potential biases. Our analysis improves understanding of parasite dynamics and provides a novel background for optimizing future drug efficacy trials in Chagas disease. Trial Registration: original trial registered with ClinicalTrials.gov, number NCT01489228.

The lipidome of Crithidia fasciculataand its plasticity.

Cerone M, Roberts M, Smith TK.
28-20-2022
Front Cell Infect Microbiol.
https://pubmed.ncbi.nlm.nih.gov/36405970/

Crithidia fasiculata belongs to the trypanosomatidae order of protozoan parasites, bearing close relation to other kinetoplastid parasites such as *Trypanosoma brucei* and *Leishmania spp.* As an early diverging lineage of eukaryotes, the study of kinetoplastid parasites has provided unique insights into alternative mechanisms to traditional eukaryotic metabolic pathways. *Crithidia* are a monogenetic parasite for mosquito species and have two distinct lifecycle stages both taking place in the mosquito gut. These consist of a motile choanomastigote form and an immotile amastigote form morphologically similar to amastigotes in *Leishmania*. Owing to their close relation to *Leishmania, Crithidia* are a growing research tool, with continuing interest in its use as a model organism for kinetoplastid research with the added benefit that they are non-pathogenic to humans and can be grown with no special equipment or requirements for biological containment. Although comparatively little research has taken place on *Crithidia*, similarities to other kinetoplast species has been shown in terms of energy metabolism and genetics. *Crithidia* also show similarities to kinetoplastids in their production of the monosaccharide D-arabinopyranose similar to Leishmania, which is incorporated into a lipoarabinogalactan a major cell surface GPI-anchored molecule. Additionally, *Crithidia* have been used as a eukaryotic expression system to express proteins from other kinetoplastids and potentially other eukaryotes including human proteins allowing various co- and post-translational protein modifications to the recombinant proteins. Despite the obvious usefulness and potential of this organism very little is known about its lipid metabolism. Here we describe a detailed lipidomic analyses and demonstrate the possible placidity of *Crithidia's* lipid metabolis. This could have important implications for biotechnology approaches and how other kinetoplastids interact with, and scavenge nutrients from their hosts.

Recent progress in diagnosis and treatment of Human African Trypanosomiasis has made the elimination of this disease a realistic target by 2030.

Álvarez-Rodríguez A, Jin BK, Radwanska M, Magez S.
03-1-2022
Front Med (Lausanne).
https://pubmed.ncbi.nlm.nih.gov/36405602/

Human African Trypanosomiasis (HAT) is caused by unicellular flagellated protozoan parasites of the genus Trypanosoma brucei. The subspecies T. b. gambiense is mainly responsible for mostly chronic anthroponotic infections in West- and Central Africa, accounting for roughly 95% of all HAT cases. Trypanosoma b. rhodesiense results in more acute zoonotic infections in East-Africa. Because HAT has a two-stage pathogenesis, treatment depends on clinical assessment of patients and the determination whether or not parasites have crossed the blood brain barrier. Today, ultimate confirmation of parasitemia is still done by microscopy analysis. However, the introduction of diagnostic lateral flow devices has been a major contributor to the recent dramatic drop in T. b. gambiense HAT. Other techniques such as loop mediated isothermal amplification (LAMP) and recombinant polymerase amplification (RPA)-based tests have been published but are still not widely used in the field. Most recently, CRISPR-Cas technology has been proposed to improve the intrinsic diagnostic characteristics of molecular approaches. This will become crucial in the near future, as preventing the resurgence of HAT will be a priority and will require tools with extreme high positive and negative predicted values, as well as excellent sensitivity and specificity. As for treatment, pentamidine and suramin have historically been the drugs of choice for the treatment of blood-stage gambiense-HAT and rhodesiense-HAT, respectively. For treatment of second-stage infections, drugs that pass the blood brain barrier are needed, and melarsoprol has been effectively used for both forms of HAT in the past. However, due to the high occurrence of post-treatment encephalopathy, the drug is not recommended for use in T. b. gambiense HAT. Here, a combination therapy of eflornithine and nifurtimox (NECT) has been the choice of treatment since 2009. As this treatment requires IV perfusion of eflornithine, efforts were launched in 2003 by the drugs for neglected disease initiative (DNDi) to find an oral-only therapy solution, suitable for rural sub-Saharan Africa treatment conditions. In 2019 this resulted in the introduction of fexinidazole, with a treatment regimen suitable for both the blood-stage and non-severe second-stage T. b. gambiense infections. Experimental treatment of T. b. rhodesiense HAT has now been initiated as well.

Molecular identification of Trypanosoma cruzi in domestic animals in municipalities of the State of Rio Grande do Norte, Brazil.

de Araújo-Neto VT, Barbosa-Silva AN, Medeiros Honorato NR, Sales LML, de Cassia Pires R, do Nascimento Brito CR, da Matta Guedes PM, da Cunha Galvão LM, da Câmara ACJ.
21-11-2022
Parasitol Res.
https://pubmed.ncbi.nlm.nih.gov/36404367/

Trypanosoma cruzi, the etiologic agent of American trypanosomiasis, is a vector-borne zoonotic parasite which has been little studied regarding its infection in domestic animals. In this study, we evaluated the occurrence of natural infection by T. cruzi in farm animals using molecular markers and phylogenetic analysis in blood clot samples of 60 sheep (Ovis aires), 22 goats (Capra hircus), and 14 horses (Equus caballus) in eight municipalities located in an infection risk area in the state of Rio Grande do Norte (RN), Northeast Region of Brazil. Trypanosoma spp. infection was identified by amplifying the rRNA 18S SSU gene in 48.9% of the samples. The SH022 sample showed 99.8% similarity with the Y strain of T. cruzi in phylogeny, grouped in the DTU II clade. Blood clots of sheep, goats, and horses detected T. cruzi kDNA in 28.3% (17/60), 22.7% (5/22), and 15.4% (2/14) of the samples, respectively. These animals were distributed in the three studied mesoregions throughout the state of RN. The identification of natural infection in domestic animals contributes to expand the epidemiological transmission scenario in an area where T. brasiliensis is the main vector.

Disentangling the contributions of biotic and abiotic predictors in the niche and the species distribution model of Trypanosoma cruzi, etiological agent of Chagas disease.

Rengifo-Correa L, González-Salazar C, Stephens CR.
16-11-2022
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/36402171/

The potential benefits of incorporating biotic, as well as abiotic, predictors in niche and species distribution models (SDMs), as well as how to achieve this, is still debated, with their interpretability and explanatory potential being particularly questioned. It is therefore important to stress test modelling methodologies that include biotic factors against use cases where there is ample knowledge of the potential biotic component of the niche. Relatively well studied and important vector-borne diseases offer just such an opportunity, where knowledge of the agents involved in the transmission cycle -vectors and hosts- can serve to calibrate and test the niche model and corresponding SDM. Here, we study the contributions of biotic -14 vectors, 459 potential hosts- and abiotic -258 climatic categories- predictors to the explanatory and predictive features of the niche and corresponding SDM for the etiological agent of Chagas disease, Trypanosoma cruzi, in Mexico. Using an established spatial data mining technique, we generate biotic, abiotic and biotic+abiotic niche and SDM models. We test our models by comparing predictions of the most important probable hosts of Chagas disease with a previously published list of confirmed hosts. We quantify, compare, and contrast the individual and total contributions of predictors to the niche and distribution of Chagas disease in Mexico. We assess the relative predictive potential of these variables to model performance, showing that models that include relevant biotic niche variables lead to more predictive, more ecologically realistic SDMs. Our research illustrates a useful general procedure for identifying and ranking potential biotic interactions and for assessing the relative importance of biotic and abiotic predictors. We conclude that the inclusion of both abiotic and biotic predictors in SDMs not only provides more predictive and accurate models but also models that are more understandable and explainable from an ecological niche perspective.

Heme-deficient metabolism and impaired cellular differentiation as an evolutionary trade-off for human infectivity in Trypanosoma brucei gambiense.

Horáková E, Lecordier L, Cunha P, Sobotka R, Changmai P, Langedijk CJM, Abbeele JVD, Vanhollebeke B, Lukeš J.
18-11-2022
Nat Commun.
https://pubmed.ncbi.nlm.nih.gov/36400774/

Resistance to African trypanosomes in humans relies in part on the high affinity targeting of a trypanosome lytic factor 1 (TLF1) to a trypanosome haptoglobin-hemoglobin receptor (HpHbR). While TLF1 avoidance by the inactivation of HpHbR contributes to Trypanosoma brucei gambiense human infectivity, the evolutionary trade-off of this adaptation is unknown, as the physiological function of the receptor remains to be elucidated. Here we show that uptake of hemoglobin via HpHbR constitutes the sole heme import pathway in the trypanosome bloodstream stage. T. b. gambiense strains carrying the inactivating mutation in HpHbR, as well as genetically engineered T. b. brucei HpHbR knock-out lines show only trace levels of intracellular heme and lack hemoprotein-based enzymatic activities, thereby providing an uncommon example of aerobic parasitic proliferation in the absence of heme. We further show that HpHbR facilitates the developmental progression from proliferating long slender forms to cell cycle-arrested stumpy forms in T. b. brucei. Accordingly, T. b. gambiense was found to be poorly competent for slender-to-stumpy differentiation unless a functional HpHbR receptor derived from T. b. brucei was genetically restored. Altogether, we identify heme-deficient metabolism and disrupted cellular differentiation as two distinct HpHbR-dependent evolutionary trade-offs for T. b. gambiense human infectivity.

Impact of pulmonary African trypanosomes on the immunology and function of the lung.

Mabille D, Dirkx L, Thys S, Vermeersch M, Montenye D, Govaerts M, Hendrickx S, Takac P, Van Weyenbergh J,

Pintelon I, Delputte P, Maes L, Pérez-Morga D, Timmermans JP, Caljon G.
18-11-2022
Nat Commun.
https://pubmed.ncbi.nlm.nih.gov/36400767/

Approximately 20% of sleeping sickness patients exhibit respiratory complications, however, with a largely unknown role of the parasite. Here we show that tsetse fly-transmitted Trypanosoma brucei parasites rapidly and permanently colonize the lungs and occupy the extravascular spaces surrounding the blood vessels of the alveoli and bronchi. They are present as nests of multiplying parasites exhibiting close interactions with collagen and active secretion of extracellular vesicles. The local immune response shows a substantial increase of monocytes, macrophages, dendritic cells and γδ and activated αβ T cells and a later influx of neutrophils. Interestingly, parasite presence results in a significant reduction of B cells, eosinophils and natural killer cells. T. brucei infected mice show no infection-associated pulmonary dysfunction, mirroring the limited pulmonary clinical complications during sleeping sickness. However, the substantial reduction of the various immune cells may render individuals more susceptible to opportunistic infections, as evident by a co-infection experiment with respiratory syncytial virus. Collectively, these observations provide insights into a largely overlooked target organ, and may trigger new diagnostic and supportive therapeutic approaches for sleeping sickness.

KRGG1 function in RNA editing in Trypanosoma brucei.

Carnes J, Gendrin C, McDermott SM, Stuart K.
Nov-2022
RNA
https://pubmed.ncbi.nlm.nih.gov/36400448/

The discovery and characterization of two novel structural motifs on the C-terminal domain of kinetoplastid RNA editing ligases.

Moses D, Mehta V, Salavati R.
Nov-2022
RNA
https://pubmed.ncbi.nlm.nih.gov/36400447/

Withaferin A-silyl ether analogs as potential anti-kinetoplastid agents targeting the programmed cell death.

San Nicolás-Hernández D, Bethencourt-Estrella CJ, López-Arencibia A, Hernández-Álvarez E, Sifaoui I, Bazzocchi IL, Lorenzo-Morales J, Jiménez IA, Piñero JE.
16-11-2022
Biomed Pharmacother.
https://pubmed.ncbi.nlm.nih.gov/36399830/

Current therapies of leishmaniasis and Chagas disease, two of the most widespread neglected tropical diseases, have limited efficacy and toxic side effects. In this regard, natural products play an important role in overcoming the current need for new antiparasitic agents. The present study reports the leishmanicidal and trypanocidal activities of twenty-four known silyl-ether derivatives of withaferin A. Eleven compounds from this series (4, 7, 8, 10, 12, 15, 17, 18, 20, 22 and 25) showed a potent dose-dependent inhibitory effect on the proliferation of Leishmania amazonensis promastigotes and Trypanosoma cruzi epimastigotes respectively, even higher than the references drugs, miltefosine and benznidazole. Among them, the most promising compound, derivative 10, exhibited approximately 34-fold higher leishmanicidal activity and 49-fold higher trypanocidal activity compared to the reference drugs, as well as lower cytotoxicity. Moreover, compounds 4, 7, 10, 12 and 15 were more active than the reference drugs against the amastigote forms of L. amazonensis, presenting a high selectivity index. Assays performed to study the ATP levels, mitochondrial membrane potential, plasma membrane permeability, chromatin condensation, reactive oxygen species and autophagy indicated that these withaferin A-silyl analogs appear to induce events characteristic of apoptosis-like and also autophagy leading to programmed cell death. These findings support the therapeutic potential of withaferin A-related steroids as anti-Leishmania and Trypanosoma agents.

Trypanosoma brucei Mitochondrial DNA Polymerase POLIB Contains a Novel Polymerase Domain Insertion That Confers Dominant Exonuclease Activity.

Delzell SB, Nelson SW, Frost MP, Klingbeil MM.
18-11-2022
Biochemistry.
https://pubmed.ncbi.nlm.nih.gov/36399653/

Chagas cardiomyopathy is associated with a high susceptibility to T. cruzi infection in monocyte-derived macrophages and a predominance of $CD4^+CD45RO^+$ T-cells with immunoregulatory patterns.

Carvalho AMRS, Ferraz IA, Hojo-Souza NS, Medeiros FAC, Viana LA, Bartholomeu DC, Chaves AT, de Souza TM, Costa E Silva MF, Mendes TAO, Duarte MC, Rocha MODC, Menezes-Souza D.
Jan-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/36370753/

The pathogenesis of Chronic Chagas Cardiomyopathy (CCC) is still not fully understood, and the persistence of the parasite in tissues seems to be essential for the onset and progression of heart disease, tissue destruction, and chronic inflammation. It is clear that the polarity found between the asymptomatic (IND) and cardiac clinical forms refers mainly to the mechanisms involved in the regulation of the host's immune response. Thus, to elucidate aspects of the susceptibility of host phagocytes to T. cruzi infection, the present study explored novel aspects of innate immune response, integrating data on susceptibility to infection and intracellular replication, using monocyte-derived macrophages from CCC patients,

together with memory $CD4^+$ T-cells ($CD45RO^+$). The isolation of PBMC was conducted by means of in vitro infection assay with T. cruzi trypomastigotes and flow cytometry analysis of the intracytoplasmic cytokine production by $CD4^+$T-cells. Our findings indicated that monocytes derived from individuals with CCC are more susceptible to the infection and replication of intracellular amastigotes. Moreover, the stimulation of $CD4^+$ T-cells from CCC patients, together with T. cruzi trypomastigotes, induces a predominance of a regulatory response over a type 1 response, demonstrated by an increase in IL-10 production and a reduction in the IFN-γ and IFN-γ/IL-10. Suppression of the function of monocyte-derived macrophages, from CCC patients, to control trypomastigote infection and intracellular replication sheds light on a potential susceptibility of these cells isolated from peripheral blood, which may reflect the ineffectiveness of parasite control by phagocytes in cardiac tissues, which can subsequently result in serious heart disease.

Characterization of Feeding Behavior and its Relationship With the Longevity of Wild and Peridomestic Triatoma dimidiata, Latreille 1811 (Hemiptera, Reduviidae) Under Laboratory Conditions.

Marín-Ortiz JC, Parra-Henao G, Altamiranda-Saavedra M, Jaramillo-O N.
16-11-2022
J Med Entomol.
https://pubmed.ncbi.nlm.nih.gov/35980342/

Triatoma dimidiata (Latreille 1811) is considered the second most important vector of the Trypanosa cruzi etiological agent of Chagas disease in Colombia. It has a life cycle that involves a domiciled, peridomiciled, and wild distribution. The study of feeding behavior and its influence on the survival of sylvatic and peridomestic populations can help identify a possible differential risk in the transmission of Chagas disease to humans, mainly in northwestern and east-central Colombia. We characterize the main parameters of feeding behavior and their influence on the longevity and survival of two rat-fed populations of T. dimidiata from Colombia, one in the north-west (from palms in a tropical dry forest area) and the other in the center-east (peridomiciliated), under controlled environmental conditions. The palm population took considerably longer than the peridomestic population to complete its life cycle under experimental laboratory conditions, being both populations univoltine since they have only one life cycle per year. Statistically significant differences were evidenced using Box-Cox model between the survival rates of T. dimidiata populations when the parameters related to blood intake and behavior were incorporated, in contrast to the survival models in which the origin only was considered as a factor. Our results could be used to generate recommendations to guide prevention strategies in communities near sylvatic and peridomiciliated populations of T. dimidiata.

Leishmaniose

Antileishmania and immunomodulatory potential of cashew nut shell liquid and cardanol.

Ribeiro IMM, de Sousa VC, Melo ECS, de Cássia Viana de Carvalho R, de Sousa Dos Santos M, de Oliveira Nery Neto JA, de Melo DS, de Araújo Teixeira LS, das Graças Lopes Citó AM, Moura AKS, Arcanjo DDR, de Amorim Carvalho FA, de Moraes Alves MM, de Mendonça IL.
13-11-2022
Toxicol In Vitro
https://pubmed.ncbi.nlm.nih.gov/36435415/

Conventional treatments for leishmaniasis have caused serious adverse effects, poor tolerance, development of resistant strains. Natural products have been investigated as potential therapeutic alternatives. The cashew nut shell liquid (CNSL) is a natural source of phenolic compounds with several biological activities, where cardanol (CN) is considered one of the most important and promising compounds. This study aimed to evaluate antileishmanial, cytotoxic and immunomodulatory activities of CNSL and CN. Both showed antileishmanial potential, with IC_{50} for CNSL and CN against Leishmania infantum: 148.12 and 56.74 µg/mL; against Leishmania braziliensis: 85.71 and 64.28 µg/mL; against Leishmania major: 153.56 and 122.31 µg/mL, respectively. The mean cytotoxic concentrations (CC_{50}) of CNSL and CN were 37.51 and 31.44 µg/mL, respectively. CNSL and CN significantly reduced the percentage of infected macrophages, with a selectivity index (SI) >20 for CN. CNSL and cardanol caused an increase in phagocytic capacity and lysosomal volume. Survival rates of Zophobas morio larvae at doses of 3; 30 and 300 mg/kg were: 85%, 75% and 60% in contact with CNSL and 85%, 60% and 40% in contact with CN, respectively. There was a significant difference between the survival curves of larvae when treated with CN, demonstrating a significant acute toxicity for this substance. Additional investigations are needed to evaluate these substances in the in vivo experimental infection model.

Leishmania mexicana Lipophosphoglycan Activates Dermal γδ T Cells with Participation of TLR2.

Soto-Olguín N, Zamora-Chimal J, Delgado-Domínguez J, Becker I.
25-11-2022
Acta Parasitol.
https://pubmed.ncbi.nlm.nih.gov/36434381/

Antileishmanial Effects of Bunium Persicum Crude Extract, Essential Oil, and Cuminaldehyde on Leishmania Major: In Silico and In Vitro Properties.

Mohamadi N, Sharifi I, Afgar A, Sharififar F, Sharifi F.
24-11-2022
Acta Parasitol.
https://pubmed.ncbi.nlm.nih.gov/36434380/

Purpose: Cuminaldehyde (CA), an oxidized aldehyde monoterpene, is a major essential oil component in cumin seeds, which has shown different promising medical effects. In this study, we comprehensively evaluated the antileishmanial potential of Bunium persicum (Boiss) B. Fedtsch (Apiaceae) and one of its main essential oil constituents, CA, focus on the mechanisms of action. **Methods:** We used a molecular docking approach to examine the capability of CA for binding to IL-12P40 and TNF-α. The colorimetric assay was performed to assess the effect of B. persicum crude extract, essential oil, and CA, against Leishmania major promastigotes and intracellular amastigotes. The expression of IFN-γ, IL-12P40, TNF-α, and IL-10 genes was detected using quantitative real-time polymerase chain reaction qPCR. **Results:** Docking analyses in the current study indicated CA binds to IL-12P40 and TNF-α. These products were safe, extremely antileishmanial, and significantly promoted Th1-related cytokines (IFN-γ, IL-12P40, TNF-α), while downregulating the Th2 phenotype (IL-10). **Conclusion:** Cumin essential oil and its major component, CA, possessed powerful antileishmanial activity. The primary mechanism of activity involves an immunomodulatory role toward Th1 cytokine response. Therefore, cumin essential oil and CA deserve further explorations as promising medications for treating leishmaniasis.

Repurposing the Antibacterial Agents Peptide 19-4LF and Peptide 19-2.5 for Treatment of Cutaneous Leishmaniasis.

El-Dirany R, Fernández-Rubio C, Peña-Guerrero J, Moreno E, Larrea E, Espuelas S, Abdel-Sater F, Brandenburg K, Martínez-de-Tejada G, Nguewa P.
20-11-2022
Pharmaceutics
https://pubmed.ncbi.nlm.nih.gov/36432719/

The lack of safe and cost-effective treatments against leishmaniasis highlights the urgent need to develop improved leishmanicidal agents. Antimicrobial peptides (AMPs) are an emerging category of therapeutics exerting a wide range of biological activities such as anti-bacterial, anti-fungal, anti-parasitic and anti-tumoral. In the present study, the approach of repurposing AMPs as antileishmanial drugs was applied. The leishmanicidal activity of two synthetic anti-lipopolysaccharide peptides (SALPs), so-called 19-2.5 and 19-4LF was characterized in *Leishmania major*. In vitro, both peptides were highly active against intracellular *Leishmania major* in mouse macrophages without exerting toxicity in host cells. Then, q-PCR-based gene profiling, revealed that this activity was related to the downregulation of several genes involved in drug resistance (*yip1*), virulence (*gp63*) and parasite proliferation (*Cyclin 1* and *Cyclin 6*). Importantly, the treatment of BALB/c mice with any of the two AMPs caused a significant reduction in *L. major* infective burden. This effect was associated with an increase in Th1 cytokine levels (*IL-12p35*, *TNF-α*, and *iNOS*) in the skin lesion and spleen of the *L. major* infected mice while the Th2-associated genes were downregulated (*IL-4* and *IL-6*). Lastly, we investigated the effect of both peptides in the gene expression profile of the P2X7 purinergic receptor, which has been reported as a therapeutic target in several diseases. The results showed significant repression of *P2X7R* by both peptides in the skin lesion of *L. major* infected mice to an extent comparable to that of a common anti-leishmanial drug, Paromomycin. Our in vitro and in vivo studies suggest that the synthetic AMPs 19-2.5 and 19-4LF are promising candidates for leishmaniasis treatment and present P2X7R as a potential therapeutic target in cutaneous leishmaniasis (CL).

The Trypanosoma cruzi TcrNT2 Nucleoside Transporter Is a Conduit for the Uptake of 5-F-2'-Deoxyuridine and Tubercidin Analogues.

Aldfer MM, Alfayez IA, Elati HAA, Gayen N, Elmahallawy EK, Milena Murillo A, Marsiccobetre S, Van Calenbergh S, Silber AM, de Koning HP.
19-11-2022
Molecules.
https://pubmed.ncbi.nlm.nih.gov/36432150/

Synthesis and Anti-Leishmanial Properties of Quinolones Derived from Zanthosimuline.

Jézéquel G, Cardoso LNF, Olivon F, Dennemont I, Apel C, Litaudon M, Roussi F, Pomel S, Desrat S.
15-11-2022
Molecules
https://pubmed.ncbi.nlm.nih.gov/36431992/

Quinoline derivatives and especially quinolones are considered as privileged structures in medicinal chemistry and are often associated with various biological properties. We recently isolated a series of original monoterpenyl quinolones from the bark of *Codiaeum peltatum*. As this extract was found to have a significant inhibitory activity against a *Leishmania* species, we decided to study the anti-leishmanial potential of this type of compound. Leishmaniasis is a serious health problem affecting more than 12 million people in the world. Available drugs cause harmful side effects and resistance for some of them. With the aim of finding anti-leishmanial compounds, we developed a synthetic strategy to access natural quinolones and analogues derived from zanthosimuline. We showed the versatility of this natural compound toward cyclization conditions, leading to various polycyclic quinolone-derived structures. The natural and synthetic compounds were evaluated against amastigote forms of *Leishmania infantum*. The results obtained confirmed the interest of this family of natural compounds but also revealed promising activities for some intermediates deriving from zanthosimuline. Following the same synthetic strategy, we then prepared 14 new analogues. In this work, we identified two promising molecules with good activities against intramacrophage *L. infantum* amastigotes without any cytotoxicity. We also showed that slight changes in amide functional groups affect drastically their anti-parasitic activity.

Prevalence of visceral leishmaniasis among people with HIV: a systematic review and meta-analysis.

Kantzanou M, Karalexi MA, Theodoridou K, Kostares E, Kostare G, Loka T, Vrioni G, Tsakris A.
24-11-2022
Eur J Clin Microbiol Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/36427170/

Leishmaniasis is a parasitic infection expressing different clinical phenotypes. Visceral leishmaniasis (VL) is considered an opportunistic infection among people with human immunodeficiency virus (HIV). The objective of this review was to identify published data on the prevalence of Leishmania spp. infection among PWH and to define particular determinants that affect critically the epidemiological characteristics of VL-HIV coinfection and, potentially, its burden on public health. Two independent reviewers conducted a systematic literature search until June 30, 2022. Meta-analyses were conducted using random-effects models to calculate the summary prevalence and respective 95% confidence intervals (CI) of leishmaniasis among PWH. Meta-regression analysis was performed to investigate the impact of putative effect modifiers, such as the mean CD4 cell count, on the major findings. Thirty-four studies were eligible, yielding a summary prevalence of 6% (95%CI, 4-11%) for leishmaniasis (n = 1583) among PWH (n = 85,076). Higher prevalence rates were noted in Asia (17%, 95%CI, 9-30%) and America (9%, 95%CI, 5-17%) than in Europe (4%, 95%CI, 2-8%). Prevalence rates were significantly mediated by the age, sex, and CD4 cell count of participants. Heterogeneity remained significant in all meta-analyses ($p < 0.0001$). In the majority of included studies, people were coinfected with HIV and Leishmania species associated with VL, as opposed to those associated with cutaneous leishmaniasis. No sign of publication bias was shown ($p = 0.06$). Our summary of published studies on leishmaniasis among PWH is important to provide prevalence estimates and define potential underlying factors that could guide researchers to generate and further explore specific etiologic hypotheses.

Holanamine, a Steroidal Alkaloid from the Bark of Holarrhena pubescens Wall. ex G. Don Inhibits the Growth of Leishmania donovani by Targeting DNA Topoisomerase 1B.

Goel N, Gupta VK, Garg A, Bhoumik A, Biswas R, Natarajan R, Majumder HK, Jaisankar P.
23-11-2022
ACS Infect Dis
https://pubmed.ncbi.nlm.nih.gov/36417798/

Leishmaniasis is a group of neglected tropical diseases (NTDs) caused by about 20 species of obligate intracellular protozoan parasites of the genus *Leishmania*, which occurs in cutaneous, mucocutaneous, and visceral forms. Many researchers have sought to utilize natural products for novel and effective treatments to combat many infectious diseases, including leishmaniasis. *Holarrhena pubescens* Wall. ex G. Don (Apocynaceae) bark is a rich source of bioactive steroidal alkaloids. The total alkaloidal extract (IC_{50} 6.12 ± 0.117 μg/mL), and the isolated alkaloid, holanamine, showed significant antileishmanial activity (IC_{50} 2.66 ± 0.112 μM against AG83 and 3.80 ± 0.126 μM against BHU-575) against the *Leishmania donovani* parasite, better than miltefosine (IC_{50} 19.61 ± 0.093 μM against AG83 and 23.20 ± 0.094 μM against BHU-575). Holanamine inhibited the *L. donovani* topoisomerase 1B (LdToP1B) in a non-competitive manner (IC_{50} 2.81 ± 0.105 μM), indicating that it interacts with the free enzyme and enzyme-DNA complex without inhibiting human topoisomerase. Hydrogen bonding and hydrophobic interactions of holanamine with the N-terminal and hinge region of the large subunit of LTop1B is responsible for its potent antileishmanial activity, as shown by docking studies. Treatment with holanamine causes apoptotic-like cell death by generating cellular and mitochondrial reactive oxygen species, disrupting the mitochondrial membrane potential and inducing ultrastructural alterations in the promastigotes. Holanamine effectively clears intracellular amastigotes but minimally affects host macrophages with no significant cytotoxicity in HEK 293 and L929 cell lines. Thus, our studies show that holanamine can further be used to develop effective antileishmanial agents against evolving drug-resistant parasites.

Case Report: Simple Nodular Cutaneous Leishmaniasis Caused by Autochthonous Leishmania (Mundinia) orientalis in an 18-Month-Old Girl: The First Pediatric Case in Thailand and Literature Review.

Anugulruengkitt S, Songtaweesin WN, Thepnarong N, Tangthanapalakul A, Sitthisan M, Chatproedprai S, Wititsuwannakul J, Likitnukul S, Jariyapan N, Weedall GD, Siriyasatien P, Preativatanyou K.
21-11-2022
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/36410322/

We report an autochthonous case of simple, localized cutaneous leishmaniasis in a healthy 18-month-old girl from southern Thailand. The patient presented with a solitary chronic cutaneous nodular lesion on her left cheek for approximately 1 year. Histopathological dissection of the cheek skin biopsy demonstrated remarkably nodular and interstitial infiltrates of lymphocytes and histiocytes full of intracellular oval-shaped amastigotes, consistent with cutaneous leishmaniasis. The Leishmania promastigotes were also cultured successfully from the lesion biopsy and were designated with the WHO code MHOM/TH/2021/CULE5. Using internal transcribed spacer 1-specific polymerase chain reaction, the parasite DNA was demonstrated in both saliva and lesion biopsy. Based on the BLASTn and phylogenetic analysis, the parasite was identified as Leishmania orientalis, clustered in the Mundinia subgenus. The patient responded well to a 6-week course of oral itraconazole, without recurrence. To our knowledge, this is the fourth case of autochthonous leishmaniasis resulting from L. orientalis and the youngest patient of leishmaniasis ever reported in Thailand. More importantly, we also demonstrate the clinical course of the lesion according to the timeline before and after treatment, which can help physicians better understand and provide an accurate diagnosis with appropriate treatment of this emerging parasitic disease.

Thermosensitive system formed by poloxamers containing carvacrol: An effective carrier system against Leishmania amazonensis.

Costa AMB, Silva ARST, Santos AJ, Galvão JG, Andrade-Neto VV, Torres-Santos EC, Ueki MM, Almeida LE, Sarmento VHV, Dolabella SS, Scher R, Lira AAM, Nunes RS.

Jan-2023

Acta Trop.

https://pubmed.ncbi.nlm.nih.gov/36375398/

The drugs used in the treatment of leishmaniasis show problems concerning side effects and toxicity. As a result, the search for new actives is necessary, and natural products like carvacrol - 5-isopropyl-2-methylphenol, become a relevant alternative. To enable the use of carvacrol as an antileishmanial agent, thermosensitive hydrogels were developed from poloxamer triblock copolymers 407 (P407) and 188 (P188). Carvacrol-free and carvacrol-containing hydrogels were obtained from P407 alone and from the mixture of P407 and P188. The hydrogels were subjected to Differential scanning calorimetry, Small-angle X-ray scattering, Scanning electron microscopy, and Rheology analysis. The activity of hydrogels and carvacrol isolated against promastigotes and intracellular amastigotes of Leishmania amazonensis and their cytotoxicity in mammalian cells was determined. The sol-gel transition temperature for the binary hydrogel containing carvacrol (HG407/188CA) was 37.04 ± 1.35 °C. HG407/188CA presented lamellar structure at temperatures of 25 °C and 37 °C. HG407/188CA and carvacrol presented IC50 against Leishmania amazonensis promastigotes of 18.68 ± 1.43 µg/mL and 23.83 ± 3.32 µg/mL, respectively, and IC50 against Leishmania amazonensis amastigotes of 35.08 ± 0.75 µg/mL and 29.32 ± 0.21 µg/mL, respectively. HG407/188CA reduced the toxicity of carvacrol in all mammalian cells evaluated, raising the CC50 in murine peritoneal macrophages from 40.23 ± 0.21 µg/mL to 332.6 ± 4.89 µg/mL, obtaining a Selectivity Index (SI) of 9.5 against 1.37 of the isolated carvacrol. HG407/188CA provided higher selectivity of carvacrol for the parasite. Thus, the binary hydrogel obtained may enable the use of carvacrol as a potential antileishmanial agent.

Identification of 1,2,3-triazolium salt-based inhibitors of Leishmania infantum trypanothione disulfide reductase with enhanced antileishmanial potency in cellulo and increased selectivity.

de Lucio H, Revuelto A, Carriles AA, de Castro S, García-González S, García-Soriano JC, Alcón-Calderón M, Sánchez-Murcia PA, Hermoso JA, Gago F, Camarasa MJ, Jiménez-Ruiz A, Velázquez S.

15-12-2022

Eur J Med Chem.

https://pubmed.ncbi.nlm.nih.gov/36332553/

N-methylation of the triazole moiety present in our recently described triazole-phenyl-thiazole dimerization disruptors of Leishmania infantum trypanothione disulfide reductase (LiTryR) led to a new class of potent inhibitors that target different binding sites on this enzyme. Subtle structural changes among representative library members modified their mechanism of action, switching from models of classical competitive inhibition to time-dependent mixed noncompetitive inhibition. X-ray crystallography and molecular modeling results provided a rationale for this distinct behavior. The remarkable potency and selectivity improvements, particularly against intracellular amastigotes, of the LiTryR dimerization disruptors 4c and 4d reveal that they could be exploited as leishmanicidal agents. Of note, L. infantum promastigotes treated with 4c significantly reduced their low-molecular-weight thiol content, thus providing additional evidence that LiTryR is the main target of this novel compound.

Leishmania infantum NTPDase1 and NTPDase2 play an important role in infection and nitric oxide production in macrophages.

da Silva W, Ribeiro IC, Agripino JM, da Silva VHF, de Souza LÂ, Oliveira TA, Bressan GC, Vasconcellos RS, Dumas C, Pelletier J, Sévigny J, Papadopoulou B, Fietto JLR.

Jan-2023

Acta Trop.

https://pubmed.ncbi.nlm.nih.gov/36309108/

Leishmania infantum, the causative agent of American Visceral Leishmaniasis (VL), is known for its ability to modulate the host immune response to its own favor. Ecto-nucleoside triphosphate diphosphohydrolase (ENTPDase) represents a family of enzymes that hydrolyze nucleotides and are involved in nucleotide-dependent biological processes. L. infantum has two ENTPDases, namely LiNTPDase1 and LiNTPDase2. Here, we used genetic tools to overexpress or abolish the expression of LiNTPDase1 and -2 to assess their role in parasite growth in culture and macrophage infection. While LiNTPDase1 or 2-overexpressing clones showed no morphological or growth changes in promastigotes, LiNTPDase2 overexpression increased macrophage adhesion and infection by 50% and 30%, respectively. The individual LiNTPDase1 and 2 knockout mutants showed lag in growth profile, which was reversed by the addition of adenine and guanine to the culture media. Moreover, the morphology of the knockout mutants even in supplemented media was changed to an amastigote-like form. The double knockout of both genes was lethal and a mechanism of compensation of deletion of one isoform was detected in these mutants. Correspondingly, the absence of LiNTPDase1 or LiNTPDase2 led to a dramatic reduction in in vitro infection (~90%). Interestingly, nitric oxide production was decreased in both knockout mutants during infection, which suggests that both LiNTPDases can inhibit macrophage responses against the parasite. Overall, our results show important roles of LiNTPDase1 and -2 concerning in vitro macrophage infection and reinforce their use as potential targets to control Leishmania infections.

A global perspective on non-autochthonous canine and feline Leishmania infection and leishmaniosis in the 21st century.

Rocha R, Pereira A, Maia C.
Jan-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/36198329/

Leishmaniosis is a high-burden vector-borne disease caused by Leishmania parasites that affect humans and other animals, including dogs and cats. Globalization is one of the main factors that largely contributes to the spread of leishmaniosis to non-endemic areas. A comprehensive review of scientific literature published between 2000 and 2021 was conducted to identify the epidemiological situation and clinical management of imported animal Leishmania infection and leishmaniosis as a fundamental step to better manage individual cases and traveler animal health from a global and One Health perspective. A total of 31 articles were selected, representing 1403 canine, and 25 feline imported cases. Canine and feline leishmanioses in non-endemic areas remain a challenge for veterinarians. Thus, diagnostic and management algorithms for veterinary clinical decision support are proposed. Increased surveillance of non-autochthonous cases, including relocated companion animals, could improve individual health, and mitigate the public and animal health risk of introducing Leishmania species into new areas.

Identification of protein biomarkers of attenuation and immunogenicity of centrin or p27 gene deleted live vaccine candidates of Leishmania against visceral leishmaniasis.

Tandon R, Reyaz E, Roshanara, Jadhav M, Gandhi M, Dey R, Salotra P, Nakhasi HL, Selvapandiyan A.
29-08-2022
Parasitol Int.
https://pubmed.ncbi.nlm.nih.gov/36049661/

Currently, no licensed vaccine is available for human visceral leishmaniasis (VL), a fatal disease caused by the protozoan parasite Leishmania donovani. Two of our live attenuated L. donovani vaccine candidates, either deleted for Centrin1 (LdCen1-/-) or p27 gene (Ldp27-/-), that display reduced growth in macrophages were studied to be safe, immunogenic and protective against VL in various animal models. This report involves the identification of differentially expressed proteins, their related pathways and its underlying mechanism in the intracellular stage of these parasites, using Isobaric Tags for Relative and Absolute Quantitation (iTRAQ) methods. Out of 50-60 proteins, found to be differentially expressed in these mutant parasites, 36 were found to be common in both the parasites. Such proteins mainly belong to the functional categories viz. metabolic enzymes, chaperones and stress proteins, proteins involved in translation, processing and transport and proteins involved in nucleic acid processing. Proteins known to be host protective, like Glyceraldehyde-3-phosphate dehydrogenase (GAPDH), cytochrome c, calreticulin and those responsible for inducing immune response, namely tubulins, DEAD box RNA helicases, HSP70 and tryparedoxin, have been detected to be modulated in these parasites. Such proteins could be predicted as biomarkers, with further scope of study for their role in growth attenuation. SIGNIFICANCE: This study aims at predicting proteomic biomarkers of Leishmania parasite growth attenuation, that have immunomodulatory role in the disease leishmaniasis. Advanced studies could be helpful in establishing the role of these identified proteins in parasitic virulence and to predict the host interaction at molecular level. Also, these proteins could be exploited as attenuation markers during the development of genetically modified live attenuated parasites as vaccine candidates. These could be cross validated in varied species of Leishmania and other tyrpanosomatids for similar response towards identifying them as universal biomarkers of attenuation.

Measuring the sero-prevalence of Leishmania donovani induced cutaneous leishmaniasis: A method comparison study.

Deepachandi B, Ejazi SA, Bhattacharyya A, Ali N, Soysa P, Siriwardana Y.
Feb-2023
Parasitol Int.
https://pubmed.ncbi.nlm.nih.gov/36038060/

An in-house enzyme-linked immunosorbent assay (ELISA) based on crude antigen of Leishmania reported a high sero-prevalence (82.0%) in Leishmania donovani induced cutaneous leishmaniasis (CL) in Sri Lanka. ELISA was further compared with established serological tools to identify a suitable point of care diagnostic tool. Sero-prevalence of 100 CL samples were analyzed using in-house ELISA, Indian dipstick test and rK39 strip test. Results obtained were further compared with direct agglutination test (DAT) for 40 CL. Test performance was evaluated using Kappa index value. Clinico-epidemiological characteristics of patients were analyzed using SPSSv25.0. Cost analysis of tests was carried out. ELISA showed a high sero-positivity of 81.0% (n = 81/100) while DAT (57.5%,n = 23/40), Indian dipstick test (22.0%,n = 22/100) and rK39 test (15.0%,n = 15/100) showed a comparatively less sero-positivity. According to Kappa index values, there were no perfect agreement between tests. Among ELISA positive patients (n = 81/100), DAT, Indian dipstick test and rK39 demonstrated sero-positivity rates of 61.3% (n = 19/31), 25.9% (n = 21/81) and 16.0% (n = 13/81) respectively. Among ELISA negative patients (n = 19/100), three assays demonstrated sero-positivity rates of 44.4% (n = 4/9), 5.3% (n = 1/9) and 10.5% (n = 2/19) respectively. DAT can be used as an alternative test when ELISA is not available or negative. Clinico-epidemiological profiles of patients that showed sero-positivity by each assay were different. Cost per patient was approximately 5.5 USD for DAT and 3.0 USD for each other tests. Established serological tests demonstrated different and relatively lower detection rates. Species, strain and antigen heterogeneity, inconsistency in amount of used antigens, sera, antibody expression patterns and testing methodologies could be responsible. This study

highlighted the importance of designing an in-house serological assay based on local parasite.

Wharton Jelly Derived Mesenchymal Stem Cell's Exosomes Demonstrate Significant Antileishmanial and Wound Healing Effects in Combination with Aloe-Emodin: An in Vitro Study.

Koken GY, Abamor ES, Allahverdiyev A, Karaoz E.
Dec-2022
J Pharm Sci.
https://pubmed.ncbi.nlm.nih.gov/35995206/

Cysticercose

An alternating current electrokinetics biosensor for rapid on-site serological screening of Taenia solium cysticercosis infection

Lin X, Jiang X, Wu JJ, Eda S, Wan N
26-11-2022
Mikrochim Acta
https://pubmed.ncbi.nlm.nih.gov/36435891/

Cysticercosis, caused by Taenia solium infection, is a leading cause of acquired epilepsy in many developing countries. Several types of immunoassays have been developed for the detection of Taenia solium infection in both infected humans and livestock animals. However, these methods require central laboratory facilities and are both time- and labor-consuming with longer than desired turnaround time. In this work, we demonstrated that AC electrokinetics (ACEK) capacitive sensing can be used to realize point-of-care immunosensor in general, with the on-site screening of Taenia solium infection as an example here. The sensor employs interdigitated microelectrodes (IDME) functionalized with a recombinant Taenia solium antigen, rT24H, to detect anti-rT24H antibodies in clinical serum samples. ACEK capacitive sensing method interrogates the IDME sensors with a special AC signal, which serves the dual purposes of enriching target antibodies by ACEK effects and directly measuring the capacitance change induced by specific binding. First, to characterize the ACEK biosensor as an immunosensor in general, IgG in phosphate-buffered saline buffer was tested against IDME sensors functionalized with anti-IgG. The limit of detection of the sensor was 24.1 fg/mL, and the linear dynamic range was 0.1-100 pg/mL. To test the clinical usage of this sensor, ACEK capacitive sensors with rT24H probe were used to test clinical serum samples from patients with or without Taenia solium infection. The diagnostic sensitivity of the ACEK capacitive sensor for Taenia solium infection was found to be 88.24%. ACEK capacitive immunosensors have shown good potential for point-of-care diagnostics.

Echinococcose

Experimental treatment of cystic echinococcosis: Combination therapy with carvacrol and thymol versus albendazole.

Albani C, Patricia P, Julia F, Adriana A, Antonela P, Celina EM.
23-11-2022
Exp Parasitol.
https://pubmed.ncbi.nlm.nih.gov/36435216/

Serum Level of egr-miR-2a-3p as a Potential Diagnostic Biomarker for Cystic Echinococcosis.

Karami MF, Beiromvand M, Rafiei A, Dayer D, Rahdar M, Bahreini A, Dastyar AA.
4-11-2022
Acta Parasitol
https://pubmed.ncbi.nlm.nih.gov/36434379/

Data on the combined effect of atovaquone, mefloquine, and 3-bromopyruvic acid against Echinococcus multilocularis protoscoleces.

Kouguchi H, Enkai S, Matsuyama H, Hidaka M, Inaoka DK, Kita K, Yagi K.
28-10-2022
Data Brief.
https://pubmed.ncbi.nlm.nih.gov/36426011/

The dataset presented here is related to a previous research article titled "Mitochondrial Complex III in Larval Stage of *Echinococcus multilocularis* as a Potential Chemotherapeutic Target and in vivo Efficacy of Atovaquone Against Primary Hydatid Cysts"[1]. In this report, data were collected from aerobic and anaerobic culture assays of *E. multilocularis* protoscoleces in the presence of three anti-echinococcal drug candidates (atovaquone, mefloquine, and 3-bromopyruvic acid). The data were analyzed for viability of the protoscoleces between day 0 and day 7 upon adding drug candidates. In aerobic condition, all drug candidates caused damage to the protoscoleces, as described previously [1], [2], [3], [4], [5], [6]. Mefloquine, alone as well as in combination with atovaquone, immediately eliminated the protoscoleces, whereas combination of atovaquone with 3-bromopyruvic acid did not show clear synergy. In anaerobic condition, mefloquine, alone as well as in combination with atovaquone, eliminated protoscoleces immediately. 3-Bromopyruvic acid showed stronger efficacy in anaerobic condition than in aerobic condition. Combination of atovaquone with 3-bromopyruvic acid eliminated the protoscoleces, indicating that synergy occurred only under anaerobic condition. The data clarified that combined use of the three drugs eliminated protoscoleces in both aerobic and anaerobic conditions, hence suggesting that these could inhibit aerobic and anaerobic respiration pathways of *Echinococcus multilocularis* in vivo. The obtained data would be useful for the development of new drug dosing method for alveolar echinococcosis.

Establishment of primary cystic echinococcosis in laboratory mice: our results in the Balb/c strain.

Sohraby SA, Moazeni M, Rakhshandehroo E.
2022
Iran J Vet Res.
https://pubmed.ncbi.nlm.nih.gov/36425602/

In Silico Evaluation of the Haplotype Diversity, Phylogenetic Variation and Population Structure of Human E. granulosus sensu stricto (G1 Genotype) Sequences.

Selcuk MA, Celik F, Kesik HK, Gunyakti Kilinc S, Ahmed H, Jiang N, Simsek S, Cao J.
14-11-2022
Pathogens
https://pubmed.ncbi.nlm.nih.gov/36422598/

Echinococcus granulosus sensu lato is the causative agent of cystic echinococcosis (CE), which is a neglected zoonotic disease with an important role in human morbidity. In this study, we aimed to investigate the haplotype diversity, genetic variation, population structure and phylogeny of human *E. granulosus sensu stricto* (s.s.) (G1 genotype) isolates submitted to GenBank from different parts of the world by sequencing the mitochondrial CO1 and ND1 genes. The sequences of the mt-CO1 (401 bp; *n* = 133) and mt-ND1 (407 bp; *n* = 140) genes were used to analyze the haplotype, polymorphism and phylogenetic of 273 *E. granulosus s.s.* (G1 genotype) isolates. Mutations were observed at 31 different points in the mt-CO1 gene sequences and at 100 different points in the mt-ND1 gene sequences. Furthermore, 34 haplotypes of the mt-CO1 sequences and 37 haplotypes of the mt-ND1 sequences were identified. Tajima's D, Fu's Fs, and Fu's LD values showed high negative values in both mt-CO1 and mt-ND1 gene fragments. The haplotype diversities in the sequences retrieved from GenBank in this study indicate that the genetic variation in human isolates of *E. granulosus s.s.* in western countries is higher than in eastern countries. This may be due to demographic expansions due to animal trades and natural selections.

Genetic diversity and haplotype analysis of yak and sheep echinococcal cysts isolates from the mitochondrial cox1 gene in parts of Tibet, China.

Fan S, Zhao X, Danqulamu, Shi B, Tang W, Dong H, Xia C.
07-11-2022
Front Vet Sci.
https://pubmed.ncbi.nlm.nih.gov/36419727/

Very low frequency waves as selective probe for Cysticercus tenuicollis, Hydatid cyst and Coenurus cerebralis bio-analysis using single cell-signal recording.

Foroutan H, Moazeni M, Doroodmand MM, Mootabi-Alavi A.
22-11-2022
Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/36418888/

Hydatid Disease of the Liver Presenting as Spontaneous Cutaneous Fistula: A case report.

Ghabisha S, Ahmed F, Al-Wageeh S, Al-Shami E, Al-Naggar K, Askarpour MR, Eslahi A.
Nov-2022
Sultan Qaboos Univ Med J
https://pubmed.ncbi.nlm.nih.gov/36407698/

Case report: Right atrium-inferior vena cava bypass in a patient with unusual cardiac cystic echinococcosis.

Liu L, Wu B, Li M, Guo Y.
03-11-2022
Front Cardiovasc Med.
https://pubmed.ncbi.nlm.nih.gov/36407447/

Cardiovascular hydatid disease is caused by parasitic infection of Echinococcus granulosus, which could be asymptomatic or life-threatening depending on lesion site, granuloma size, and disease progression. Diagnosis and treatment of cardiac echinococcosis should be under comprehensive consideration. In this case, we reported a successful right atrium-inferior vena cava bypass surgery in a 31-year-old female with unresectable right atrial echinococcosis and inferior vena cava obstruction.

Cardiac Echinococcosis With Hepatic Involvement in a Child: A Case Report.

Akrim Y, Babokh F, El Hakkouni A.
17-10-2022
Cureus.
https://pubmed.ncbi.nlm.nih.gov/36407185/

Hydatidosis is endemic in Morocco. Cardiac localization of hydatid disease is a rare entity. Involvement of the interventricular septum is even rarer. We report the case of a 6-year-old girl with combined hepatocardiac hydatid disease. She was admitted with complaints of dyspnea, asthenia and vomiting. Ultrasound imaging and CT scan showed cystic lesions in the interventricular septum and in the liver. Serologic test results were positive. According to the biological and radiological findings, the diagnosis of echinococcosis with cardiac and hepatic involvement was suggested. Complete excision of the cardiac cyst was performed followed by anthelminthic treatment with albendazole as a supportive therapy. The confirmative diagnosis of hydatid disease was made by microscopic examination of the removed material. Our patient was referred to the department of general surgery to treat the liver lesions in the future. The postoperative period was unremarkable.

First detection of Echinococcus multilocularis in Bosnia and Herzegovina.

Omeragić J, Goletić T, Softić A, Goletić Š, Kapo N, Soldo DK, Šupić J, Škapur V, Čerkez G, Ademović E, Semren O, Alić A.
12-11-2022
Int J Parasitol Parasites Wildl.
https://pubmed.ncbi.nlm.nih.gov/36406035/

Echinococcus multilocularis has been spreading through Central Eastern Europe but has not yet been reported in Bosnia and Herzegovina (B&H). Recently, this parasite is confirmed in Croatia suggesting the movement of the parasite's distribution limit further south. Given that there is no surveillance or monitoring system for echinococcosis in B&H, our study was designed as a pilot study of E. multilocularis. A total of 57 red foxes originating from 24 localities all over the country were collected during the routine rabies monitoring, autopsied and examined for the presence of echinococcosis. Based on intestinal scraping technique and microscopy, E. multilocularis adult worms have been detected in one (1/57, 1.75%) red fox. To verify this finding and to differentiate Echinococcus spp., DNA extracted from adult worms was subjected to species-specific PCR targeting part of the mitochondrial 12S ribosomal RNA gene. E. multilocularis PCR-positive samples were further confirmed by NGS sequencing of a 203 bp amplified fragment of 12S rRNA, which has been deposited in GenBank (Accession no.: OP047920). This finding represents the first detection of E. multilocularis in B&H, strongly suggesting its presence in the country. The confirmation of the parasite in the same locality where migrants/refugees temporarily stay on their route to Western Europe highlights the need for a One Health approach in addressing all future questions. Moreover, the first detection of E. multilocularis in B&H warrants the need for the implementation of an appropriate state surveillance program.

European Haplotype of Echinococcus multilocularis in the United States.

Polish LB, O'Connell EM, Barth TFE, Gottstein B, Zajac A, Gibson PC, Bah A, Kirchgessner M, Estrada M, Seguin MA, Ramirez-Barrios R.
17-11-2022
Engl J Med.
https://pubmed.ncbi.nlm.nih.gov/36383717/

Evaluating noninvasive methods for estimating cestode prevalence in a wild carnivore population.

Brandell EE, Jackson MK, Cross PC, Piaggio AJ, Taylor DR, Smith DW, Boufana B, Stahler DR, Hudson PJ.
15-11-2022
PLoS One.
https://pubmed.ncbi.nlm.nih.gov/36378663/

Helminth infections are cryptic and can be difficult to study in wildlife species. Helminth research in wildlife hosts has historically required invasive animal handling and necropsy, while results from noninvasive parasite research, like scat analysis, may not be possible at the helminth species or individual host levels. To increase the utility of noninvasive sampling, individual hosts can be identified by applying molecular methods. This allows for longitudinal sampling of known hosts and can be paired with individual-level covariates. Here we evaluate a combination of methods and existing long-term monitoring data to identify patterns of cestode infections in gray wolves in Yellowstone National Park. Our goals were: (1) Identify the species and apparent prevalence of cestodes infecting Yellowstone wolves; (2) Assess the relationships between wolf biological and social characteristics and cestode infections; (3) Examine how wolf samples were affected by environmental conditions with respect to the success of individual genotyping. We collected over 200 wolf scats from 2018-2020 and conducted laboratory analyses including individual wolf genotyping, sex identification, cestode identification, and fecal glucocorticoid measurements. Wolf genotyping success rate was 45%, which was higher in the winter but decreased with higher precipitation and as more time elapsed between scat deposit and collection. One cestode species was detected in 28% of all fecal samples, and 38% of known individuals. The most common infection was Echinococcus granulosus sensu lato (primarily E. canadensis). Adult wolves had 4x greater odds of having a cestode infection than pups, as well as wolves sampled in the winter. Our methods provide an alternative approach to estimate cestode prevalence and to linking parasites to known individuals in a wild host system, but may be most useful when employed in existing study systems and when field collections are designed to minimize the time between fecal deposition and collection.

Single-Cell Heterogeneity of the Liver-Infiltrating Lymphocytes in Individuals with Chronic Echinococcus multilocularis Infection.

Jiang T, Sun W, Aji T, Shao Y, Guo C, Zhang C, Ran B, Hou J, Yasen A, Guo Q, Wang H, Qu K, Wen H.
17-11-2022
Infect Immun.
https://pubmed.ncbi.nlm.nih.gov/36317875/

Human alveolar echinococcosis (AE) is a tumor-like disease predominantly located in the liver. The cellular composition and heterogeneity of the lesion-infiltrating lymphocytes which produce an "immunosuppressive" microenvironment are poorly understood. Here, we profiled 83,921 CD45+ lymphocytes isolated from the peripheral blood (PB), perilesion (PL), and adjacent normal (AN) liver tissue of four advanced-stage AE patients using single-cell RNA and T-cell receptor (TCR) sequencing technology. We identified 23 large clusters, and the distributions and transcriptomes of these cell clusters in the liver and periphery were different. The cellular proportions of exhausted CD8+ T cells and group 2 innate lymphoid cells (ILC2s) were notably higher in PL tissue, and the expression features of these cell subsets were related to neoplasm metastasis and immune response suppression. In the 5 CD8+ T-cell populations, only CD8+ mucosa-associated invariant T (MAIT) cells were enriched in PL samples and the TRAV1-2_TRAJ33_TRAC TCR was clonally expanded. In the 11 subsets of CD4+ T cells, Th17 cells and induced regulatory T cells (iTregs) were preferentially enriched in PL samples, and their highly expressed genes were related to cell invasion, tumor metastasis, and inhibition of the inflammatory immune response. Exhaustion-specific genes (TIGIT, PD-1, and CTLA4) were upregulated in Tregs. Interestingly, there was a close contact between CD8+ T cells and iTregs or Th17

cells, especially for genes related to immunosuppression, such as PDCD1-FAM3C, which were highly expressed in PL tissue. This transcriptional data set provides valuable insights and a rich resource for deeply understanding the immune microenvironment in AE, which could provide potential target signatures for AE diagnosis and immunotherapies.

The impact of natural environment on human alveolar echinococcosis: A township-level modeling study in Qinghai-Tibet Plateau.

Yin J, Wu X, Han J, Torgerson PR.
15-01-2023
Sci Total Environ.
https://pubmed.ncbi.nlm.nih.gov/36179829/

Human alveolar echinococcosis (AE) is a lethal helminthic infection caused by the tapeworms Echinococcus multilocularis. The Qinghai-Tibet Plateau has the greatest endemicity of human AE globally, but the natural risk factors and its impact mechanism are still unclear. Generalized linear models and generalized additive models are used to select key linear and non-linear environmental factors associated with cases of AE. The interactive effect between different factors is identified using concurvity test. From fifty-nine variables analyzed, four key factors and one interaction term were identified associated with AE. Considering interaction terms between climatic and geographical landscape factors can significantly improve model fitting. Minimum winter precipitation, percentage of grassland cover, and minimum elevation have significant positive linear relationship with human AE incidence. The relationship between maximum summer precipitation and human AE is non-linear with high AE incidence associated with moderate precipitation. The interaction term of maximum summer precipitation and number of patches of grassland on human AE indicates that human AE incidence is highest when both factors were high. The climatic and landscape risk factors together are associated with the local transmission of human AE in Qinghai-Tibet Plateau. This study provides a scientific basis for human intervention in AE from fine-scale ecological environment.

Cerebral hydatid cyst in children: A case series of 21 patients and review of literature.

Assamadi M, Benantar L, Hamadi H, Ksiks O, El Hadwe S, Aniba K.
Dec.2022
Neurochirurgie.
https://pubmed.ncbi.nlm.nih.gov/35907445/

Pigmented congenital vitreous cyst in a patient with positive Echinococcus serology.

Patil NS, Rayat JS.
Dec.2022
Can J Ophthalmol.
https://pubmed.ncbi.nlm.nih.gov/35202572/

Progress Toward Global Eradication of Dracunculiasis - Worldwide, January 2021-June 2022.

Hopkins DR, Weiss AJ, Yerian S, Sapp SGH, Cama VA.
25-11-2022
MMWR Morb Mortal Wkly Rep.
https://pubmed.ncbi.nlm.nih.gov/36417302/

Dracunculiasis (Guinea worm disease), caused by the parasite Dracunculus medinensis, is acquired by drinking water containing small crustacean copepods (water fleas) infected with D. medinensis larvae. Recent evidence suggests that the parasite also appears to be transmitted by eating fish or other aquatic animals. About 1 year after infection, the worm typically emerges through the skin on a lower limb of the host, causing pain and disability (1). No vaccine or medicine is available to prevent or treat dracunculiasis. Eradication relies on case containment* to prevent water contamination and other interventions to prevent infection, including health education, water filtration, treatment of unsafe water with temephos (an organophosphate larvicide), and provision of safe drinking water (1,2). CDC began worldwide eradication efforts in October 1980, and in 1984 was designated by the World Health Organization (WHO) as the technical monitor of the Dracunculiasis Eradication Program (1). In 1986, with an estimated 3.5 million cases† occurring annually in 20 African and Asian countries§ (3), the World Health Assembly called for dracunculiasis elimination. The Guinea Worm Eradication Program (GWEP),¶ led by The Carter Center and supported by partners that include WHO, UNICEF, and CDC, began assisting ministries of health in countries with endemic disease. In 2021, a total of 15 human cases were identified and three were identified during January-June 2022. As of November 2022, dracunculiasis remained endemic in five countries (Angola, Chad, Ethiopia, Mali, and South Sudan); cases reported in Cameroon were likely imported from Chad. Eradication efforts in these countries are challenged by infection in animals, the COVID-19 pandemic, civil unrest, and insecurity. Animal infections, mostly in domestic dogs, some domestic cats, and in Ethiopia, a few baboons, have now surpassed human cases, with 863 reported animal infections in 2021 and 296 during January-June 2022. During the COVID-19 pandemic all national GWEPs remained fully operational, implementing precautions to ensure safety of program staff members and community members. In addition, the progress toward eradication and effectiveness of interventions were reviewed at the 2021 and 2022 annual meetings of GWEP program managers, and the 2021 meeting of WHO's International Commission for the Certification of Dracunculiasis Eradication. With only 15 human cases identified in 2021 and three during January-June 2022, program efforts appear to be closer to reaching the goal of eradication. However, dog infections and impeded access because of civil unrest and insecurity in Mali and South Sudan continue to be the greatest challenges for the program. This report describes progress during January 2021-June 2022 and updates previous reports (2,4).

The Complete Genome Sequence of Amorphophallus titanum, the Corpse Flower.

Frisse L, Martinez MA, Pirro S.
2022
Biodivers Genomes.
https://pubmed.ncbi.nlm.nih.gov/36415484/

Potential of Lemna minor and Eichhornia crassipes for the phytoremediation of water contaminated with Nickel (II).

Moreno-Rubio N, Ortega-Villamizar D, Marimon-Bolívar W, Bustillo-Lecompte C, Tejeda-Benítez LP.
18-11-2022
Environ Monit Assess.
https://pubmed.ncbi.nlm.nih.gov/36396866/

Phytoextraction of Nickel (II) in water by two types of aquatic macrophytes (Lemna minor and Eichhornia crassipes) was investigated using synthetic aqueous solutions of NiSO4 at concentrations of 0.5, 1.5 and 2.5 mg/L. The toxic effects of nickel salt in plants were evaluated through the presence of necrosis and chlorosis. The bioconcentration factor, Nickel (II) removal efficiency and kinetics of removal were also calculated. Results of this study show bioconcentration factors higher than 1000, which categorize L. minor and E. crassipes as hyperaccumulators. Besides, L. minor presented a removal percentage higher than 68%, compared to E. crassipes that did not exceed 50% in any of the three concentrations studied. However, E. crassipes showed better resistance to the effects of nickel and obtained a greater removal capacity during the phytoremediation process that lasted for 10 days. In contrast, L. minor suffered necrosis and chlorosis in a concentration-dependent way. Consequently, both macrophytes are sustainable alternatives for nickel removal from contaminated water.

Alleviation of aqueous nitrogen loss from paddy fields by growth and decomposition of duckweed (Lemna minor L.) after fertilization.

Wang Y, Chen X, Guo B, Liu C, Liu J, Qiu G, Fu Q, Li H.
Jan. 2023
Chemosphere.
https://pubmed.ncbi.nlm.nih.gov/36332733/

Runoff loss of nitrogen from paddy fields has received increasing attention in recent years. Duckweed is an aquatic plant frequently found in paddy fields. In this study, the effects of duckweed (Lemna minor L.) in floodwater on aqueous nitrogen losses from paddy fields were systematically investigated. Results demonstrated that the growth of duckweed decreased total nitrogen concentrations in floodwater and nitrogen runoff loss from paddy fields by 16.7%-18.3% and 11.2%-13.6%, respectively. Moreover, compared with NO3-, NH4+ was preferentially removed by duckweed. 15N isotope tracer experiments revealed that the growth and decomposition of duckweed acted as a "buffer" against the nitrogen variation in floodwater after fertilization. During the growth of duckweed, leaves were found to be the principal organ to assimilate NH4+ and release NO3- by using non-invasive micro-test technology. Duckweed degradation increased the content of hydrophobic acids and marine humic-like substances in floodwater, which promoted the migration of nitrogen from floodwater to soil. Redundancy analysis and structural equation models further illustrated that pH and temperature variation in floodwater caused by duckweed played a greater role in aqueous nitrogen loss reduction than the nitrogen accumulation in duckweed. This study suggested that the growth of duckweed in paddy fields was an effective supplementary method for controlling aqueous nitrogen loss during agricultural production.

Dualistic effects of bisphenol A on growth, photosynthetic and oxidative stress of duckweed (Lemna minor).

Liang J, Li Y, Xie P, Liu C, Yu L, Ma X.
Dec. 2022
Environ Sci Pollut Res Int.
https://pubmed.ncbi.nlm.nih.gov/35819675/

In this study, we exposed duckweed (Lemna minor), a floating freshwater plant, to BPA at different concentrations (0, 1, 5, 20, and 50 mg/L) for 7 days so as to investigate the effects of BPA on its growth, photosynthesis, antioxidant system, and osmotic substances. It was found that BPA had the acute toxic effects of "low promotion and high inhibition" on growth and photosynthesis. Specifically, BPA at a low concentration (5 mg/L) significantly promoted the plant growth and improved the concentration of photosynthetic pigments (chlorophyll a, b, and total Chl) of L. minor. However, BPA at a high concentration (50 mg/L) significantly inhibited the plant growth, the Chl content, and the maximal photochemical efficiency (F_v/F_m). Furthermore, BPA with high concentration (50 mg/L) induced ROS accumulation and increased the activities of antioxidant enzymes (SOD, CAT, POD, APX, and GR) and the contents of antioxidant substances (GSH, proline, and T-AOC), which indicated that L. minor might tolerate BPA toxicity by activating an antioxidant defense system. The correlation analysis revealed that the fresh weight of L. minor was significantly and positively correlated with photosynthesis and the contents of soluble protein and sugar, while it was negatively correlated with the content of H_2O_2. Totally, these results showed that BPA at different concentrations had dualistic effects on the growth of L. minor, which was attributed to the alterations of photosynthesis, oxidative stress, and osmotic regulation systems and provided a novel insight for studying the effects of BPA on aquatic plant physiology.

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

Filariose lymphatique

RNAi-mediated knockdown of arginine kinase genes leads to high mortality and negatively affect reproduction and blood-feeding behavior of Culex pipiens pallens.

Qian K, Guan Q, Zhang H, Zhang N, Meng X, Liu H, Wang J.
22-11-2022
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/36413567/

Background: Arginine kinase (AK) is one of the crucial enzymes involved in energy metabolism in invertebrates, and has been proposed as the target for RNA interference (RNAi)-based control of agricultural insect pests. While there is only one AK gene in most insects, two AK genes were identified in Culex pipiens pallens, the primary vector of lymphatic filariasis and epidemic encephalitis. Methods: The full-length cDNA sequences of CpAK1 and CpAK2 genes were obtained by reverse transcription PCR(RT-PCR) and rapid amplification of cDNA ends (RACE). The expression levels of CpAK1 and CpAK2 in different developmental stages and tissues were detected by reverse transcription quantitative PCR (RT-qPCR). The role of CpAK1 and CpAK2 in the reproduction and blood feeding behavior was analyzed using RNA interference (RNAi). Results: Full-length cDNAs of CpAK1 and CpAK2 were isolated from Cx. pipiens pallens. Analysis of the expression pattern revealed that the mRNA level of CpAK1 was significantly higher than CpAK2 in all development stages and tissues examined, and the expressions of both CpAK1 and CpAK2 were upregulated in response to blood feeding. The co-knockdown of CpAK1 and CpAK2 mediated by RNAi led to high mortality (74.3%) of adult female mosquitoes and decreased hatchability (59.9%). Remarkably, the blood feeding rate and the engorgement rate of the female mosquitoes were negatively affected by co-injection of dsRNAs targeting CpAK1 and CpAK2. Conclusion: CpAK1 and CpAK2 were detected in all developmental stages and tissues, but showed divergence in expression level. RNAi-mediated knockdown of AK genes leads to high mortality and negatively affect blood-feeding behavior of Cx. pipiens pallens, suggesting that AK could be used for the target of RNAi-based mosquito control in the future.

Knowledge, attitude, and practice regarding mosquito-borne diseases among migrant laborers from a migrant settlement in Ponekkara, Ernakulam Kerala.

Bhardwaj R, Mohandas KS, Mathew MM.
Nov-22
Indian J Public Health
https://pubmed.ncbi.nlm.nih.gov/36412475/

Background: Mosquito-borne diseases (MBDs) such as Malaria, Dengue, Chikungunya, lymphatic filariasis, and Japanese Encephalitis are important public health problems in India. Ernakulam in Kerala being a hub of construction activities has a large influx of migrants from Odisha, West Bengal, Bihar, Assam, U. P., Jharkhand, T. N., and Karnataka. Hence, the objective of this study was to assess the knowledge, attitude, and practice related to MBDs and the associated factors among the migrant laborers from a migrant settlement in Ponekkara, Ernakulam Kerala. Materials and methods: A cross-sectional study was done among 179 migrant laborers from a migrant settlement in Ponekkara, Kerala, from September 2021 to November 2021 using a pretested semi-structured questionnaire to collect information regarding socio-demographic details and their knowledge, attitude, and practice regarding mosquito borne diseases. After taking verbal consent, the questionnaire was administered by the investigator. Descriptive and univariate analysis was done using SPSS Version 20. Results: It was found that 58.4% of the migrant laborers had poor knowledge, 55.9% had poor attitude, and 61.5% of them had poor practice regarding MBDs. On univariate analysis, a statistically significant association was observed between attitude score and the level of education. Conclusion: The findings showed that migrant laborers had an overall poor knowledge, attitude, and practices regarding MBDs. Consequently, there is a need to plan an awareness program among the migrant settlements regarding MBDs.

Correction: India can consider integration of three eliminable disease control programmes on malaria, lymphatic filariasis, and visceral leishmaniasis.

Rahi M, Chaturvedi R, Das P, Sharma A.
21-11-2022
PLoS Pathog
https://pubmed.ncbi.nlm.nih.gov/36409694/

Eosinophils in filarial infections: Inducers of protection or pathology?

Ehrens A, Hoerauf A, Hübner MP.
31-10-2022
Front Immunol.
https://pubmed.ncbi.nlm.nih.gov/36389745/

Filariae are parasitic roundworms, which can cause debilitating diseases such as lymphatic filariasis and onchocerciasis. Lymphatic filariasis, also known as elephantiasis, and onchocerciasis, commonly referred to

as river blindness, can lead to stigmatizing pathologies and present a socio-economic burden for affected people and their endemic countries. Filariae typically induce a type 2 immune response, which is characterized by cytokines, i.e., IL-4, IL-5 and IL-13 as well as type 2 immune cells including alternatively activated macrophages, innate lymphoid cells and Th2 cells. However, the hallmark characteristic of filarial infections is a profound eosinophilia. Eosinophils are innate immune cells and pivotal in controlling helminth infections in general and filarial infections in particular. By modulating the function of other leukocytes, eosinophils support and drive type 2 immune responses. Moreover, as primary effector cells, eosinophils can directly attack filariae through the release of granules containing toxic cationic proteins with or without extracellular DNA traps. At the same time, eosinophils can be a driving force for filarial pathology as observed during tropical pulmonary eosinophilia in lymphatic filariasis, in dermatitis in onchocerciasis patients as well as adverse events after treatment of onchocerciasis patients with diethylcarbamazine. This review summarizes the latest findings of the importance of eosinophil effector functions including the role of eosinophil-derived proteins in controlling filarial infections and their impact on filarial pathology analyzing both human and experimental animal studies.

Assessing seroprevalence and associated risk factors for multiple infectious diseases in Sabah, Malaysia using serological multiplex bead assays.

Chan YL, Patterson CL, Priest JW, Stresman G, William T, Chua TH, Tetteh K, Lammie P, Drakeley C, Fornace KM.
25-10-2022
Front Public Health.
https://pubmed.ncbi.nlm.nih.gov/36388287/

Background: Infectious diseases continue to burden populations in Malaysia, especially among rural communities where resources are limited and access to health care is difficult. Current epidemiological trends of several neglected tropical diseases in these populations are at present absent due to the lack of habitual and efficient surveillance. To date, various studies have explored the utility of serological multiplex beads to monitor numerous diseases simultaneously. We therefore applied this platform to assess population level exposure to six infectious diseases in Sabah, Malaysia. Furthermore, we concurrently investigated demographic and spatial risk factors that may be associated with exposure for each disease. Methods: This study was conducted in four districts of Northern Sabah in Malaysian Borneo, using an environmentally stratified, population-based cross-sectional serological survey targeted to determine risk factors for malaria. Samples were collected between September to December 2015, from 919 villages totaling 10,100 persons. IgG responses to twelve antigens of six diseases (lymphatic filariasis- Bm33, Bm14, BmR1, Wb123; strongyloides- NIE; toxoplasmosis-SAG2A; yaws- Rp17 and TmpA; trachoma- Pgp3, Ct694; and giardiasis- VSP3, VSP5) were measured using serological multiplex bead assays. Eight demographic risk factors and twelve environmental covariates were included in this study to better understand transmission in this community. Results: Seroprevalence of LF antigens included Bm33 (10.9%), Bm14+ BmR1 (3.5%), and Wb123 (1.7%). Seroprevalence of Strongyloides antigen NIE was 16.8%, for Toxoplasma antigen SAG2A was 29.9%, and Giardia antigens GVSP3 + GVSP5 was 23.2%. Seroprevalence estimates for yaws Rp17 was 4.91%, for TmpA was 4.81%, and for combined seropositivity to both antigens was 1.2%. Seroprevalence estimates for trachoma Pgp3 + Ct694 were 4.5%. Age was a significant risk factors consistent among all antigens assessed, while other risk factors varied among the different antigens. Spatial heterogeneity of seroprevalence was observed more prominently in lymphatic filariasis and toxoplasmosis. Conclusions: Multiplex bead assays can be used to assess serological responses to numerous pathogens simultaneously to support infectious disease surveillance in rural communities, especially where prevalences estimates are lacking for neglected tropical diseases. Demographic and spatial data collected alongside serosurveys can prove useful in identifying risk factors associated with exposure and geographic distribution of transmission.

Assessment of factors related to individuals who were never treated during mass drug administration for lymphatic filariasis in Ambon City, Indonesia.

Titaley CR, Worrell CM, Ariawan I, Taihuttu YMJ, de Lima F, Naz SF, Que BJ, Krentel A.
11-11-2022
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/36367853/

Mycétome

Mycetoma of the right foot: a rare clinical image.

Shaikh MK, Borkar S.
11-08-2022
Pan Afr Med J.
https://pubmed.ncbi.nlm.nih.gov/36405660/

Cytomorphology of Deep Mycoses in Dogs and Cats.

Dehghanpir SD.
Jan-2023
Vet Clin North Am Small Anim Pract.
https://pubmed.ncbi.nlm.nih.gov/36270845

The purpose of this review is to familiarize clinical pathologists and clinicians with the cytomorphologic features associated with deep mycoses in dogs and cats. The goals are to develop a more unified approach to the description and interpretation of fungal cytomorphology and to facilitate the categorization of fungi that do not produce unique morphologic structures in tissue.

Onchocercose

Direct proteomic detection and prioritization of 19 onchocerciasis biomarker candidates in humans.

Rosa BA, Curtis K, Erdmann Gilmore P, Martin J, Zhang Q, Sprung R, Weil GJ, Townsend RR, Fischer PU, Mitreva M.
23-11-2022
Mol Cell Proteomics.
https://pubmed.ncbi.nlm.nih.gov/36435333/

Onchocerca volvulus, the causative agent of onchocerciasis, infects over 20 million people and can cause severe dermatitis and ocular conditions including blindness. Current treatments employed in mass drug administration programs do not kill adult female worms, and common diagnostic tests cannot reliably assess viability of adult worms. There is an urgent need for better diagnostic tests to facilitate monitoring the efficacy of new treatments and disease elimination efforts. Here, eight plasma samples collected from individuals infected with O. volvulus and seven from uninfected individuals were analyzed by MS/MS spectrometry to directly identify O. volvulus proteins present in infected but absent in uninfected control samples. This direct proteomic approach for biomarker discovery had not been previously employed for onchocerciasis. Among all detected proteins, 19 biomarker candidates were supported by two or more unique peptides, identified in the plasma of at least three O. volvulus-infected human samples and absent in all control samples. Comprehensive analysis and ranking of these candidates included detailed functional annotation and a review of RNA-seq gene expression profiles. Isotope-labeled standard peptides were ran in parallel and validated MS/MS peptide identifications for 15 peptides from 11 of the 19 proteins, and two infected urine and one uninfected urine sample was used for additional validation. A major antigen / OVOC11613 was identified as the most promising candidate with eight unique peptides across five plasma samples and one urine sample. Additional strong candidates included OVOC1523 / ATP synthase, OVOC247 / laminin and OVOC11626 / PLK5, and along with OVOC11613, and were also detected in urine samples from onchocerciasis patients. This study has identified a promising novel set of proteins that will be carried forward to develop assays that can be used for diagnosis of O. volvulus infections and for monitoring treatment efficacy.

Molecular detection of Loxodontofilaria spp. in Asian elephants (Elephas maximus) from elephant training camps in Thailand.

Saengsawang P, Desquesnes M, Yangtara S, Chalermwong P, Thongtip N, Jittapalapong S, Inpankaew T.
11-11-2022
Comp Immunol Microbiol Infect Dis
https://pubmed.ncbi.nlm.nih.gov/36427455/

Filarial infection is an important disease in human and animal medicine. Several filarial worms are of importance, especially nematodes in the Onchocercidae. The Asian elephant (Elephas maximus) is an endangered animal and is very important from several socio-economic and ecological aspects in Thailand. Various parasites can be found in elephants; however, data related to filarial infections in elephants is limited. The objective of this study was to detect filaria in the blood of Asian elephants in Thailand, based on a polymerase chain reaction (PCR) technique. Blood samples were collected from 208 Asian elephants and detected for filaria using PCR, targeting the region of the internal transcribed spacer 2 (ITS2), the cytochrome c oxidase subunit 1 (cox1), and the RNA polymerase II large subunit (rbp1). In total, 4.33% (9 out of 208) of the sampled elephants had Loxodontofilaria spp. DNA with 100% query coverage. In addition, the obtained cox1 and rbp1 sequences matched with Loxodontofilaria sp., Onchocerca sp., and Dirofilaria sp. There were no identified risk factors (sex, age, location, and packed cell volume) related to Loxodontofilaria infection in elephants. The analyses of the phylogeny of ITS2 sequences demonstrated that the Loxodotofilaria-positive sequences were closely related to Onchocerca dewittei japonica and Onchocerca dewittei dewittei with 100% query coverage. Notably, the concatenated phylogenetic trees of ITS2 and the cox1 and rbp1 genes were closely similar to Loxodontofilaria sp. To describe in detail the genomic DNA of Loxodontofilaria spp., other genes should be additionally studied using a more discriminatory technique, such as DNA barcoding or whole genome sequencing.

Morphological description and multilocus genotyping of Onchocerca spp. in red deer (Cervus elaphus) in Switzerland.

Manzanell R, Stocker AS, Deplazes P, Mathis A.
03-11-2022
Int J Parasitol Parasites Wildl.
https://pubmed.ncbi.nlm.nih.gov/36420351/

Onchocercosis is a parasitic disease caused by over 30 *Onchocerca* spp. (Nematoda: Filarioidea) and predominantly affecting ungulates. Four *Onchocerca* spp. have been described in the European red deer (*Cervus elaphus*). *Onchocerca flexuosa* and *Onchocerca jakutensis* form subcutaneous nodules in the back region. The other two species, *Onchocerca skrjabini* and the lesser-known *Onchocerca garmsi*, are found freely in the subcutaneous tissue of carpal and tarsal joints, and the sternal region, respectively. The presence of *Onchocerca* spp. in eight red deer shot in the hunting season during September 2020 in the Grisons region, Switzerland, was investigated by analysing nodules and free worms in the subcutaneous tissue. The obtained worms were morphologically and genetically identified as *O. jakutensis*, *O. flexuosa* and *O. skrjabini*. The latter two are first reports from Switzerland, and morphological redescriptions of these two species are presented. *Onchocerca skrjabini* and *O. jakutensis* are newly described from the sternal region of deer. One female of *O. jakutensis* was found free in the subcutaneous tissue of the sternal region, an atypical

presentation for this species. Phylogenetic analyses were based on four mitochondrial and one nuclear loci, revealing that *O. jakutensis* belongs to a clade which so far only included non-cervid *Onchocerca* spp. Analysis of sequences from this study and GenBank entries revealed two distinct subpopulations of *O. skrjabini*: one from European red deer and another from Japanese serow and sika deer. Morphological identification can be challenging, also because worm location in the host is less strictly determined than previously described. Genetic identification is straightforward for *O. flexuosa*, *O. jakutensis* and *O. skrjabini* for which complete data of five loci are now available whereas genetic data of *O. garmsi* is still lacking.

LupiQuant: A real-time PCR based assay for determining host-to-parasite DNA ratios of Onchocerca lupi and host Canis lupus from onchocercosis samples.

Roe CC, Urbanz J, Auten C, Verocai GG, Upshaw-Bia K, Holiday O, Hepp C, Sahl JW.
21-11-2022
PLoS One.
https://pubmed.ncbi.nlm.nih.gov/36409718/

Onchocerca lupi is a filarial nematode that causes ocular onchocercosis in canines globally including North America and areas of Europe, North Africa, and the Middle East. Reported incidence of this parasite in canines has continued to steadily escalate since the early 21st century and was more recently documented in humans. Whole genome sequencing (WGS) of this parasite can provide insight into gene content, provide novel surveillance targets, and elucidate the origin and range expansion. However, past attempts of whole genome sequencing of other Onchocerca species reported a substantial portion of their data unusable due to the variable over-abundance of host DNA in samples. Here, we have developed a method to determine the host-to-parasite DNA ratio using a quantitative PCR (qPCR) approach that relies on two standard plasmids each of which contains a single copy gene specific to the parasite genus Onchocerca (major body wall myosin gene, myosin) or a single copy gene specific to the canine host (polycystin-1 precursor, pkd1). These plasmid standards were used to determine the copy number of the myosin and pkd1 genes within a sample to calculate the ratio of parasite and host DNA. Furthermore, whole genome sequence (WGS) data for three O. lupi isolates were consistent with our host-to-parasite DNA ratio results. Our study demonstrates, despite unified DNA extraction methods, variable quantities of host DNA within any one sample which will likely affect downstream WGS applications. Our quantification assay of host-to-parasite genome copy number provides a robust and accurate method of assessing canine host DNA load in an O. lupi specimen that will allow informed sample selection for WGS. This study has also provided the first whole genome draft sequence for this species. This approach is also useful for future focused WGS studies of other parasites.

Identification of the onchocerciasis vector in the Kakoi-Koda focus of the Democratic Republic of Congo.

Post RJ, Laudisoit A, Mandro M, Lakwo T, Laemmer C, Pfarr K, Hoerauf A, Tortosa P, Gomard Y, Ukety T, Mande C, Farovitch L, Amazigo U, Bakajika D, Oguttu DW, Awaca N, Colebunders R.
04-11-2022
PLoS Negl Trop Dis.
https://pubmed.ncbi.nlm.nih.gov/36331979/

Background: The objective of this study was to characterise the vector in a small hyper-endemic focus of onchocerciasis (the Kakoi-Koda focus) which has recently been discovered on the western slopes of the rift valley above Lake Albert. Methodology/principal findings: Aquatic stages of blackflies were collected by hand from streams and rivers, and anthropophilic adult females were collected by human landing catches. Using a combination of morphotaxonomy and DNA barcoding, the blackflies collected biting humans within the focus were identified as Simulium dentulosum and Simulium vorax, which were also found breeding in local streams and rivers. Simulium damnosum s.l., Simulium neavei and Simulium albivirgulatum were not found (except for a single site in 2009 where crabs were carrying S. neavei). Anthropophilic specimens from the focus were screened for Onchocerca DNA using discriminant qualitative real-time triplex PCR. One specimen of S. vorax was positive for Onchocerca volvulus in the body, and out of 155 S. dentulosum, 30% and 11% were infected and infective (respectively). Conclusions/significance: Simulium dentulosum currently appears to be the main vector of human onchocerciasis within the Kakoi-Koda focus, and S. vorax may be a secondary vector. It remains possible that S. neavei was the main (or only) vector in the past having now become rare as a result of the removal of tree-cover and land-use changes. Simulium vorax has previously been shown to support the development of O. volvulus in the laboratory, but this is the first time that S. dentulosum has been implicated as a probable vector of onchocerciasis, and this raises the possibility that other blackfly species which are not generally considered to be anthropophilic vectors might become vectors under suitable conditions. Because S. dentulosum is not a vector in endemic areas surrounding the Kakoi-Koda focus, it is probable that the Kakoi-Koda focus is significantly isolated.

Feline ocular onchocercosis by Onchocerca lupi: Phylogenetic insights and implication for veterinary health.

Tudor P, Ionașcu I, Mateescu CI, Bezerra-Santos MA, Gurău MR, Mateescu RE, Gagniuc E, Tudor N, Otranto D.
Jan-2023
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/36283498/

Onchocerca lupi is a vector-borne filaroid which affects wild (i.e., wolves, coyotes) and domestic carnivores (i.e., dogs, cats), and occasionally humans. This nematode causes ocular damage due to the location of adult worms embedded in the eye connective tissues. Several human

cases of onchocercosis by O. lupi have been reported in Europe, Asia, north Africa, and the USA where the infection thrives in dogs and less frequently in cats. In this study, we review clinical aspects of feline infestation by O. lupi, and report the first case of this onchocercid in a cat from Romania, showing a subconjunctival mass located at the medial canthus of the right eye; worms were surgically removed from the ocular nodule and morphologically and molecularly identified. Lesions were examined and characterized using histological procedures. Nematodes were identified as O. lupi based on their morphology at the direct observation as well as at the histological examination. Molecular and phylogenetic analysis confirmed the identification of this onchocercid, with the cox 1 sequence obtained clustering with those available in public repositories, including isolates from dogs and cats from Europe and USA. Despite the few reports available on the occurrence of this parasite on domestic cats, these felines are regarded as potential hosts of O. lupi in Portugal and USA. Moreover, the spread of feline ocular onchocercosis in Eastern Europe countries draw attention on the need of additional studies to confirm the potential vectors involved in its transmission cycle.

Status of Onchocerca volvulus (Spirurida: Onchocercidae) Transmission and Effect of Climatic Variables on the Vector Population Dynamics After Two Decades of Ivermectin-based Preventive Chemotherapy in the Mbam Valley (Centre Region, Cameroon).

Domche A, Nwane PB, Nana Djeunga HC, Njitchouang GR, Pion SD, Boussinesq M, Njiokou F, Kamgno J.
16-11-2022
J Med Entomol.
https://pubmed.ncbi.nlm.nih.gov/36111691/

Entomological indicators of onchocerciasis transmission and the effect of climatic variables on the vector population dynamics were investigated in two first-line villages after more than two decades of mass drug administration with ivermectin. Female blackflies were collected in two villages (Bayomen and Biatsota) using human landing method for a period of 12 months. Blackflies were dissected and entomological indices were computed. Monthly temperature, precipitation, and humidity were collected and the Spearman correlation rank test was used to assess the relationship between biting rates and climatic variables. The highest biting rates (62,280 bites/human/month in Bayomen and 42,090 bites/human/month in Biatsota) were recorded during the long rainy season (November). The Onchocerca volvulus transmission was greater during the long dry season in both villages, with a peak at the beginning of the long dry season in Biatsota (100 infective larvae/human/month), and at the middle of the long dry season in Bayomen (92 infective larvae/human/month). No correlation was found between biting rates and selected climatic variables in the two villages. This study revealed that onchocerciasis transmission is ongoing in the study area despite almost 25 years of Community-Directed Treatment with Ivermectin. In accordance with WHO recommendations, vector control should be used in combination with mass drug administration to accelerate transmission interruption of onchocerciasis. To be optimal, this vector control should be implemented during the long dry season (November to March) when water volumes are low and transmission potentials are high.

Schistosomiase

Establishing and Integrating a Female Genital Schistosomiasis Control Programme into the Existing Health Care System.

Nemungadi TG, Furumele TE, Gugerty MK, Djirmay AG, Naidoo S, Kjetland EF.
16-11-2022
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/36422933/

Female genital schistosomiasis (FGS) is a complication of *Schistosoma haematobium* infection, and imposes a health burden whose magnitude is not fully explored. It is estimated that up to 56 million women in sub-Saharan Africa have FGS, and almost 20 million more cases will occur in the next decade unless infected girls are treated. Schistosomiasis is reported throughout the year in South Africa in areas known to be endemic, but there is no control programme. We analyze five actions for both a better understanding of the burden of FGS and reducing its prevalence in Africa, namely: (1) schistosomiasis prevention by establishing a formal control programme and increasing access to treatment, (2) introducing FGS screening, (3) providing knowledge to health care workers and communities, (4) vector control, and (5) water, sanitation, and hygiene. Schistosomiasis is focal in South Africa, with most localities moderately affected (prevalence between 10% and 50%), and some pockets that are high risk (more than 50% prevalence). However, in order to progress towards elimination, the five actions are yet to be implemented in addition to the current (and only) control strategy of case-by-case treatment. The main challenge that South Africa faces is a lack of access to WHO-accredited donated medication for mass drug administration. The establishment of a formal and funded programme would address these issues and begin the implementation of the recommended actions.

Intestinal Helminth Infections in Ghanaian Children from the Ashanti Region between 2007 and 2008-A Retrospective Cross-Sectional Real-Time PCR-Based Assessment.

Akenten CW, Weinreich F, Paintsil EK, Amuasi J, Fosu D, Loderstädt U, May J, Frickmann H, Dekker D.
14-11-2022
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/36422925/

In spite of ongoing eradication programs, helminth infections are still a medical issue in Ghana. For follow-up assessments on the decline of regional helminth infections, historic baseline prevalence values obtained

with standardized diagnostic procedures can be helpful. In this retrospective cross-sectional study, real-time PCR targeting the nematodes *Ancylostoma* spp. (ITS2), *Ascaris lumbricoides* (ITS1), *Enterobius vermicularis* (ITS1), *Necator americanus* (ITS2), *Strongyloides stercoralis* (18S rRNA) and *Trichuris trichiura* (18S rRNA), the trematodes *Schistosoma* spp. (ITS2) as well as the cestodes *Hymenolepis nana* (ITS1), *Taenia saginata* (ITS1) and *Taenia solium* (ITS1) was applied with 2046 DNA eluates from stool samples of Ghanaian children from the Ashanti region collected between 2007 and 2008 in order to retrospectively define prevalence values. The overall prevalence was low with 3.8% (*n* = 77) and only 0.1% (*n* = 2) double infections with helminths were recorded. The three most frequently detected enteric helminth species comprised 2% *S. stercoralis* (*n* = 41), 0.8% *H. nana* (*n* = 16), and 0.7% *N. americanus* (*n* = 14), while only sporadic infection events were recorded for other helminth species comprising 0.1% *E. vermicularis* (*n* = 2), 0.1% *Schistosoma* spp. (*n* = 2), 0.1% *T. saginata* (*n* = 1) and 0.1% *T. trichiura* (*n* = 1). *A. lumbricoides*, *Ancylostoma* spp. and *T. solium* were not detected at all. In conclusion, the retrospective assessment suggests a low prevalence of enteric helminth infections in Ghanaian children from the Ashanti Region within the assessment period between 2007 and 2008.

Schistosomiasis and Recurrent Arthritis: A Systematic Review of the Literature.

Mortier C, Mehadji M, Amrane S, Demoux AL, L'Ollivier C.
17-11-2022
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/36422620/

Effects of Schistosoma mansoni and Praziquantel Treatment on the Lower Gastrointestinal Mucosa: A Cohort Study in Tanzania.

Pham K, Mtalitinya GS, Aristide C, Airewele EA, Nyakaru DK, McMahon P, Mulaki GM, Corstjens PLAM, de Dood C, van Dam GJ, Changalucha JM, Mazigo HD, Lee MH, Jaka H, Downs JA.
18-11-2022
Acta Trop.
https://pubmed.ncbi.nlm.nih.gov/36410422/

Schistosomes infect over 200 million people worldwide, but few studies have characterized the effects of Schistosoma mansoni infection and effective treatment on the lower gastrointestinal mucosa. In this prospective cohort study, we compared the clinical findings on sigmoidoscopy and laboratory measures in Tanzanian adults with and without S. mansoni infection at baseline and 6 months after praziquantel treatment. Grading of the endoscopic findings was done using the Mayo Scoring System for Assessment of Ulcerative Colitis Activity. Schistosome infection was confirmed by stool microscopy and serum circulating anodic antigen (CAA). Baseline comparisons were performed in Stata using Fisher's exact and Wilcoxon rank-sum tests, and pre- and post-treatment comparisons using Wilcoxon matched-pairs signed-rank and McNemar's tests. We investigated the clinical characteristics of 48 individuals: 32 with and 16 without S. mansoni infection. Infected individuals had greater severity of sigmoid and rectal mucosal abnormalities and higher Mayo scores and serum eosinophils (all $p<0.05$) than uninfected individuals at initial evaluation. At 6 months, 28 individuals completed repeat blood tests and sigmoidoscopy. Of these, 14 cleared their baseline infection (n=7) or experienced a greater than 7-fold decrease in serum CAA (n=7). Follow-up sigmoidoscopies revealed some improvements in sigmoid and rectal mucosal findings, although Mayo scores were not significantly lower. Both the median erythrocyte sedimentation rates (32.5→12.5 mm/hr) and percent of eosinophils (7.1→3.1%) decreased in this group from baseline to follow-up. S. mansoni infection was associated with mild-to-moderate lower gastrointestinal mucosal abnormalities that were grossly visible during sigmoidoscopy, and these improved partially 6 months after effective treatment with praziquantel. Additional studies, of longer duration and focused on both clinical and mucosal immunologic effects of S. mansoni, could provide additional insight.

In vivo efficiency of praziquantel treatment of single-sex Schistosoma japonicum aged three months old in mice.

Wang N, Peng HQ, Gao CZ, Cheng YH, Sun MT, Qu GL, Webster JP, Lu DB.
12-11-2022
Int J Parasitol Drugs Drug Resist.
https://pubmed.ncbi.nlm.nih.gov/36403362/

Schistosomiasis is a major neglected tropical disease mainly caused by Schistosoma haematobium, S. japonicum and S. mansoni, and results in the greatest disease burden. Mass drug administration (MDA) with praziquantel (PZQ), a single drug only available for the disease, has played a vital role in schistosomiasis control. Therefore, any possibility of selection of the parasites for PZQ resistance or low sensitivity may hamper the 2030's target of global disease elimination. We had experimentally demonstrated the long-term survival and reproductive potential of single-sex (of either sex) S. japonicum infections in definitive hosts mice. What has not yet been adequately addressed is whether the long live single-sex schistosomes remain sensitive to PZQ, and what reproduction potential for those schistosomes surviving treatment may have. We therefore performed experimental mice studies to explore the treatment effectiveness of PZQ (at total doses of 200 or 400 mg/kg, corresponding to the sub-standard or standard treatment doses in humans) for single-sex S. japonicum aged three months old. The results showed that no treatment efficiency was observed on female schistosomes, whereas on male schistosomes only at PZQ 400 mg/kg a significant higher efficiency in reducing worm burdens was observed. Moreover, either schistosome males or females surviving PZQ treatment remained their reproduction potential as normal. The results indicate that long (i.e., three months) live single-sex S. japonicum can easily survive the current treatment strategy, and moreover, any schistosomes, if with PZQ resistance or low sensitivity, could be easily

transmitted in nature. Therefore, in order to realize the target for the national and the global schistosomiasis elimination, there is undoubtedly a great need for refining PZQ administration and dosage, looking for alternative therapies, and/or developing vaccines against schistosome.

CaMKII regulates neuromuscular activity and survival of the human blood fluke Schistosoma mansoni.

Hirst NL, Lawton SP, Walker AJ.
18-11-2022
Sci Rep.
https://pubmed.ncbi.nlm.nih.gov/36400915/

Calcium/calmodulin dependant protein kinase II (CaMKII), an important transducer of Ca^{2+} signals, orchestrates multiple cellular functions in animals. Here we investigated the importance of CaMKII to Schistosoma mansoni, a blood parasite that causes human schistosomiasis. We demonstrate that phosphorylated (activated) CaMKII is present in cercariae, schistosomula and adult worms, and show that striking activation occurs in the nervous tissue of these parasite life-stages; CaMKII was also activated in the tegument and muscles of adult worms and the vitellaria of females. Exposure of worms to the anti-schistosomal drug praziquantel (PZQ) induced significant CaMKII activation and depletion of CaMKII protein/activation in adult worms resulted in hypokinesia, reduced vitality and death. At medium confidence (global score ≥ 0.40), S. mansoni CaMKII was predicted to interact with 51 proteins, with many containing CaMKII phosphorylation sites and nine mapped to phosphoproteome data including sites within a ryanodine receptor. The CaMKII network was functionally enriched with mitogen-activated protein kinase, Wnt, and notch pathways, and ion-transport and voltage-dependent channel protein domains. Collectively, these data highlight the intricacies of CaMKII signalling in S. mansoni, show CaMKII to be an active player in the PZQ-mediated response of schistosomes and highlight CaMKII as a possible target for the development of novel anti-schistosome therapeutics.

Pathology and molecular mechanisms of Schistosoma japonicum-associated liver fibrosis.

Liu Z, Zhang L, Liang Y, Lu L.
28-10-2022
Front Cell Infect Microbiol.
https://pubmed.ncbi.nlm.nih.gov/36389166/

Schistosomiasis has been widely disseminated around the world, and poses a significant threat to human health. Schistosoma eggs and soluble egg antigen (SEA) mediated inflammatory responses promote the formation of egg granulomas and liver fibrosis. With continuous liver injuries and inflammatory stimulation, liver fibrosis can develop into liver cirrhosis and liver cancer. Therefore, anti-fibrotic therapy is crucial to increase the survival rate of patients. However, current research on antifibrotic treatments for schistosomiasis requires further exploration. In the complicated microenvironment of schistosome infections, it is important to understand the mechanism and pathology of schistosomiasis-associated liver fibrosis(SSLF). In this review, we discuss the role of SEA in inhibiting liver fibrosis, describe its mechanism, and comprehensively explore the role of host-derived and schistosome-derived microRNAs (miRNAs) in SSLF. Inflammasomes and cytokines are significant factors in promoting SSLF, and we discuss the mechanisms of some critical inflammatory signals and pro-fibrotic cytokines. Natural killer(NK) cells and Natural killer T(NKT) cells can inhibit SSLF but are rarely described, therefore, we highlight their significance. This summarizes and provides insights into the mechanisms of key molecules involved in SSLF development.

Performance Evaluation of the Schistoscope 5.0 for (Semi-)automated Digital Detection and Quantification of Schistosoma haematobium Eggs in Urine: A Field-based Study in Nigeria.

Meulah B, Oyibo P, Bengtson M, Agbana T, Lontchi RAL, Adegnika AA, Oyibo W, Hokke CH, Diehl JC, van Lieshout L.
17-10-2022
Am J Trop Med Hyg.
https://pubmed.ncbi.nlm.nih.gov/36252803/

Conventional microscopy is the standard procedure for the diagnosis of schistosomiasis, despite its limited sensitivity, reliance on skilled personnel, and the fact that it is error prone. Here, we report the performance of the innovative (semi-)automated Schistoscope 5.0 for optical digital detection and quantification of Schistosoma haematobium eggs in urine, using conventional microscopy as the reference standard. At baseline, 487 participants in a rural setting in Nigeria were assessed, of which 166 (34.1%) tested S. haematobium positive by conventional microscopy. Captured images from the Schistoscope 5.0 were analyzed manually (semiautomation) and by an artificial intelligence (AI) algorithm (full automation). Semi- and fully automated digital microscopy showed comparable sensitivities of 80.1% (95% confidence interval [CI]: 73.2-86.0) and 87.3% (95% CI: 81.3-92.0), but a significant difference in specificity of 95.3% (95% CI: 92.4-97.4) and 48.9% (95% CI: 43.3-55.0), respectively. Overall, estimated egg counts of semi- and fully automated digital microscopy correlated significantly with the egg counts of conventional microscopy ($r = 0.90$ and $r = 0.80$, respectively, $P < 0.001$), although the fully automated procedure generally underestimated the higher egg counts. In 38 egg positive cases, an additional urine sample was examined 10 days after praziquantel treatment, showing a similar cure rate and egg reduction rate when comparing conventional microscopy with semiautomated digital microscopy. In this first extensive field evaluation, we found the semiautomated Schistoscope 5.0 to be a promising tool for the detection and monitoring of S. haematobium infection, although further improvement of the AI algorithm for full automation is required.

Prevalence and correlates of urogenital schistosomiasis in school-going children at Maramba Primary School in Livingstone District, Zambia.

Kapanga S, Mulemena JA, Kamvuma K, Phiri CN, Chanda W.
Nov-2022
Infect Dis Now.
https://pubmed.ncbi.nlm.nih.gov/36130702/

Objectives: To determine the presence and correlates of S. haematobium in urine specimens of school-going children at Maramba Primary School in Livingstone, Zambia. Methods and subjects: A structured questionnaire was administered to children with signed consent from their guardians/parents, and spot urine specimens were collected in sterile containers for macroscopic/microscopic examination by an experienced laboratory technologist. Results: A total of 173 school-going children participated in the study. Parasitic eggs were detected in six specimens with prevalence of 3.47 %, which was strongly associated with presence of microscopic red blood cells ($p < 0.01$) and washing clothes in a stream ($p = 0.01$). Conclusion: Low prevalence of urogenital schistosomiasis among school-going children was noted with correlates such as washing in a stream, while an older age group showed much stronger disease association.

Evaluation of lignan-loaded poly(ε-caprolactone) nanoparticles: synthesis, characterization, in vivo and in silico schistosomicidal activity.

Lima TC, Magalhães LG, Paula LAL, Cunha WR, Januário AH, Pauletti PM, Bastos JK, Dos Santos FF, Forim MR, Laurentiz RS, Santos FA, Orenha RP, Parreira RLT, Fuzo CA, Molina EF, Santos MFC, Silva MLAE.
Nov-2022
Nat Prod Res.
https://pubmed.ncbi.nlm.nih.gov/34963393/

The formulations showed a size distribution with monodisperse systems formation. In vivo evaluation of schistosomicidal activity against Schistosoma mansoni showed that DNHK, when incorporated into nanoparticles, caused egg number reduction of 4.2% and 28.1% at 40 mg/kg an

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

Intestinal Parasite Infections and Associated Risk Factors among Pre-School Aged Children in Kibera Informal Settlement, Nairobi, Kenya.

Njenga D, Mbugua AK, Okoyo C, Njenga SM.
2022
East Afr Health Res.
https://pubmed.ncbi.nlm.nih.gov/36424950/

Intestinal Helminth Infections in Ghanaian Children from the Ashanti Region between 2007 and 2008-A Retrospective Cross-Sectional Real-Time PCR-Based Assessment.

Akenten CW, Weinreich F, Paintsil EK, Amuasi J, Fosu D, Loderstädt U, May J, Frickmann H, Dekker D.
14-11-2022
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/36422925/

In spite of ongoing eradication programs, helminth infections are still a medical issue in Ghana. For follow-up assessments on the decline of regional helminth infections, historic baseline prevalence values obtained with standardized diagnostic procedures can be helpful. In this retrospective cross-sectional study, real-time PCR targeting the nematodes *Ancylostoma* spp. (ITS2), *Ascaris lumbricoides* (ITS1), *Enterobius vermicularis* (ITS1), *Necator americanus* (ITS2), *Strongyloides stercoralis* (18S rRNA) and *Trichuris trichiura* (18S rRNA), the trematodes *Schistosoma* spp. (ITS2) as well as the cestodes *Hymenolepis nana* (ITS1), *Taenia saginata* (ITS1) and *Taenia solium* (ITS1) was applied with 2046 DNA eluates from stool samples of Ghanaian children from the Ashanti region collected between 2007 and 2008 in order to retrospectively define prevalence values. The overall prevalence was low with 3.8% ($n = 77$) and only 0.1% ($n = 2$) double infections with helminths were recorded. The three most frequently detected enteric helminth species comprised 2% *S. stercoralis* ($n = 41$), 0.8% *H. nana* ($n = 16$), and 0.7% *N. americanus* ($n = 14$), while only sporadic infection events were recorded for other helminth species comprising 0.1% *E. vermicularis* ($n = 2$), 0.1% *Schistosoma* spp. ($n = 2$), 0.1% *T. saginata* ($n = 1$) and 0.1% *T. trichiura* ($n = 1$). *A. lumbricoides*, *Ancylostoma* spp. and *T. solium* were not detected at all. In conclusion, the retrospective assessment suggests a low prevalence of enteric helminth infections in Ghanaian children from the Ashanti Region within the assessment period between 2007 and 2008.

Intestinal Parasitic Infection and Nutritional Status in Children under Five Years Old: A Systematic Review.

Fauziah N, Aviani JK, Agrianfanny YN, Fatimah SN.
12-11-2022
Trop Med Infect Dis.
https://pubmed.ncbi.nlm.nih.gov/36422922/

Intestinal parasitic infections are common infectious diseases causing many health problems and impaired growth and physical development.. Children under five years old are the most vulnerable to infections, due to their immature immunity and feeding and exploratory behaviours. This systematic review aimed to assess the relationship between intestinal parasitic infections and undernutrition among children under 5 years old. Fifteen studies met the inclusion and exclusion criteria and were classified as high-quality studies. Twelve parasites were

reported, including *Ascaris lumbricoides*, *Cryptosporodium* spp., *Entamoeba histolytica*, *Enterobius vermicularis*, *Giardia lamblia*, hookworm, *Hymenolepis nana*, *Strongyloides sterocalis*, *Taenia* spp. and *Trichuris trichuria*. Ascariasis is the most reported infection, with a prevalence ranging from 10.77% in Ethiopia to 57.14% in Malaysia, and is correlated with stunting (OR 2.17 (95% CI 1.14, 4.13), p = 0.02). Giardiasis is the second most reported infection, with a prevalence ranging from 4.43% in Ethiopia to 66.33% in the Central African Republic, and is related to an increased risk of stunting (OR 2.34 (95% CI 1.07, 5.10), p = 0.03)), wasting (OR 2.90 (95% CI 1.12, 7.49, p = 0.03)), and being underweight (OR 1.53 (95% CI 1.02, 2.29, p = 0.04)). The third and fourth most prevalent infections are *T. trichiura* and hookworm infections. Intestinal parasitic infections can occur very early in life and cause significant growth retardation. It is important to understand the prevalence and effects of infection based on the parasite species in order to implement therapeutic interventions and prevention controls.

A New Comestible Formulation of Parasiticide Fungi to Reduce the Risk of Soil-Transmitted Helminth Infections in a Canine Shelter.

Viña C, Salmo R, Pena MV, Palomero AM, Hernández JÁ, Cazapal-Monteiro C, Arias MS, Sánchez-Andrade R, Paz-Silva A.
21-22-2022
Pathogens.
https://pubmed.ncbi.nlm.nih.gov/36422641/

Dogs cared for in a shelter are dewormed every three-four months, but they all become infected one-two months later by the soil-transmitted helminths (STHs) *Toxocara canis*, *Toxascaris leonina*, *Trichuris vulpis,* and *Ancylostoma caninum*. For the purpose of reducing their risk of infection by decreasing the survival of helminths' infective stages in soil, chlamydospores of two parasiticide fungi, *Mucor circinelloides* (ovicide) and *Duddingtonia flagrans* (larvicide) were formulated as handmade edible gelatins and given three days per week for 17 months to 18 dogs (DRF, dogs receiving fungi); a second group was maintained without fungi (CD, control dogs). All individuals were dewormed at months 0, 3, 7, 10 and 13, and it was observed that the levels of helminths egg-output were reduced by 96-98% fourteen days after each treatment. Fecal egg counts of STHs were similar in both groups until the 6th-8th months, and then remained significantly lower in DRF than in CD (42-100% ascarids; 30-100% trichurids and ancylostomatids). According to the results, and considering that gelatin treats have always been fully accepted, it is concluded that this new formulation offers an efficient solution to decrease the risk of infection among dogs maintained in shelters, and is therefore recommended.

Elimination of probable praziquantel-resistant Dipylidium caninum with nitroscanate in a mixed-breed dog: a case report.

Loftus JP, Acevedo A, Bowman DD, Liotta JL, Wu T, Zhu M.
22-11-2022
Parasit Vectors.
https://pubmed.ncbi.nlm.nih.gov/36419194/

Background: Praziquantel is the drug of choice for treating the tapeworm Dipylidium caninum in dogs; however, resistance is possible, and regular, non-targeted administration of praziquantel may select for anthelminthic-resistant populations. Methods: The zinc sulfate fecal floatation procedure was conducted. Gross visualization was used to identify Dipylidium spp. segments, and capsule endoscopy was used to visualize adult tapeworms within the intestinal tract. Results: An 18-month-old spayed female terrier mix was presented due to diarrhea, hematochezia and weight loss. The dog received appropriate anthelmintic therapy for Giardia spp., Ancylostoma spp. and Dipylidium spp. The dog's clinical signs resolved, and elimination of Ancylostoma spp. was confirmed by subsequent fecal analysis. However, Dipylidium spp. segments were repeatedly present in the stool. Observation of the segments confirmed the presence of adult Dipylidium spp in feces. Treatment with praziquantel and epsiprantel were unsuccessful in eliminating the organism but was apparently successful in flea prevention. A single dose of nitrosconate was administered and eliminated Dipylidium spp. infection in the dog. Conclusions: Nitrosconate can be an effective treatment for praziquantel-resistant dipylidiasis in dogs. The novel application of capsule endoscopy confirmed the anthelmintic efficacy of this treatment.

Ovicidal activity of the hydroalcoholic extract of Brazilian peppertree (Schinus terebinthifolia Raddi) against Ancylostoma spp. from naturally parasitized dogs.

Añaña DC, Waller SB, Giordani C, Perera SC, de Almeida Capella G, Berne N, Strothmann AL, Freitag RA, Cleff MB.
Nov-2022
Nat Prod Res.
https://pubmed.ncbi.nlm.nih.gov/34969328/

Gale

Lessons to learn from the analysis of routine health data from Moria Refugee Camp on Lesvos, Greece.

Hart PL, Zahos H, Salt N, Schofield R, Mahroof-Shaffi S, Simonek T, Harkensee C.
22-11-2022
J Public Health (Oxf).
https://pubmed.ncbi.nlm.nih.gov/36415082/

On-site detection of fish furunculosis by combining DNAzyme and carboxyl-functionalized graphene.

Ding W, Miao Q, Bao X, Wang S, Lu J, Lyu M, Wang S.

08-09-2022
Front Chem.
https://pubmed.ncbi.nlm.nih.gov/36405323/

Contagious Itch, Disgust and Empathy in a Family with Scabies and their Treating Medical Staff: An Exploratory Study.

Sutter M, Kamber M, Navarini A, Mueller SM.
21-11-2022
Acta Derm Venereol.
https://pubmed.ncbi.nlm.nih.gov/36281810/

Morsures de serpent

Isolation, Characterization and Anticancer Activity of Two Bioactive Compounds from *Arisaema flavum* (Forssk.) Schott

Sobia Nisa, Yamin Bibi, Saadia Masood, Ashraf Ali, Sadia Alam, Maimoona Sabir, Abdul Qayyum, Waqas Ahmed, Sarah Alharthi, Eman Y Santali, Saif A Alharthy, Waleed M Bawazir, Majed N Almashjary
2022
Molecules
https://www.mdpi.com/1420-3049/27/22/7932

Medicinal plants play important role in the public health sector worldwide. Natural products from medicinal plants are sources of unlimited opportunities for new drug leads because of their unique chemical diversity. Researchers have focused on exploring herbal products as potential sources for the treatment of cancer, cardiac and infectious diseases. *Arisaema flavum* (Forssk.) is an important medicinal plant found in the northwest Himalayan regions of Pakistan. It is a poisonous plant and is used as a remedy against snake bites and scorpion stings. In this study, two bioactive compounds were isolated from *Arisaema flavum* (Forssk.) and their anticancer activity was evaluated against human breast cancer cell line MCF-7 using an MTT assay. The crude extract of *Arisaema flavum* (Forssk.) was subjected to fractionation using different organic solvents in increasing order of polarity. The fraction indicating maximum activity was then taken for isolation of bioactive compounds using various chromatographic and spectroscopic techniques such as column chromatography, thin-layer chromatography (TLC), gas chromatography-mass spectrometry (GC-MS), Fourier transform infrared spectroscopy (FTIR) and nuclear magnetic resonance spectroscopy (NMR). Crude extract of *Arisaema flavum* (Forssk.), as well as various fractions extracted in different solvents such as n-hexane, chloroform and ethyl acetate, were tested against human breast cancer cell line MCF-7 using an MTT assay. The crude extract exhibited significant dose-dependent anticancer activity with a maximum activity of 78.6% at 500 µg/mL concentration. Two compounds, hexadecanoic acid ethyl ester with molecular formula $C_{18}H_{36}O_7$ and molar mass 284 and 5-Oxo-19 propyl-docosanoic acid methyl ester with molecular formula $C_{26}H_{50}O_3$ and molecular mass 410, were isolated from chloroform fraction. These compounds were tested against the MCF-7cell line for cytotoxic activity and exhibited a significant (*p* < 0.00l) decrease in cell numbers for MCF-7 cells with IC_{50} of 25 µM after 48 h of treatment. Results indicated that *Arisaema flavum* (Forssk.) possesses compounds with cytotoxic activity that can further be exploited to develop anticancer formulations.