



TRYLEIDIAG PRESS REVIEW

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R&D in Africa - A new network says it can be done

ANDI: African Network for Drugs and Diagnostics Innovation
Creating a sustainable platform for R&D innovation in Africa



EVENTS HIGHLIGHTS

Microarrays: Methods and Applications for Genome Analysis

19 - 28 April 2009

Wellcome Trust, Hinxton Cambridge, UK

Course summary

The course will provide a comprehensive overview and practical experience of the production and uses of DNA microarrays for a broad range of applications. While complete details of microarray fabrication will be covered in theoretical sessions and demonstrations, the main theme of the course will be the applications of DNA microarrays for state-of-the-art genome analysis as detailed below.

Closing date for applications: 29 November 2008

Read more at:

<http://www.wellcome.ac.uk/Professional-resources/Courses-and-conferences/Advanced-Courses/Courses/WTX026218.htm>



RESEARCH NEWS

Cardiac involvement in African and American trypanosomiasis.

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Lancet Infect Dis. 2008 Oct;8(10):631-41.

American trypanosomiasis (Chagas disease) and human African trypanosomiasis (HAT; sleeping sickness) are both caused by single-celled flagellates that are transmitted by arthropods. Cardiac problems are the main cause of morbidity in chronic Chagas disease, but neurological problems dominate in HAT. Physicians need to be aware of Chagas disease and HAT in patients living in or returning from endemic regions, even if they left those regions long ago. Chagas heart disease has to be taken into account in the differential diagnosis of cardiomyopathy, primarily in patients with pathological electrocardiographic (ECG) findings, such as right bundle branch block or left anterior hemiblock, with segmental wall motion abnormalities or aneurysms on echocardiography, and in young patients with stroke in the absence of arterial hypertension. In HAT patients, cardiac involvement as seen by ECG alterations, such as repolarisation changes and low voltage, is frequent. HAT cardiopathy in general is benign and does not cause relevant congestive heart failure and subsides with treatment. We review the differences between the American and African trypanosomiasis with the main focus on the heart.

Trypanosoma brucei rhodesiense Transmitted by a Single Tsetse Fly Bite in Vervet Monkeys as a Model of Human African Trypanosomiasis.

Thuita JK, Kagira JM, Mwangangi D, Matovu E, Turner CM, Masiga D.

Trypanosomiasis Research Centre, (KARI-TRC), Kikuyu, Kenya.

PLoS Negl Trop Dis. 2008;2(5):e238. Epub 2008 May 14.

We have investigated the pathogenicity of tsetse (*Glossina pallidipes*)-transmitted cloned strains of *Trypanosoma brucei rhodesiense* in vervet monkeys. Tsetse flies were confirmed to have mature trypanosome infections by xenodiagnosis, after which nine monkeys were infected via the bite of a single infected fly. Chancres developed in five of the nine (55.6%) monkeys within 4 to 8 days post infection (dpi). All nine individuals were successfully infected, with a median pre-patent period of 4 (range = 4-10) days, indicating that trypanosomes migrated from the site of fly bite to the systemic circulation rapidly and independently of the development of the chancre. The time lag to detection of parasites in cerebrospinal fluid (CSF) was a median 16 (range = 8-40) days, marking the onset of central nervous system (CNS, late) stage disease. Subsequently, CSF white cell numbers increased above the pre-infection median count of 2 (range = 0-9) cells/microl, with a positive linear association between their numbers and that of CSF trypanosomes. Haematological changes showed that the monkeys experienced an early microcytic-hypochromic anaemia and severe progressive thrombocytopaenia. Despite a 3-fold increase in granulocyte numbers by 4 dpi, leucopaenia occurred



early (8 dpi) in the monkey infection, determined mainly by reductions in lymphocyte numbers. Terminally, leucocytosis was observed in three of nine (33%) individuals. The duration of infection was a median of 68 (range = 22-120) days. Strain and individual differences were observed in the severity of the clinical and clinical pathology findings, with two strains (KETRI 3741 and 3801) producing a more acute disease than the other two (KETRI 3804 and 3928). The study shows that the fly-transmitted model accurately mimics the human disease and is therefore a suitable gateway to understanding human African trypanosomiasis (HAT; sleeping sickness).

T cells and immunopathogenesis of experimental African trypanosomiasis.

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Immunol Rev. 2008 Oct;225(1):128-39.

SUMMARY: African trypanosomes are pathogens for humans and livestock. They are single-cell, extra-cellular parasites that cause persistent infections of the blood and induce profound immunosuppression. Here, we review recent work on experimental African trypanosomiasis, especially infections with *Trypanosoma congolense*, in mice with regard to mechanisms of immunosuppression and immunopathology. The center of the immunopathology is the T-cell-independent production of antibodies to the variant surface glycoprotein (VSG) of trypanosomes, the anti-VSG antibody-mediated phagocytosis of trypanosomes by macrophages, and the subsequent profound dysregulation of the macrophage system. Depending on the genetics of the host and the parasite load, the malfunction of the macrophage system is enhanced by interferon-gamma produced by parasite-specific, major histocompatibility complex class II-restricted, matrix-adherent CD4(+) T cells or downregulated by interleuin-10 produced by parasite-specific, CD4(+)CD25(high) Forkhead box protein 3(+) regulatory T cells. There is a physiological conflict of the two relevant cytokines interleukin-10 and interferon-gamma in regulating the immunopathology versus regulating the induction and effect of protective immune responses. On the basis of very recent work in our laboratory, we propose a hypothetical model suggesting a cross-regulation of natural killer T cells and CD4(+)CD25(high) Forkhead box protein 3(+) regulatory T cells in experimental infections with *T. congolense*.

Cytokines in central nervous system trypanosomiasis: cause, effect or both?

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Trans R Soc Trop Med Hyg. 2008 Sep 22. [Epub ahead of print]

The late, or encephalitic, stage of human African trypanosomiasis (HAT), or sleeping sickness, is typified by a diffuse meningoencephalitis characterised neuropathologically by perivascular infiltration of inflammatory cells. While the cause of this neuroinflammatory reaction is not understood, there is evidence for the roles of pro-inflammatory cytokines such as IFN-gamma and TNF-alpha and counter-



inflammatory cytokines such as IL-10, with the balance of these influencing disease outcome. Because of the practical difficulties of obtaining serial measurements in patients, it has proved difficult to assign either cause or effect properties to measured cytokines, but mechanistic animal modelling studies are proving helpful.

Kinetoplastida: new therapeutic strategies.

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Parasite. 2008 Sep;15(3):522-7.

New formulations and therapeutic switching of the established drugs, amphotericin B and paromomycin, together with the discovery of miltefosine, have significantly improved the opportunities for treatment of visceral leishmaniasis (VL) chemotherapy. However, for human African trypanosomiasis (HAT), Chagas disease and cutaneous leishmaniasis there has been limited progress. For HAT, a novel diamidine, parfuramidine, is in phase III clinical trial for early-stage disease, but for the treatment of late-stage disease there are no new drugs and combinations of eflornithine with melarsoprol or nifurtimox have been the focus of clinical studies. For Chagas disease, different classes of compounds that have validated biochemical targets, sterol biosynthesis methylases and cysteine proteases, are in various stages of development. The genome sequences that are now available for the pathogens that cause the leishmaniasis and trypanosomiasis, and new methods for rapid validation of targets, are part of the solution to discover new drugs. The integration of medicinal chemistry, pharmacokinetics, project planning and interaction with the pharma/biotech sector are essential if progress is to be made. Although there are financial constraints, the appearance of new funding sources and not-for-profit product development partnerships offers hope for drug development.

Molecular epidemiology of African trypanosomiasis: the contributions of David George Godfrey OBE to the biochemical characterization of trypanosomes.

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Parasite. 2008 Sep;15(3):233-6.

The accurate identification of the causative organisms of disease is fundamental to the study of epidemiology. Hence molecular tools are now widely used to detect and distinguish pathogens, and have greatly improved our understanding of epidemiology. David Godfrey pioneered the use of molecular markers in the epidemiology of African trypanosomiasis, thus enabling the light of reliable evidence to shine on this previously problematic and controversial subject area. From the early 1970's David's group employed first isoenzyme electrophoresis and subsequently DNA-based characterization methods to aid identification of trypanosomes collected from a range of endemic countries across Africa. These investigations had a major impact on our understanding of the zoonotic nature of human trypanosomiasis in Africa and of the genetic diversity of African trypanosomes.



Development of drug resistance in *Trypanosoma brucei rhodesiense* and *Trypanosoma brucei gambiense*. Treatment of human African trypanosomiasis with natural products (Review).

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Int J Mol Med. 2008 Oct;22(4):411-9.

Human African trypanosomiasis is an infectious disease which has resulted in the deaths of thousands of people in Sub-Saharan Africa. Two subspecies of the protozoan parasite *Trypanosoma brucei* are the causative agents of the infection, whereby *T. b. gambiense* leads to chronic development of the disease and *T. b. rhodesiense* establishes an acute form, which is fatal within months or even weeks. Current chemotherapy treatment is complex, since special drugs have to be used for the different development stages of the disease, as well as for the parasite concerned. Melarsoprol is the only approved drug for effectively treating both subspecies of human African trypanosomiasis in its advanced stage, however, the drug's potency is constrained due to an unacceptable side effect: encephalopathy, which develops in one out of every 20 patients who are treated with the drug. In addition to the deleterious treatment with melarsoprol, the number of drug-resistant strains of *T. brucei* spp. increases. Mechanisms of drug resistance have been elucidated and involve decreased drug import through the loss of the purine transporter P2 as well as enhanced drug export, mediated by a multidrug resistance-associated protein called TbMRPA. Thereby, the medical treatment with the available chemotherapeutics becomes exceedingly difficult. A promising strategy for research into new drugs and moreover, to overcome drug resistance, are compounds derived from natural sources. This study provides an overview of the recently discovered small molecules with trypanocidal activity against *T. b. gambiense* and *T. b. rhodesiense*. In addition, former promising compounds are touched upon.

Glycosylphosphatidylinositol-phospholipase C regulates transferrin endocytosis in the African Trypanosome.

Subramanya S, Hardin FC, Steverding D, Mensa-Wilmot K.

Biochem J. 2008 Sep 11. [Epub ahead of print]

Glycosylphosphatidylinositol phospholipase C (GPI-PLC) is expressed in bloodstream form *Trypanosoma brucei*, a protozoan that causes human African trypanosomiasis. Loss of GPI-PLC genes reduces virulence of a pleomorphic strain of the parasite, for reasons that are not clear. Herein, we report that GPI-PLC stimulates endocytosis of Transferrin (Tfn) 300-to-500%. Surprisingly, GPI-PLC is not detected at endosomes, suggesting that the enzyme does not interact directly with the endosomal machinery. Therefore, we hypothesized that a diffusible product of GPI-PLC enzyme reaction (possibly diacylglycerol (DAG)) mediated biological effects of the protein. Two sets of data support this assertion. First, a catalytically inactive Gln81Leu mutant of GPI-PLC, expressed in a GPI-PLC null background, had no effect on endocytosis, indicating that enzyme activity is essential for the protein to stimulate endocytosis. Second, exogenous DAGs 1-oleyl 2-acetyl-sn-glycerol (OAG) and dimyristoylglycerol (DMG), independently stimulated endocytosis of Tfn. Further, the DAG mimic



phorbol-12-myristate-13-acetate (PMA), a phorbol ester also activated endocytosis in *T. brucei*. DAG-stimulated endocytosis is a novel pathway in the trypanosome. We surmise that (i) GPI-PLC regulates Tfn endocytosis in *T. brucei*, (ii) GPI-PLC is a signaling enzyme, and (iii) DAG is a second messenger for GPI-PLC. We propose that regulation of endocytosis as a physiological function of GPI-PLC in bloodstream *T. brucei*.

The continuing problem of human African trypanosomiasis (sleeping sickness).

Kennedy PG.

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Ann Neurol. 2008 Aug;64(2):116-26.

Human African trypanosomiasis, also known as sleeping sickness, is a neglected disease, and it continues to pose a major threat to 60 million people in 36 countries in sub-Saharan Africa. Transmitted by the bite of the tsetse fly, the disease is caused by protozoan parasites of the genus *Trypanosoma* and comes in two types: East African human African trypanosomiasis caused by *Trypanosoma brucei rhodesiense* and the West African form caused by *Trypanosoma brucei gambiense*. There is an early or hemolymphatic stage and a late or encephalitic stage, when the parasites cross the blood-brain barrier to invade the central nervous system. Two critical current issues are disease staging and drug therapy, especially for late-stage disease. Lumbar puncture to analyze cerebrospinal fluid will remain the only method of disease staging until reliable noninvasive methods are developed, but there is no widespread consensus as to what exactly defines biologically central nervous system disease or what specific cerebrospinal fluid findings should justify drug therapy for late-stage involvement. All four main drugs used for human African trypanosomiasis are toxic, and melarsoprol, the only drug that is effective for both types of central nervous system disease, is so toxic that it kills 5% of patients who receive it. Eflornithine, alone or combined with nifurtimox, is being used increasingly as first-line therapy for gambiense disease. There is a pressing need for an effective, safe oral drug for both stages of the disease, but this will require a significant increase in investment for new drug discovery from Western governments and the pharmaceutical industry.

Multiple-strain infections of *Trypanosoma brucei* across Africa.

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Acta Trop. 2008 Sep;107(3):275-279. Epub 2008 Jul 12.

It is becoming increasingly clear that parasitic infections frequently contain multiple strains of the same parasite species. This may have important consequences for the parasite dynamics in the host and thus alter disease and transmission dynamics. In *Trypanosoma brucei*, the causal agent of human African trypanosomiasis (sleeping sickness), multiple-strain infections have previously been demonstrated to occur. Here, we analyzed field isolates of *T. b. gambiense*, *T. b. rhodesiense*, and *T. b. brucei*, isolated throughout Africa to assess the commonness of multiple-strain infections across the natural range of this parasite. Using eight highly variable microsatellite loci, we found multiple strains



in 8.8% of our isolates. Due to the technical challenges of detecting multiple infections this number represents a minimum estimate and the true frequency of multiple-strain infections is likely to be higher. Multiple-strain infections occurred across the entire East-West range of the parasite. Together with previous results, these findings strongly suggest that multiple-strain infections are common for this parasite and that their consequences for epidemiology and parasite evolution should be investigated in detail.

Glycogen synthase kinase 3 is a potential drug target for African trypanosomiasis therapy.

Ojo KK, Gillespie JR, Riechers AJ, Napuli AJ, Verlinde CL, Buckner FS, Gelb MH, Domostoj MM, Wells SJ, Scheer A, Wells TN, Van Voorhis WC.

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Antimicrob Agents Chemother. 2008 Oct;52(10):3710-7. Epub 2008 Jul 21.

Development of a safe, effective, and inexpensive therapy for African trypanosomiasis is an urgent priority. In this study, we evaluated the validity of *Trypanosoma brucei* glycogen synthase kinase 3 (GSK-3) as a potential drug target. Interference with the RNA of either of two GSK-3 homologues in bloodstream-form *T. brucei* parasites led to growth arrest and altered parasite morphology, demonstrating their requirement for cell survival. Since the growth arrest after RNA interference appeared to be more profound for *T. brucei* GSK-3 "short" (Tb10.161.3140) than for *T. brucei* GSK-3 "long" (Tb927.7.2420), we focused on *T. brucei* GSK-3 short for further studies. *T. brucei* GSK-3 short with an N-terminal maltose-binding protein fusion was cloned, expressed, and purified in a functional form. The potency of a GSK-3-focused inhibitor library against the recombinant enzyme of *T. brucei* GSK-3 short, as well as bloodstream-form parasites, was evaluated with the aim of determining if compounds that inhibit enzyme activity could also block the parasites' growth and proliferation. Among the compounds active against the cell, there was an excellent correlation between activity inhibiting the *T. brucei* GSK-3 short enzyme and the inhibition of *T. brucei* growth. Thus, there is reasonable genetic and chemical validation of GSK-3 short as a drug target for *T. brucei*. Finally, selective inhibition may be required for therapy targeting the GSK-3 enzyme, and a molecular model of the *T. brucei* GSK-3 short enzyme suggests that compounds that selectively inhibit *T. brucei* GSK-3 short over the human GSK-3 enzymes can be found.

A longitudinal study on the transmission dynamics of human *Leishmania (Leishmania) infantum chagasi* infection in Amazonian Brazil, with special reference to its prevalence and incidence.

Silveira FT, Lainson R, Pereira EA, de Souza AA, Campos MB, Chagas EJ, Gomes CM, Laurenti MD, Corbett CE.

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Parasitol Res. 2008 Oct 21. [Epub ahead of print]



This was a longitudinal study carried out during a period over 2 years with a cohort of 946 individuals of both sexes, aged 1 year and older, from an endemic area of American visceral leishmaniasis (AVL) in Pará State, Brazil. The object was to analyze the transmission dynamics of human *Leishmania* (*Leishmania*) *infantum* *chagasi* infection based principally on the prevalence and incidence. For diagnosis of the infection, the indirect fluorescent antibody test (IFAT) and leishmanin skin test (LST) were performed with amastigote and promastigote antigens of the parasite, respectively. The prevalence by LST (11.2%) was higher ($p < 0.0001$) than that (3.4%) by IFAT, and the combined prevalence by both tests was 12.6%. The incidences by LST were also higher ($p < 0.05$) than those by IFAT at 6 (4.7% x 0.6%), 12 (4.7% x 2.7%), and 24 months (2.9% x 0.3%). Moreover, there were no differences ($p > 0.05$) between the combined incidences by both tests on the same point surveys, 5.2%, 6.3%, and 3.6%. During the study, 12 infected persons showed high IFAT IgG titers with no LST reactions: five children and two adults developed AVL (2,560-10,120), and two children and three adults developed subclinical oligosymptomatic infection (1,280-2,560). The combined tests diagnosed a total of 231 cases of infection leading to an accumulated prevalence of 24.4%.

Hematological profile in pyrexia of unknown origin: role of bone marrow trephine biopsy vis-à-vis aspiration.

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Hematology. 2008 Oct;13(5):307-12.

BACKGROUND: Bone marrow examination, by aspiration and/or trephine biopsy, is an important procedure in arriving at a diagnosis for long-duration febrile illness. The role of trephine biopsy in immunocompromised host, especially HIV-positive patients, has been well studied in the literature. However, its utility in immunocompetent patients is still shrouded by controversy. Thus, the authors attempted to evaluate the utility of marrow aspirate vis-à-vis trephine biopsy in establishing a diagnosis in cases of pyrexia of unknown origin in immunocompetent individuals, along with an analysis of haematological alterations in these patients. **MATERIALS AND METHODS:** Over a period of 8 years, 121 patients with pyrexia of unknown origin underwent both bone marrow aspiration and trephine biopsy as a part of diagnostic work-up. These cases were reviewed for their clinical data and hematological findings, including detailed morphological features in aspiration smears and trephine biopsies. Bone marrow aspiration and biopsy were compared for their diagnostic efficacy in these patients. **RESULTS:** A wide age range (2-65 years) was noted with a slight male predominance (2 : 1). Anemia was the most common feature in peripheral blood findings, seen in 97.5% of patients. Bone marrow aspiration was diagnostic in only 16.5% of cases, which revealed leishmaniasis or pure red cell aplasia. Granulomas were infrequent in marrow aspiration smears, as only two cases (1.6%) showed ill defined epithelioid cell collections. Compared to this, trephine biopsy offered a diagnosis in 76% of the cases. Granulomas were a frequent finding in the trephine biopsy, being present in 70% of the cases included. Additional cases diagnosed on biopsy (over those diagnosed with aspiration smears) included lymphoma, tuberculosis, fungal infection, sarcoidosis and hypocellular marrow. **CONCLUSION:** Bone marrow trephine biopsy is an important adjunct to aspiration in arriving at an aetiological diagnosis of patient with long-duration febrile illness, and should be routinely performed in such cases. The presence of granulomas in trephine biopsy increases the likelihood of an etiologic diagnosis in these patients.

Decreased IL-10 and IL-13 production and increased CD44(hi) T



cell recruitment contribute to Leishmania major immunity induced by non-persistent parasites.

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Eur J Immunol. 2008 Oct 16. [Epub ahead of print]

Leishmaniasis is currently classified as category 1 disease, i.e. emerging and uncontrolled. Since the importance of persistent infection for maintaining an effective long-lasting protective response is controversial, the present study asks whether immunisation with non-persistent parasites leads to protection against Leishmania infection and to the recruitment of T cells of a specific phenotype. Our study shows that vaccination of susceptible BALB/c mice with live Leishmania major phosphomannomutase-deficient parasites, which are avirulent and non-persistent in vivo, leads to protection against infection. Immunisation with phosphomannomutase-deficient parasites neither leads to differences in IFN-gamma, IL-12, IL-4 production nor alters the expression of effector and memory markers, including CD62L, IL-7Ralpha and IL-2Ralpha, when compared with unvaccinated controls. Observed protection is due to the ability of vaccinated animals to suppress early IL-10 and IL-13 production and to recruit a higher number of antigen-experienced CD44(hi)CD4(+) and CD44(hi)CD8(+) T cells into draining LN following infection. Thus, expansion of T-cell numbers and their rapid recruitment to LN upon infection as well as the restriction of IL-13 and IL-10 production leading to high IFN-gamma/IL-10 ratio play an important role in protection against Leishmania affecting the outcome of the disease in favour of the host.

Cutaneous leishmaniasis: progress towards a vaccine.

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Expert Rev Vaccines. 2008 Oct;7(8):1277-87.

Leishmaniasis are vector-borne diseases due to the protozoan parasite Leishmania. Since no prevention method is available and as current therapy is costly, often poorly tolerated and not always efficacious, the development of alternative therapies, including vaccines, constitutes the priority in the fight of Leishmania infection. This review focuses on recent advances in the development of vaccines against leishmaniasis, with emphasis on the cutaneous form. Indeed, the fact that recovery from leishmaniasis is associated with immunity against new infection provides a rational basis for the development of vaccination strategy against infection with Leishmania. Evidence from animal studies demonstrate that protection can be achieved following infection with live-attenuated Leishmania as well as through immunization with purified proteins or DNA vaccines. In addition, recent results have shown that immunization against the saliva of the insect vector could have synergistic effects with conventional vaccination. Finally, vaccination using dendritic cells was recently demonstrated as a possible tool for Leishmania vaccination.

Diffuse skin spread of HIV-associated visceral leishmaniasis: cumbersome diagnostic and therapeutic issues.



Manfredi R, Passarini B, D'Antuono A, Misciali C, Marinacci G, Calza L.

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G Ital Dermatol Venereol. 2008 Oct;143(5):339-46.

An infrequent and atypical case report of HIV-associated visceral leishmaniasis complicated by a diffuse, aspecific maculo-papular cutaneous involvement was characterized by a prolonged course, and a lack of response to repeated attack/maintenance cycles performed with liposomal amphotericin B, despite a satisfactory immune response maintained thanks to a concurrent, potent combination antiretroviral treatment. Only a very prolonged administration of the older i.v. pentamidine isethionate together with oral paromomycin led to a slow, but complete cure of both visceral leishmaniasis and its related skin dissemination, in absence of adverse events and long-term disease relapses.

Differentiation and Gene Flow among European Populations of *Leishmania infantum* MON-1.

Kuhls K, Chicharro C, Cañavate C, Cortes S, Campino L, Haralambous C, Soteriadou K, Pratloug F, Dedet JP, Mauricio I, Miles M, Schaar M, Ochsenreither S, Radtke OA, Schönian G.

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PLoS Negl Trop Dis. 2008 Jul 9;2(7):e261.

BACKGROUND: *Leishmania infantum* is the causative agent of visceral and cutaneous leishmaniasis in the Mediterranean region, South America, and China. MON-1 *L. infantum* is the predominating zymodeme in all endemic regions, both in humans and dogs, the reservoir host. In order to answer important epidemiological questions it is essential to discriminate strains of MON-1. **METHODOLOGY/PRINCIPAL FINDINGS:** We have used a set of 14 microsatellite markers to analyse 141 strains of *L. infantum* mainly from Spain, Portugal, and Greece of which 107 strains were typed by MLEE as MON-1. The highly variable microsatellites have the potential to discriminate MON-1 strains from other *L. infantum* zymodemes and even within MON-1 strains. Model- and distance-based analysis detected a considerable amount of structure within European *L. infantum*. Two major monophyletic groups-MON-1 and non-MON-1-could be distinguished, with non-MON-1 being more polymorphic. Strains of MON-98, 77, and 108 were always part of the MON-1 group. Among MON-1, three geographically determined and genetically differentiated populations could be identified: (1) Greece; (2) Spain islands-Majorca/Ibiza; (3) mainland Portugal/Spain. All four populations showed a predominantly clonal structure; however, there are indications of occasional recombination events and gene flow even between MON-1 and non-MON-1. Sand fly vectors seem to play an important role in sustaining genetic diversity. No correlation was observed between *Leishmania* genotypes, host specificity, and clinical manifestation. In the case of relapse/re-infection, only re-infections by a strain with a different MLMT profile can be unequivocally identified, since not all strains have individual MLMT profiles. **CONCLUSION:** In the present study for the first time several key epidemiological questions could be addressed for the MON-1 zymodeme, because of the high discriminatory power of microsatellite markers, thus creating a basis for further epidemiological investigations.



Political and regulatory

Burden Of Neglected Tropical Diseases In Latin America And Caribbean May Exceed That Of HIV/AIDS, TB And Malaria

ScienceDaily (Sep. 25, 2008)

According to a new analysis, neglected tropical diseases (NTDs) as a group may have surpassed HIV/AIDS, tuberculosis and malaria as the most prevalent infectious diseases in Latin America and the Caribbean.

The analysis found that NTDs are the most common infections of approximately 200 million of the poorest people in the region. They include tens of millions of cases of intestinal worm infections, and almost 10 million cases of Chagas disease, as well as schistosomiasis, trachoma, dengue fever, leishmaniasis, lymphatic filariasis (LF), and onchocerciasis.

NTDs produce extreme poverty by adversely impacting child development, pregnancy outcomes and worker productivity. In some cases in Latin America and the Caribbean, NTDs also represent a living legacy of slavery, because they were first introduced into the region through the global slave trade, and even today they predominantly affect people of African descent and indigenous groups, as well as other vulnerable groups such as women and children.

"Our findings indicate that the combined disease burden of NTDs in Latin America and Caribbean appears to exceed that of HIV/AIDS, tuberculosis, or malaria. Yet, we have the proven effective, low cost tools at our fingertips to eliminate at least three of this devastating diseases," said one of the authors of the analysis Dr. Peter Hotez, M.D., Ph.D., F.A.A.P., President of the Sabin Vaccine Institute, Walter G. Ross Professor and Chair of Microbiology, Immunology, and Tropical Medicine at George Washington University and co-author of the analysis. "It's time to invest in this region and end the needless suffering."

The analysis states that in the coming years, schistosomiasis transmission could be eliminated in the Caribbean, and that transmission of lymphatic filariasis and onchocerciasis could be eliminated in Latin America and the Caribbean with proven successful, cost effective and low-cost treatments. The most burdensome NTDs, such as Chagas disease, intestinal worm infections, and schistosomiasis may first require scale-up of existing resources and/or the development of new tools in order to achieve wider control and/or elimination. Ultimately, successful wide-scale efforts for NTD elimination will require an inter-sectoral approach that bridges public health with social services and environmental interventions.

"Neglected diseases impose a huge burden on developing countries, constituting a serious obstacle for socioeconomic development and quality of life. They mostly affect people living either in shantytowns, indigenous communities or poor rural and agricultural areas," said one of the authors of the analysis Dr. Mirta Roses, Director of Pan American Health Organization (PAHO).

On Friday, September 26 during the closing session of the Clinton Global Initiative Annual Meeting, Dr. Hotez will discuss this new analysis as well as recent news from the NTD community: on Monday, UK government officials announced that they will be contributing £50 million over the next five years toward the control and elimination of NTDs, including Guinea worm. In addition, the World Health Organization announced that in 2007 alone, 546 million of the world's poorest people received



treatment for lymphatic filariasis at a cost of 10 cents per person, enabling them to live healthier more productive lives.

Throughout the CGI Annual Meeting this week, the Global Network will also call upon CGI participants to invest in efforts to help the people of Haiti who were devastated by Hurricane Ike by combating NTDs like lymphatic filariasis and soil-transmitted intestinal worms that are widespread in the country. After rainfall-induced disasters like Hurricane Ike, respiratory and intestinal infections usually increase and there is increased risk of breeding of the mosquito that transmits lymphatic filariasis in Haiti. While around three million people will be treated in Haiti in 2008 for lymphatic filariasis, additional resources are needed to step up and maintain treatment coverage in Haiti with its population of 9.5 million people, particularly in the wake of the Hurricane.



R&D in Africa — a new network says it can be done

Study outlines the gaps and opportunities

TDR press release 9 October 2008

Abuja, Nigeria -- African-based researchers and institutions have the capacity to develop new drugs and diagnostic tools for diseases affecting Africans, but are hampered by a lack of coordination and funding to the continent. At the conclusion of the first meeting of the new African Network for Drugs and Diagnostics Innovation (ANDI) in Abuja, Nigeria, participants from 21 countries committed to a network approach to increase the ability of African countries to bring forward new medicines and diagnostics.

The Vice-President of Nigeria, Dr. Goodluck Jonathan, stated that "Nigeria is in full support for ANDI. We understand the pivotal role of R&D to national development". Nigeria's minister of health, the chair of the Nigerian senate committee for health, and the minister of state for the federal capital territory of Nigeria, attended.

Communicable diseases such as tuberculosis, HIV and malaria account for about 60% of the mortality and morbidity in Africa. There are pockets of product discovery and development activities in Africa, but no one African country or institution has demonstrated the capacity to move from basic research to the commercialization of a new drug.

His Excellency Tom Mboya-Okeyo, Ambassador of Kenya in Geneva, who led the concluding session, said, "ANDI is a valuable niche in the global strategy". He was referring to the efforts by the World Health Organization to develop a plan to increase R&D and intellectual property management across the globe.

A new study mapping the R&D capacity and gaps was released at the meeting. Conducted by the Special Programme for Research and Training in Tropical Diseases (TDR), in collaboration with African institutions, it concluded that there is enough capacity on the continent to build from, with significant potential for increasing the number and quality of new tools developed, as well as providing economic development to the countries. It also highlighted the need for a systematic evaluation and validation of the biological activities of traditional medicines.

This initial report of the 4 UN organizations sponsoring TDR (UNICEF, UNDP, the World Bank and WHO), along with the commitment from the African countries, will be used to build support and collaboration with health experts, high level national officials, business leaders, international organizations, donors and policy makers. The goal is to develop locally sustainable health research and development, coordinated through an African-based and led organization. TDR Director Robert Ridley said, "ANDI will help connect people and give African scientists the opportunities to lead and manage this research and development. We believe that this approach will lead to long-term sustainability and success".

Founding meeting of the African Network for Drugs and Diagnostics Innovation (ANDI)

6 – 8 October 2008

Abuja, Nigeria "Creating a sustainable platform for R&D innovation in Africa"



ANDI objectives

ANDI aims to promote and sustain African-led R&D innovation through the discovery, development and delivery of affordable new tools, including those based on natural products and traditional medicines. ANDI will also support capacity and infrastructure development in Africa.

It is envisaged that ANDI will be a coordinated and results-driven effort that will leverage and build on existing activities in Africa. It will have strong elements of public-private partnerships. It will generate and manage intellectual property and explore innovative mechanisms that will encourage and reward local innovation. ANDI will source, manage and grant funding to support network activities, while proactively establishing sustainable funding mechanisms for its operations.

Meeting objectives and expected outcomes

- Review the landscape for product R&D in Africa: identify and share lessons on various product R&D activities and highlight gaps and new opportunities.
- Discuss the operational framework of ANDI: scope of product R&D activities, deliverables, stakeholders and possible initial structure of this proposed African network.
- Produce a publication that builds on the ANDI concept paper and the R&D landscape in Africa.
- Discuss and agree on the next steps for ANDI: creation of an interim Secretariat for ANDI; development of a strategy, business plan and implementation plan; and future process for deciding a permanent Secretariat and headquarters; resource mobilization and future meetings of ANDI.

To read more, please visit

<http://www.who.int/tdr/news-events/events/tdr/pdf/ANDI-programme.pdf>

<http://www.who.int/tdr/news-events/news/pdf/ANDI-minutes.pdf>

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