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ABSTRACT BOOK

"There will be epidemics..."

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CellMask Green. To understand the replicative capability of *T. cruzi*, we have employed a fluorescent flou-488 marker to identify incorporation of a collection of 6 thymidine analogues into *T. cruzi* DNA, visualised using click chemistry. Analogues were co-incubated with intracellular *T. cruzi* parasites over time to identify 5-ethynyl-2′-deoxyuridine (EdU) as the most effectively incorporated into parasite DNA. Identification of DNA synthesis by EdU has previously been used to label replicating mammalian cells. EdU was employed to develop a novel image-based assay to assess the activity of compounds against parasite replication. The effects of the drugs used to treat Chagas disease on *T. cruzi* replication were investigated, in addition to posaconazole, which causes a sub-efficacious effect against the parasite *in vitro* and has failed clinical trials to treat Chagas disease. Active compounds against *T. cruzi* from the Medicines for Malaria Venture (MMV) Pathogen Box were also assessed for their effect upon parasite replication. This methodology provides new insights into the MOA and static/cidal nature of the action of these compounds and drugs and is a promising tool to aid the prioritisation of compounds in drug discovery.

1400

MOLECULAR CHARACTERIZATION OF *LEISHMANIA* DNA FROM ARCHIVED GIEMSA-STAINED SLIDES OF PATIENTS FROM SALTA, ARGENTINA

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Cutaneous leishmaniasis is endemic in the northwestern province of Salta in Argentina. *Leishmania* DNA from Giemsa-stained slides of up to 12 years in storage of patients from a University based reference center in Oran, Salta was characterized through PCR-Restriction Fragment Length Polymorphism (RFLP). One hundred smears from individuals with suspicious lesions and epidemiologic exposure plus microbiologic confirmation through positive microscopy were analyzed. The samples had been originally taken 2, 3, 5, 6 and 12 years prior to performing PCR-RFLP (20 samples from each year) and were maintained at room temperature in a tropical environment. All the cases were classified in a semiquantitative scale for amastigote density, and Leishmanin skin test (LST) results were included. DNA extraction was done applying lysis buffer with proteinase K, and then DNA was amplified with ribosomal internal transcribed spacer 1(ITS1) primers. PCR products were digested with HaeIII enzyme. All PCR positive smears (74/100) belonged to *Viannia* subgenus. A statistically significant directly proportional relationship between semiquantitative microscopy and PCR results was detected ($p < 0.001$). All patients had LST positive results (induration ≥ 5 mm), and the smears of those with positive but smaller induration (LST < 19 mm) had a higher proportion of positive PCR results. This study determined that smear age did not affect PCR positivity, which allows retrospective analyzes and suggests smears might be useful for molecular complementary diagnosis. Since *Leishmania* (*Viannia*) *braziliensis* is the main circulating species in the study area, determining *Viannia* subgenus in all analyzed samples confirms previous findings. PCR positivity showed statistically significant differences according to semiquantitative microscopy, highlighting the importance of parasite burden in the diagnostic sensitivity of the method. Considering that smears of patients with smaller LST induration were more positive in PCR, a negative smear from patients with positive LST response, but < 19 mm, could actually represent a false negative smear result.

1401

PREVALENCE AND ASSOCIATION OF *LEISHMANIA* RNA VIRUS-1 (LRV-1) IN SEVERE AND NON-SEVERE PHENOTYPES OF AMERICAN TEGUMENTARY LEISHMANIASIS FROM PERU

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American tegumentary leishmaniasis (ATL) comprises a discrete set of clinical presentations of leishmaniasis endemic to Latin America. *Leishmania* RNA virus-1 (LRV-1) is a double stranded RNA virus identified in 20-25% of the *Leishmania Viannia* complex, and is believed to be a predictive biomarker of severe ATL. Our objective was to determine the baseline prevalence of LRV-1 and associations with clinical phenotypes in ATL patients from Peru. Banked clinical isolates of patients residing in or traveling to Peru between 2006 and 2016 were species identified by PCR, RFLP analysis, and Sanger sequencing, and screened for LRV-1 by real-time PCR. Patient isolates were stratified according to clinical phenotype: localized cutaneous leishmaniasis (LCL) was defined as "non-severe" ATL, whereas "severe ATL" was defined as mucosal or mucocutaneous leishmaniasis (ML/MCL); erythematous, purulent, or painful ulcers and/or lymphatic involvement (inflammatory ulcers); or multifocal/disseminated ulcers (greater than 4 in greater than 2 anatomic sites). Of 132 patients enrolled, 64 (48%) and 68 (52%) of ATL cases had the severe and non-severe phenotypes, respectively. Twenty-seven (42%) of 64 severe ATL cases and 29 (43%) of 68 non-severe ATL cases were positive for LRV-1, respectively ($p=1.00$). The severe phenotype was over-represented among older patients (median age 41.5 years vs. 29 years in non-severe ATL, $p=0.0002$), while the median age did not differ by LRV-1 status ($p=0.27$). A trend in disease severity was observed by sex, whereby 62 (59%) males had a severe phenotype compared to 10 (37%) females ($p=0.05$). No difference in LRV-1 status was observed by sex ($p=0.50$). Twenty-three (41%) of 56 quantified LRV-1 positive patients revealed greater LRV-1 copy numbers in those with ML/MCL compared to those with all forms of CL ($p=0.04$). Our findings suggest age as a contributing factor to disease severity. Although an association between LRV-1 status was clinical phenotype was not demonstrated, LRV-1 copy number was higher in patients with ML/MCL. Therefore, the role of LRV-1 viral burden in severe disease requires further exploration.

1402

TRANSCRIPTOME ANALYSIS OF SPLENIC ASPIRATES IN HUMAN VISCERAL LEISHMANIASIS REVEALS IMPAIRED TISSUE ORGANIZATION/REPAIR AND INHIBITED PARASITE KILLING

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Changes in the spleen environment that contribute to the pathogenesis of human visceral leishmaniais (VL) are under explored. We performed transcriptional profiling (RNAseq) on the remnants of diagnostic splenic aspirates from 8 Kenyan patients with visceral leishmaniasis. Differentially expressed genes were identified by comparison to splenic RNA from normal controls obtained through commercial sources. A total of 2,749 differentially expressed genes were identified with a cutoff of as 2-fold change and false discovery rate (FDR) ≤0.05. Functional analysis was done with the Ingenuity Pathways Analysis (IPA) software. We found that half of the top 10 down-regulated canonical pathways were related to cell assembly and organization with decreased expression of actin, integrins