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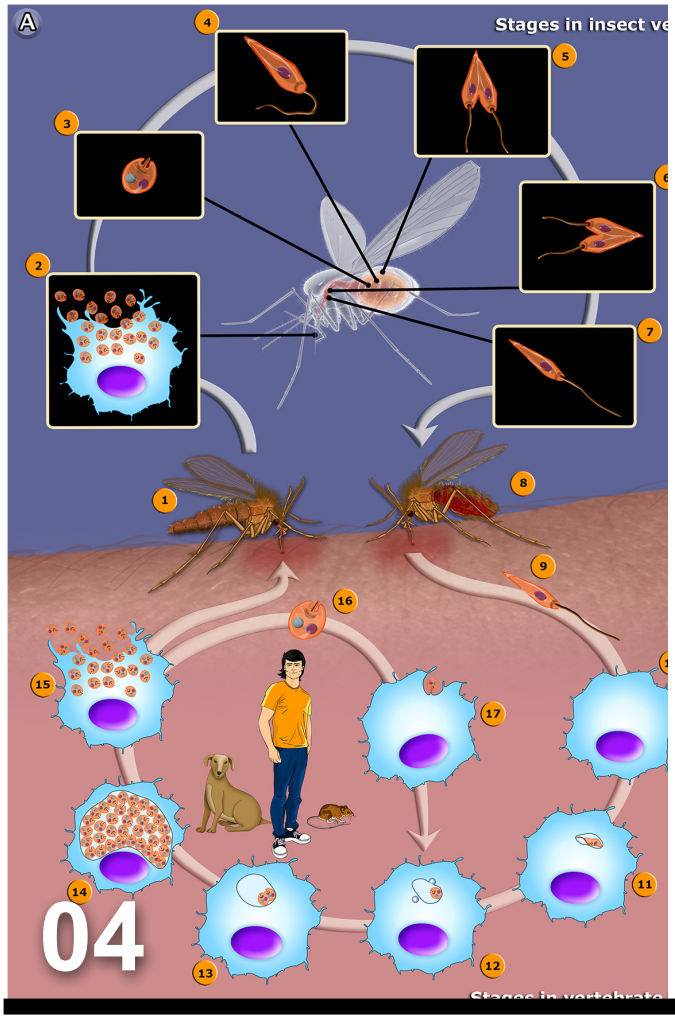
Portada



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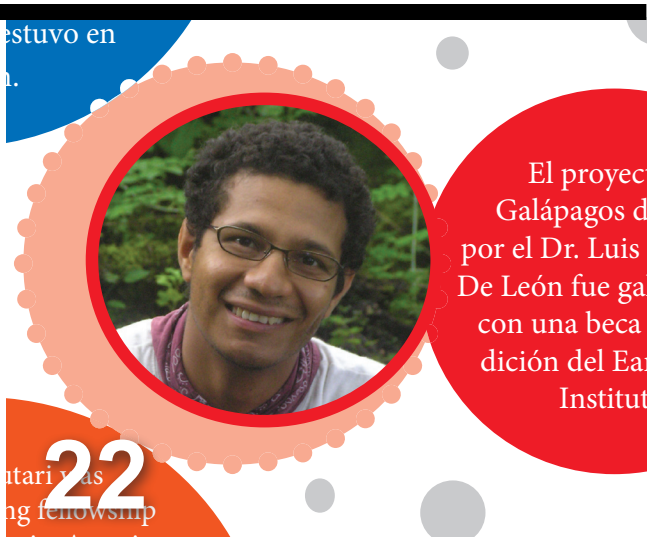


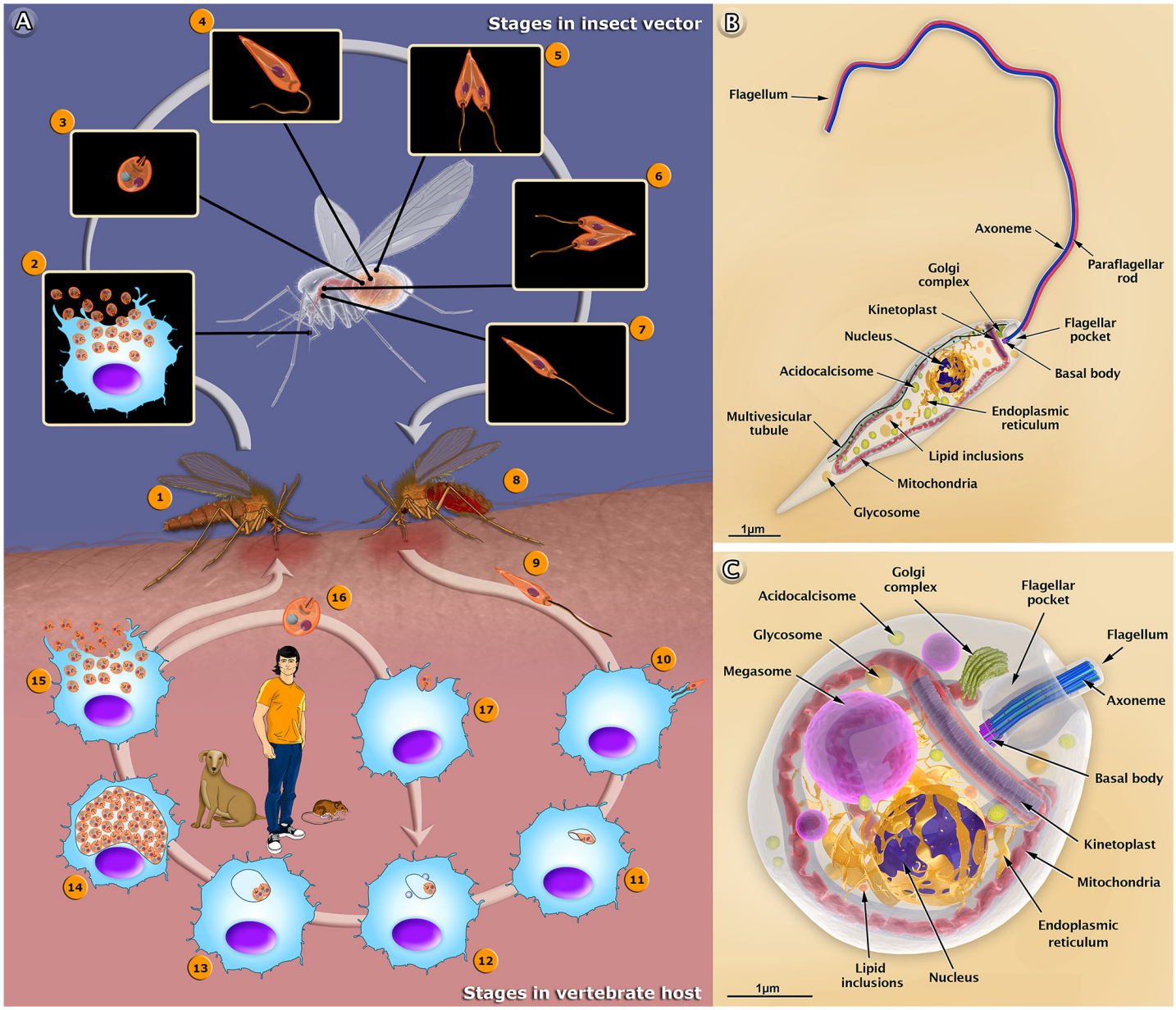
En la Portada / *Dr. Ricardo Lleonart, investigador en INDICASAT AIP.* / Fotografía y Edición por Rita Marissa Giovani.

Desarrollo y validación de una nueva herramienta molecular para el estudio del parásito *Leishmania panamensis*.

Carlos M. Restrepo y Ricardo Lleonart.
INDICASAT-AIP.

Los protozoos hemoflagelados del género Leishmania (Kinetoplastida, Trypanosomatidae) son los agentes etiológicos de la leishmaniasis, una enfermedad cuyas manifestaciones cutánea y mucocutánea son causantes de una alta morbilidad en países endémicos. Por otro lado, la forma visceral puede llegar a ser letal de no ser tratada, e incluso con acceso a tratamiento los índices de letalidad oscilan entre el 10 y 20% (1). Estimaciones recientes apuntan a una incidencia anual de entre 200,000 y 400,000 casos de leishmaniasis visceral; y 700,000 a 1.2 millones de casos de leishmaniasis cutánea (1). Sin embargo, hay que tomar en consideración que estas estimaciones son bastante conservadoras ya que existe un alto grado de sub-reporte. La incidencia de la leishmaniasis en Panamá se ha incrementado en los últimos años, hecho probablemente relacionado con la creciente urbanización de las áreas rurales y selváticas. Cada año se diagnostican aproximadamente 3,000 nuevos casos, estimándose un sub-reporte del 50% (2).

El control de la leishmaniasis se ha centrado en la quimioterapia y el control de vectores debido a la ausencia de una vacuna efectiva (3). Por más de cincuenta años, la primera línea de tratamiento contra la leishmaniasis han sido compuestos antimoniales pentavalentes. Sin embargo, estos compuestos han mostrado efectos colaterales bastante severos como son pancreatitis, toxicidad cardíaca y toxicidad renal. Adicionalmente, en algunas regiones como el subcontinente indio estas drogas se han vuelto obsoletas debido a la aparición de cepas multi-resistentes que han elevado las tasas de fallo del tratamiento hasta 65% (4). La Miltefosina (MIL) ha sido desde 2005 el medicamento oral de primera línea para el tratamiento de la leishmaniasis visceral en el subcontinente indio, pero ha demostrado baja eficacia en otras manifestaciones clínicas. A parte de su teratogenicidad, la mayor desventaja de esta droga es su larga vida media, lo que ha provocado el aumento de los casos de fallo de tratamiento debido a la aparición de resistencia (5). El antibiótico anfotericina B ha demostrado ser altamente



efectivo en el tratamiento de leishmaniasis visceral causada por cepas de *Leishmania* resistentes a los antimoniales pentavalentes, sin embargo su alta toxicidad hace necesaria la hospitalización del paciente durante las 4 semanas que dura el tratamiento. El fallo en el tratamiento utilizando anfotericina B es muy raro, excepto en el caso de los pacientes coinfectados con VIH (6). La actividad anti-*Leishmania* del aminoglicósido paromomicina ha sido evaluada durante varios años demostrando una eficacia del 95%, sin embargo debido a la falta de financiamiento los ensayos clínicos se encuentran todavía en fase IV, y es poco probable que se convierta en una monoterapia contra la leishmaniasis debido al riesgo de surgimiento de resistencia (7). A pesar de que la terapia combinada contra *Leishmania* debería reducir la aparición de resistencia y la duración del tratamiento, trabajos recientes muestran la posibilidad de que a corto plazo se desarrollen cepas doble-resistentes (8).

La resistencia a drogas por parte de los parásitos de *Leishmania* puede ser intrínseca, producto de características bioquímicas propias del parásito que les permiten sobrevivir a las drogas; o adquirida, producto de la exposición a la droga. Muchas de las observaciones clínicas y de ensayos de susceptibilidad *in vitro* han confirmado diferencias significativas en la resistencia intrínseca entre especies (9). Estas observaciones refuerzan el hecho de que la diversidad genética

entre especies y dentro de las especies tiene que ser considerada en cualquier estudio de resistencia a drogas. Además, los resultados obtenidos con una especie en particular no pueden ser transferidos a otra especie sin estudios previos.

La variabilidad genética en términos generales se mide en base a la divergencia de secuencias. La secuenciación de los genomas de varias especies de *Leishmania* ha mostrado un alto nivel de sintenia y la existencia de pocos genes especie-específicos en contraste con su alto grado de diversidad fenotípica (10). En esta especie, una gran fuente de variabilidad genética es el polimorfismo estructural de su genoma, que incluye números de copia variables de elementos repetitivos, e incluso cromosomas completos. La expansión o contracción de familias de genes y otros tipos de repeticiones en tándem origina polimorfismos de talla de los fragmentos de ADN. Además, los parásitos de *Leishmania* son capaces de generar amplificación de determinadas áreas de su genoma para producir episomas que pueden contener uno o más genes.

A pesar de que por largo tiempo se consideró que *Leishmania* era un género de parásitos diploides, estudios genómicos y de cariotipo recientes han demostrado que la aneuploidía es una característica constitutiva de estos parásitos, lo cual contribuye aún más a su variabilidad genética. Los cambios en el número cromosómico se pueden observar incluso entre individuos de un mismo cultivo (mosaicismo) (11). Aunque en muchos organismos estas variaciones cromosómicas tienen un efecto negativo en la viabilidad de los individuos, bajo determinadas condiciones adversas estas variantes pueden proveerle al parásito una ventaja adaptativa que puede convertirse en evolución a cepas resistentes a drogas. Las variaciones en el número de copias de los genes pueden atribuírsele a la ausencia de mecanismos regulatorios de la transcripción. Los genes de estos parásitos están organizados en unidades policistrónicas unidireccionales, y la regulación de la expresión genética ocurre al nivel de degradación de ARN mensajero, regulación de la traducción y/o degradación de proteínas (12).
Por lo tanto, los estudios dirigidos a la identificación de polimorfismos genéticos a nivel de secuencia, variaciones en el número de copias y cambios de la ploidía son de gran importancia para encontrar el vínculo con cambios fenotípicos de interés clínico, como por ejemplo resistencia a drogas. El conocimiento de los mecanismos genéticos que originan la resistencia a drogas puede ser de gran utilidad en el mejoramiento de los tratamientos anti-*Leishmania*, así como guiar el diseño racional de drogas menos tóxicas y vacunas.

El estudio del genoma del parásito se ha intentado empleando diferentes tipos de marcadores moleculares, entre los que se pueden mencionar la secuenciación completa o parcial de varios genes, los microsatélites, y el RFLP (del inglés "restriction fragment length polymorphism"). Cada tipo de marcador molecular permite el estudio detallado de regiones particulares del genoma y la elucidación de diversos aspectos de la biología y epidemiología del parásito. Conocer cómo se distribuye y evoluciona la variabilidad genética de un parásito es una información de gran importancia para el diseño y manejo de drogas.
Nuestro laboratorio en INDICASAT-AIP, ubicado en el Centro de Biología Molecular y Celular de Enfermedades, ha acometido la ejecución de un proyecto para el estudio de la variabilidad genética de los parásitos del género *Leishmania* aislados de pacientes panameños de leishmaniasis cutánea. Para este propósito hemos decidido emplear un marcador genético que no ha sido empleado frecuentemente en este parásito, conocido por el acrónimo AFLP (del inglés "amplified fragment length polymorphisms"). El AFLP tiene la ventaja de permitir el análisis simultáneo de cientos a miles de sitios del genoma, detectando de manera eficiente variabilidad genética sin necesidad de tener un conocimiento detallado de la secuencia de los genes involucrados en estos sitios (13).

Todos los especímenes provenientes de pacientes de leishmaniasis cutánea resultaron infectados con la especie *Leishmania panamensis*, lo cual coincide con hallazgos anteriores de otros autores y que permite concluir que esta es la especie predominante en la zona central del país (14).
Nuestros resultados de la aplicación del AFLP a muestras locales del parásito han permitido demostrar que esta metodología permite detectar gran cantidad de sitios polimórficos en su genoma, de manera

eficiente y reproducible, con niveles de error experimental bajo y semejante a los anteriormente reportados por otros autores para otras especies (14). Algunos pares de cebadores lograron detectar hasta un 89% de fragmentos polimórficos, lo cual revela que las poblaciones locales del parásito son mucho más variables de lo que se pensaba anteriormente. Una proporción importante de los fragmentos variables detectados fueron específicos para determinados grupos, bien para la especie *Leishmania panamensis*, o para las especies del subgénero *Viannia*, o para especies del subgénero *Leishmania*, con lo cual se abre la posibilidad de convertir estos fragmentos a marcadores dominantes con capacidad diagnóstica.
Los datos provenientes de AFLP en varias especies de *Leishmania*, tanto aislados locales como cepas de referencia provenientes de varias colecciones internacionales, nos han permitido también la reconstrucción de filogenias que son congruentes con la historia evolutiva aceptada para el género (Figura 1), con lo cual se puede concluir que los marcadores de AFLP son útiles para análisis genéticos tanto intra- como interespecíficos. Aunque rutinariamente hemos utilizado un panel de 13 pares de cebadores para obtener los perfiles de AFLP, resultó de gran relevancia el hecho de que algunos pares individuales de cebadores fueron capaces de reproducir árboles filogenéticos con la misma topología que la filogenia aceptada hasta el momento para el género *Leishmania*, lo cual permitiría hacer futuros análisis genéticos del parásito a un menor costo.

Los resultados de análisis estadísticos multivariados, específicamente el análisis de coordenadas principales, confirmaron los resultados de los análisis filogenéticos y además revelaron que la nueva herramienta molecular es capaz de discernir entre especies extremadamente similares como la *Leishmania panamensis* y la *Leishmania guyanensis* (Figura 2).

Estos resultados constituyen la primera caracterización genética de alta resolución en aislados de parásitos provenientes de pacientes panameños de leishmaniasis cutánea. El panel descrito de AFLP permitirá asociar

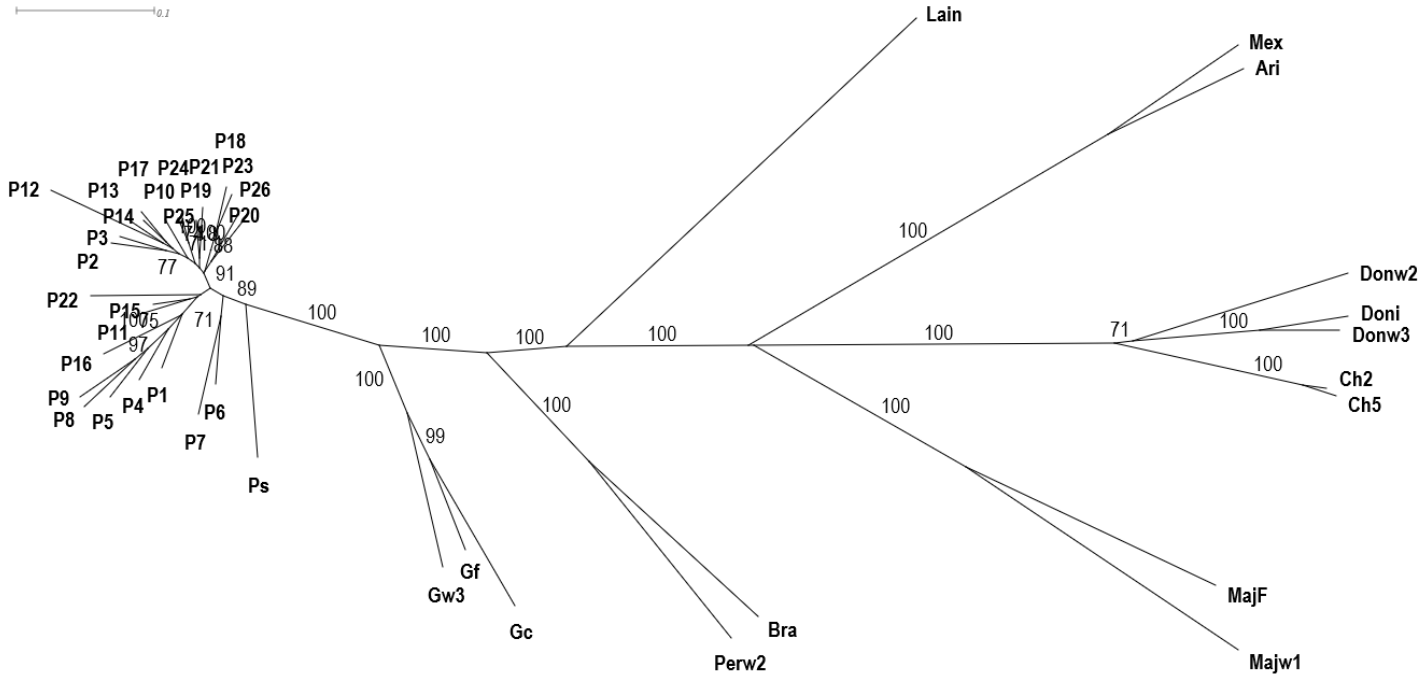


Figura 1

alelos polimórficos con determinados fenotipos de interés en el parásito, como por ejemplo, resistencia a fármacos, capacidad para desarrollar diversas presentaciones clínicas, etc. Adicionalmente, nuestros datos permiten validar una nueva herramienta para el análisis genético del parásito causante de la leishmaniasis cutánea en Panamá, demostrándose su utilidad para posteriores estudios sobre su biología, genética poblacional, epidemiología molecular y taxonomía.

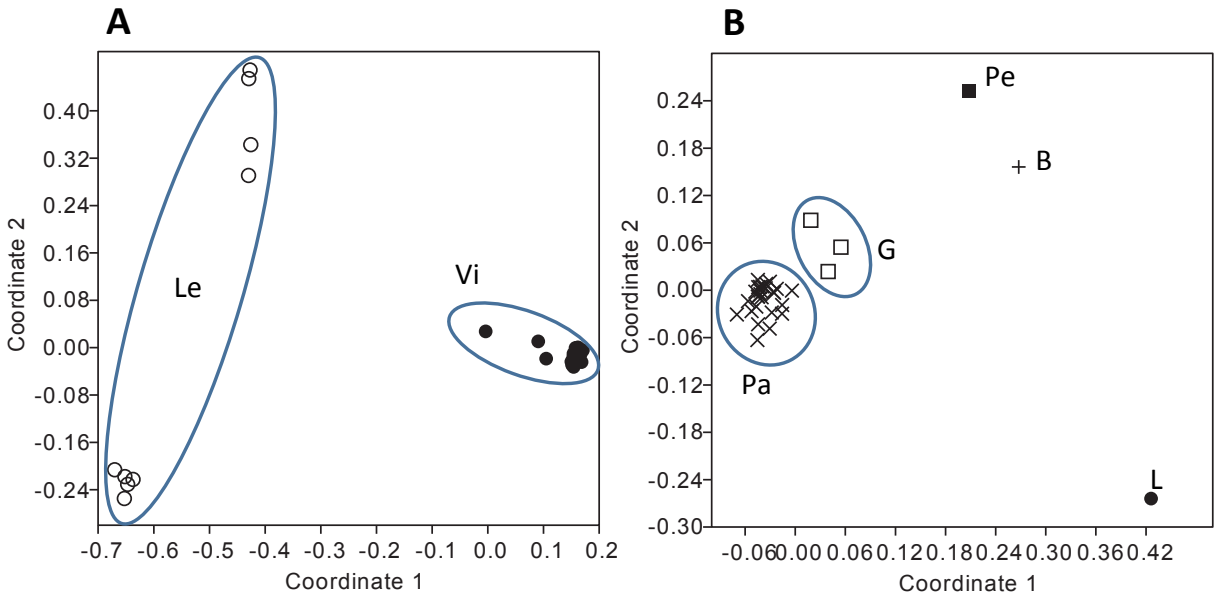


Figura 2

Referencias

1. Alvar J et al. (2012) Leishmaniasis worldwide and global estimates of its incidence. PLoS ONE 7, e35671. doi: 10.1371/journal.pone.0035671.
2. Vásquez A et al. (1998) Informe final: Estudios sobre la epidemiología de la leishmaniasis en la parte occidental de la República de Panamá. Panamá: Instituto Conmemorativo Gorgas de Estudio de la Salud, MINSA.
3. Singh N et al. (2012) Leishmaniasis: current status of available drugs and new potential drug targets. Asian Pacific Journal of Tropical Medicine 5, 485–497. doi: 10.1016/S1995-7645(12) 60084-4.
4. Sundar S et al. (2000) Failure of pentavalent antimony in visceral leishmaniasis in India: report from the center of the Indian epidemic. Clinical Infectious Diseases 31, 1104–1107. doi: 10.1086/318121.
5. Olliaro PL et al. (2005) Treatment options for visceral leishmaniasis: a systematic review of clinical studies done in India, 1980-2004. Lancet Infectious Diseases 5, 763–774. doi: 10.1016/S1473-3099(05)70296-6.
6. Berg M et al. (2013) Post-Genomic approaches to tackle drug resistance in Leishmania. Parasitology, 140, 1492–1505. doi:10.1017/S0031182013000140.
7. Hendrickx S et al. (2012) Experimental induction of Paromomycin resistance in antimony-resistant strains of *L. donovani*: outcome dependent on in vitro selection protocol. PLoS Neglected Tropical Diseases 6, e1644. doi: 10.1371/journal.pntd.0001664.
8. García-Hernández R et al (2012) *Leishmania donovani* develops resistance to drug combinations. PLOS Neglected Tropical Diseases 6, e1974. doi: 10.1371/journal.pntd.0001974.
9. Yardley V et al. (2005) The sensitivity of clinical isolates of *Leishmania* from Peru and Nepal to miltefosine. American Journal of Tropical Medicine and Hygiene 73, 272–275.
10. Peacock CS et al. (2007) Comparative genomic analysis of *three Leishmania* species that cause diverse human disease. Nature Genetics 39, 839–847. doi: 10.1038/ng2053.
11. Sterkers Y et al. (2012) Novel insights into genome plasticity in Eukaryotes: mosaic aneuploidy in *Leishmania*. Molecular Microbiology 86, 15–23. doi:10.1111/j.1365-2958.2012.08185.x.
12. Clayton C et al. (2007) Post-transcriptional regulation of gene expression in trypanosomes and leishmanias. Molecular and Biochemical Parasitology 156, 93–101. doi: 10.1016/j.molbiopara. 2007.07.007.
13. Restrepo CM et al. (2011) Amplified Fragment Length Polymorphisms Reveals High Intraspecific Variability in Field Isolates of *Leishmania panamensis*. Current Trends in Biotechnology and Pharmacy 5 (2): 1183-1192.
14. Restrepo CM et al. (2013) AFLP Polymorphisms Allow High Resolution Genetic Analysis of American Tegumentary Leishmaniasis Agents Circulating in Panama and Other Members of the *Leishmania* Genus. PLoS ONE 8(9): e73177. doi:10.1371/journal.pone.0073177

Figura 1. Resultado de los análisis de agrupamiento usando el algoritmo Bio Neighbor Joining en matrices transformadas según distancias de Jaccard. Los valores de soporte de cada rama fueron calculados a partir de 10,000 permutaciones, mostrándose solo si fueron mayores de 70%.

Figura 2: Análisis de coordenadas principales (PCOA) mostrando los grupos bien diferenciados de especímenes. Panel A: considerando todos los especímenes. Panel B: considerando solamente los especímenes del subgénero *Viannia*. Le: subgénero *Leishmania*; Vi: subgénero *Viannia*; Pa: *L. panamensis*; G: *L. guyanensis*; Pe: *L. peruviana*; B: *L. braziliensis*; L: *L. lainsoni.*

Best Teacher Award

to Prof. K.R.S. Sambasiva Rao

Prof. K.R.S. Sambasiva Rao, and Professor of Biotechnology, Acharya Nagarjuna University, India and Adjunct faculty of INDICASAT-AIP, was conferred with Best Teacher Award by Andhra Pradesh government in India on 5th September, 2013 for his distinguished service to the academics in the state of Andhra Pradesh in India. Prof.Rao is a distinguished educationist, scientist and administrator, having over 30 years of research and teaching experience. He did his Masters from Bhopal University, PhD in Zoology from S.V. University, India in Zoology. He started his career as a Research Associate at Acharya Nagarjuna University, India, and became Assistant Professor in the year 1988. Prof.Rao always keep himself learning in multidisciplinary areas with versatile research ability, he did another PhD in the field of Pharmaceutical Science from Andhra University, India in 2011 and DSc (Biotechnology) from Berhampur University, India in 2012. Prof.Rao continued his academic pursuit in doing MBA in Clinical Pharmacology and Research from ISMT, Bangalore and MSc Information Technology to improve his academic skills in the areas of Clinical Research and Bioinformatics areas.

Prof.Sambasiva Rao held several important academic positions at various Universities and organizations, as Chairman, PG BOS in Biotechnology and Zoology, Acharya Nagarjuna University, Member, PG Board of Studies in Biotechnology, SVIMS, Tirupathi, Member, PG Board of Studies in Biotechnology, Rayalaseema University, Kurnool; Member, PG Board of Studies in Biotechnology, Berhampur University, Orissa; Member, PG BOS in Biotechnology, Dravidian University, Kuppam; Member, PG Board of Studies in Biotechnology, SK University, Anantapur; Member, PG Board of

Studies in Animal Biotechnology, SV University, Tirupathi; Chairman, PG Board of Studies in Zoology, VS University, Nellore; Chairman, PG Board of Studies in Biotechnology, MG University, Nalgonda; Member, PG Board of Studies in Biotechnology, VS University, Nellore, India; Member, UG BOS in Bioinformatics, Acharya Nagarjuna University; Member, BOS in Engineering Biotechnology, Acharya Nagarjuna University. Prof. Rao is member of several professional bodies like, General Secretary and Editor of Current Trends in Biotechnology and Pharmacy; Vice-President of Indian Society of Comparative Animal Physiology (ISCAP); Vice-President, Akshara, Scientific Voluntary Organization; Member, Scientific Advisory Committee, Nireekshana (NGO); Associate Editor of International Journal of Pharmacology and Biological Sciences; Member Editor of Journal of Applied Biosciences, Member Editorial Board of Research Journal of Biological Science, Bioscan, International Journal of Pharmagenesis and The Journal of Genetics. He has been reviewer of various scientific journals, Applied Biochemistry and Biotechnology, Process Biochemistry, Bioresource Technology, African Journal of Biotechnology and Iranian Journal of Biotechnology.

Prof.Rao has more than 33 years of teaching and research experience in the fields of E nvironmental Toxicology & Physiology, Aquaculture Biotechnology, Molecular Biology and Genetic Engineering, Microbial Technology and Fermentation Technology. Prof.Rao has exceptional research credentials, published 142 research publications in peer-reviewed national and international journals, 23 general scientific articles; 67 presentations, 3 patents filed, 3 gene bank submission; 25 books and book chapters. He had successfully guided 18 Ph.Ds and 20 M.Phil students and supervised several M.Sc. and M.Tech students. Prof. Rao has successfully completed 8 research projects funded by various funding agencies.

Prof.Rao worked as a visiting scientist at Dept. of Biochemistry, Emory University, Atlanta, USA during 1999 to 2000, and also at Molecular Wood Biotechnology, Georg-Augusta Gottingen University, Germany during May to August, 2004, further at Virginia Commonwealth University, Richmond, USA during April-June, 2005. During the stay abroad, Prof.Rao worked on various advanced areas of research, such as technology relating to DNA sequencing and micro array research; cloning and expression of laccase genes, signal transduction mechanisms. Prof.Rao is an adjunct faculty at INDICASAT, from 2010 to till date.

As a scientist and academician, Prof.Rao has received several national and international awards and fellowships. These include; Talented Biotechnologist Award at ISCEPH, University of Colombo, Srilanka in 2011, Best Research Article Award from Intas Polivet published in 2004, Lion's International President Appreciation Award for 2007-08 from Lions Club International, USA. He was elected fellow of several organisation; Association of Biotechnology and Pharmacy, Andhra Pradesh Academy of Sciences, Society for Regenerative Medicine and Society for Applied Biotechnologists. Recognizing his excellent contribution to the field of research and academics, he was recently awarded with prestigious AP State government Best Teacher Award for the year 2013.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12
PANAMA

AFLP Polymorphisms Allow High Resolution Genetic Analysis of American Tegumentary Leishmaniasis Agents Circulating in Panama and other Members of the *Leishmania* Genus.

Carlos M. Restrepo, Carolina De La Guardia, Octavio E. Sousa, José E. Calzada, Patricia L. Fernández, Ricardo Lleonart.

Abstract

American Tegumentary Leishmaniasis is caused by parasites of the genus *Leishmania*, and causes significant health problems throughout the Americas. In Panama, *Leishmania* parasites are endemic, causing thousands of new cases every year, mostly of the cutaneous form. In the last years, the burden of the disease has increased, coincident with increasing disturbances in its natural sylvatic environments. The study of genetic variation in parasites is important for a better understanding of the biology, population genetics, and ultimately the evolution and epidemiology of these organisms. Very few attempts have been made to characterize genetic polymorphisms of parasites isolated from Panamanian patients of cutaneous leishmaniasis. Here we present data on the genetic variability of local isolates of *Leishmania*, as well as specimens from several other species, by means of Amplified Fragment Length Polymorphisms (AFLP), a technique seldom used to study genetic makeup of parasites. We demonstrate that this technique allows detection of very high levels of genetic variability in local isolates of *Leishmania panamensis* in a highly reproducible manner. The analysis of AFLP fingerprints generated by unique selective primer combinations in *L. panamensis* suggests a predominant clonal mode of reproduction. Using fluorescently labeled primers, many taxon-specific fragments were identified which may show potential as species diagnostic fragments. The AFLP permitted a high resolution genetic analysis of the *Leishmania* genus, clearly separating certain groups among *L. panamensis* specimens and highly related species such as *L. panamensis* and *L. guyanensis*. The phylogenetic networks reconstructed from our AFLP data are congruent with established taxonomy for the genus *Leishmania*, even when using single selective primer combinations. Results of this study demonstrate that AFLP polymorphisms can be informative for genetic characterization in *Leishmania* parasites, at both intra and inter-specific levels. **Carlos M. Restrepo, Carolina De La Guardia, Octavio E. Sousa, José E. Calzada, Patricia L. Fernández, Ricardo Lleonart. Plos One, 2013, In Press.**

In vitro evidence that an aqueous extract of *Centella asiatica* modulates α-synuclein aggregation dynamics

Rubén Berrocal, Vasudevaraju P, Indi SS, Sambasiva Rao KRS and Rao KS.

Abstract

α-Synuclein aggregation is one of the major etiological factors implicated in Parkinson's disease (PD). The prevention of aggregation of α-Synuclein is a potential therapeutic intervention for preventing PD. The discovery of natural products as alternative drugs to treat PD and related disorders is current trend. The aqueous extract of *Centella asiatica* (CA) is traditionally used as a brain tonic and CA is known to improve cognition and memory. There are limited data on the role of CA in modulating amyloid beta levels in the brain and in amyloid beta aggregation. Our study focuses on CA as a modulator of the α-Synuclein aggregation pattern *in vitro.* Our investigation is focused on: (i) whether the CA leaf aqueous extract prevents the formation of aggregates from monomers (Phase I: α-Synuclein + extract co–incubation); (ii) whether the CA aqueous extract prevents the formation of fibrils from oligomers (Phase II - extract added after oligomers formation) and (iii) whether the CA aqueous extract disintegrates the pre-formed fibrils (Phase III - extract added to mature fibrils and incubated for 9 days). The aggregation kinetics are studied using a thioflavin-T assay, and Circular Dichroism and Transmission Electron Microscopy (TEM). The results showed that the CA aqueous extract completely inhibited the α-Synuclein aggregation from monomers. Further, CA extract significantly inhibited the formation of oligomer aggregates and favored the disintegration of the preformed fibrils. The study provides an insight in finding new natural product for PD future therapeutics.

Rubén Berrocal, Vasudevaraju P, Indi SS, Sambasiva Rao KRS and Rao KS. Journal of Alzheimer's Disease (2013-in press).

Seasonal pattern of avian Plasmodium-infected mosquitoes and implications for parasite transmission in central Panama

Jose R. Loaiza, Matthew J. Miller.

Abstract

Aedeomyia squamipennis and Culex (Melanoconion) ocossa, two ubiquitous Neotropical mosquito species, are likely involved in the transmission of several bird pathogens in Gamboa, central Panama. However, knowledge on their eco-epidemiological profiles is still incomplete. Our goal in this study was to investigate temporal trends of vector density and their relationship with avian plasmodia prevalence. This information is central to identifying the risk posed by each vector species to the avian community locally. We found that A. squamipennis maintains stable population size across climatic seasons and thus maybe a more efficient vector of avian malaria than C. ocossa. In contrast, C. ocossa, which undergoes considerable population expansion in the rainy season and contraction in the dry season, is likely only an important avian malaria vector during part of the year. This is consistent with the larger number of parasite isolations and Plasmodium cyt b lineages recovered from A. squamipennis than from C. ocossa and might be explained by marked differences in their seasonality and host-feeding preferences. More Plasmodium PCR testing in mosquito communities from other areas of Panama might reveal additional vectors of avian plasmodia**. Jose R. Loaiza1, Matthew J. Miller. Parasitology Research 112(11):3743-51.**

The lipid content and fatty acid composition of four eastern central Pacific native fish species

Enrique Murillo, K.S. Rao, Armando A. Durant.

Abstract

Fish is an Important source of nutritious n-3 fatty acids, which are necessary for the prevention of cardiovascular and neurological diseases. The lipid content and fatty acid composition of economically important fishes from the eastern central Pacific, namely, *Garanx caballus, Cynoscion phoxocephalus, Lutjanus guttatus and Scomberomorus sierra, were determined.* Seasonal variations in their n-3 fatty acid composition were investigated as well. The lipid content of all these fish species was less than 4% by weight. In general, the studied species have moderate proportions of n-3 fatty acids. *C. caballus* was the fish species with the highest concentration of eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) (898mg/100g) followed by *S. sierra* (596 mg/100 g), *C. phoxocephalus* (421 mg/100g) and *L. guttatus* (342 mg/100g). The n-3/n-6 ratio of all the species studied ranged from 4.86 to 8.12. Results of this study indicate that all these fish species are highly recommended as a source of low calorie food that can meet the n-3 fatty acid dietary requirements of the Panamanian population.

Enrique Murillo, K.S. Rao, Armando A. Durant. Journal of Food Composition and Analysis, in press (2013).

Tuberculosis challenges the economic growth of Panama

Musharaf Tarajia, Amador Goodridge.

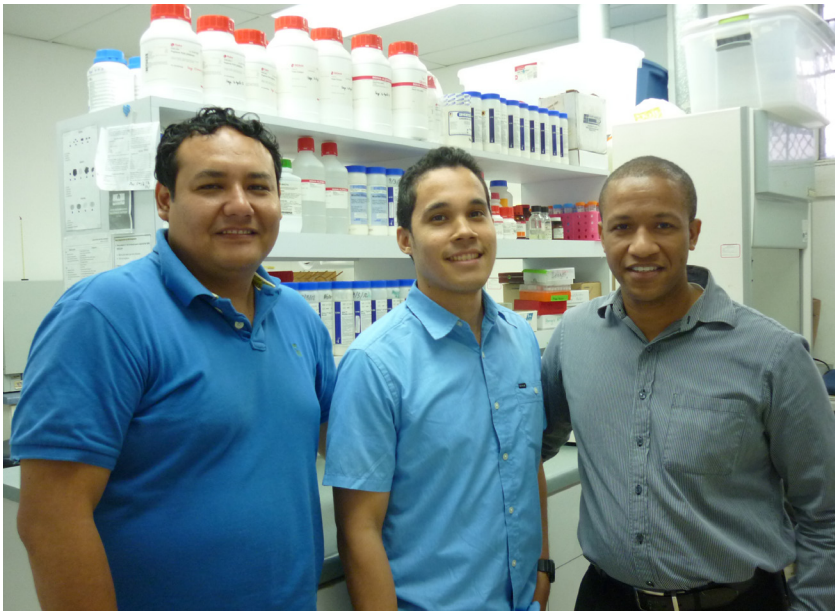
Abstract

Tuberculosis is a disease traditionally associated with inequity, and wise investment of economic resources is considered a critical factor for its control. Recently, Panama has secured its status as an upper-middle income country with robust economic growth. However, the prioritization of resources for tuberculosis control remains a major challenge. In the present notes from the field, we highlight areas that urgently require decision to effectively reduce tuberculosis burden to minimal levels. Our conclusions suggest the need for fund allocations and a multidisciplinary approach for prompt diagnosis, therapy assurance and permanent workforce complemented with applied and operational research, development and innovation.

Musharaf Tarajia, Amador Goodridge. International Journal of Tuberculosis and Lung Diseases, 2013, in press.

High clustering rates of multidrug-resistant Mycobacterium tuberculosis genotypes in Panama

Samantha Rosas, Jaime Bravo, Franklin Gonzalez, Nora de Moreno, Joel Sánchez, Ronnie G. Gavilan, Amador Goodridge.



Background: Tuberculosis continues to be one of the leading causes of death worldwide and in the American region. Although multidrug-resistant tuberculosis (MDR-TB) remains a threat to TB control in Panama, few studies have focused in typing MDR-TB strains. The aim of our study was to characterize MDR Mycobacterium tuberculosis clinical isolates using PCR-based genetic markers.
Methods: From 2002 to 2004, a total of 231 Mycobacterium tuberculosis isolates from TB cases country-wide were screened for antibiotic resistance, and MDR isolates were further genotyped by double repetitive element PCR (DRE-PCR), (GTG)5-PCR and spoligotyping.
Results: A total of 37 isolates (0.85%) were resistant to both isoniazid (INH) and rifampicin (RIF). Among these 37 isolates, only two (5.4%) were resistant to all five drugs tested. Dual genotyping using DRE-PCR and (GTG)5-PCR of MDR Mycobacterium tuberculosis isolates revealed eight clusters comprising 82.9% of the MDR strain collection, and six isolates (17.1%) showed unique fingerprints. The spoligotyping of MDR-TB clinical isolates identified 68% as members of the 42 (LAM9) family genotype.
Conclusion: Our findings suggest that MDR Mycobacterium tuberculosis is highly clustered in Panama's metropolitan area corresponding to Panama City and Colon City, and our study reveals the genotype distribution across the country. **Samantha Rosas, Jaime Bravo, Franklin Gonzalez, Nora de Moreno, Joel Sánchez, Ronnie G. Gavilan, Amador Goodridge. BMC Infectious Diseases, 2013, in press.**

Santacruzamate A, a Potent and Selective Histone Deacetylase Inhibitor from the Panamanian Marine Cyanobacterium cf. *Symploca* sp.

Christopher M. Pavlik, Christina Y. B. Wong, Sophia Ononye, Dioxelis D. Lopez, Niclas Engene, Kerry L. McPhail, William H. Gerwick, and Marcy J. Balunas

Abstract

A dark brown tuft-forming cyanobacterium, morphologically resembling the genus Symploca, was collected during an expedition to the Coiba National Park, a UNESCO World Heritage Site on the Pacific coast of Panama. Phylogenetic analysis of its 16S rRNA gene sequence indicated that it is 4.5% divergent from the type strain for Symploca and thus is likely a new genus. Fractionation of the crude extract led to the isolation of a new cytotoxin, designated santacruzamate A (1), which has several structural features in common with suberoylanilide hydroxamic acid [(2), SAHA, trade name Vorinostat], a clinically approved histone deacetylase (HDAC) inhibitor used to treat refractory cutaneous T-cell lymphoma. Recognition of the structural similarly of 1 and SAHA led to the characterization of santacruzamate A as a picomolar level selective inhibitor of HDAC2, a Class I HDAC, with relatively little inhibition of HDAC4 or HDAC6, both Class II HDACs. As a result, chemical syntheses of santacruzamate A as well as a structurally intriguing hybrid molecule, which blends aspects of both agents (1 and 2), were achieved and evaluated for their HDAC activity and specificity.

Christopher M. Pavlik, Christina Y. B. Wong, Sophia Ononye, Dioxelis D. Lopez, Niclas Engene, Kerry L. McPhail, William H. Gerwick, and Marcy J. Balunas.
Journal of Natural Products, 2013, In Press.

Comparative study on anti-oxidant and anti-inflammatory activities of *Caesalpinia crista* and *Centella asiatica* leaf extracts

Ramesh BN, Girish TK, Raghavendra RH, Naidu KA, Prasada Rao UJS, Rao KS.

Abstract

Amyloidosis, oxidative stress and inflammation have been strongly implicated in neurodegenerative disorders like Alzheimer's disease. Traditionally, *C. crista* and *C. asiatica* leaf extracts are used to treat brain related diseases in India. *C. crista* is used as a mental relaxant drink as well as to treat inflammatory diseases, while *C. asiatica* reported to be used to enhance memory and to treat dementia. The present study is aimed to understand the anti-oxidant and anti-inflammatory potential of *C. asiatica* and *C. crista* leaf extracts. The results showed that *C. asiatica* and *C. crista* antioxidant properties and inhibited 5-lipoxygenase (anti-inflammatory) in a dose dependent manner. However, leaf extracts of *C. crista* had better antioxidant and anti-inflammatory activity compared to *C. asiatica*. The better activity of *C. crista* is attributed to high gallic acid and ferulic acid compared to *C. asiatica*. Thus, the leaf extract of *C. crista* can be used as a potential therapeutic molecule for Alzheimer's disease.

Ramesh BN, Girish TK, Raghavendra RH, Naidu KA, Prasada Rao UJS, Rao KS, Journal of Pharmacy and Bioallied Sciences (In press 2014)

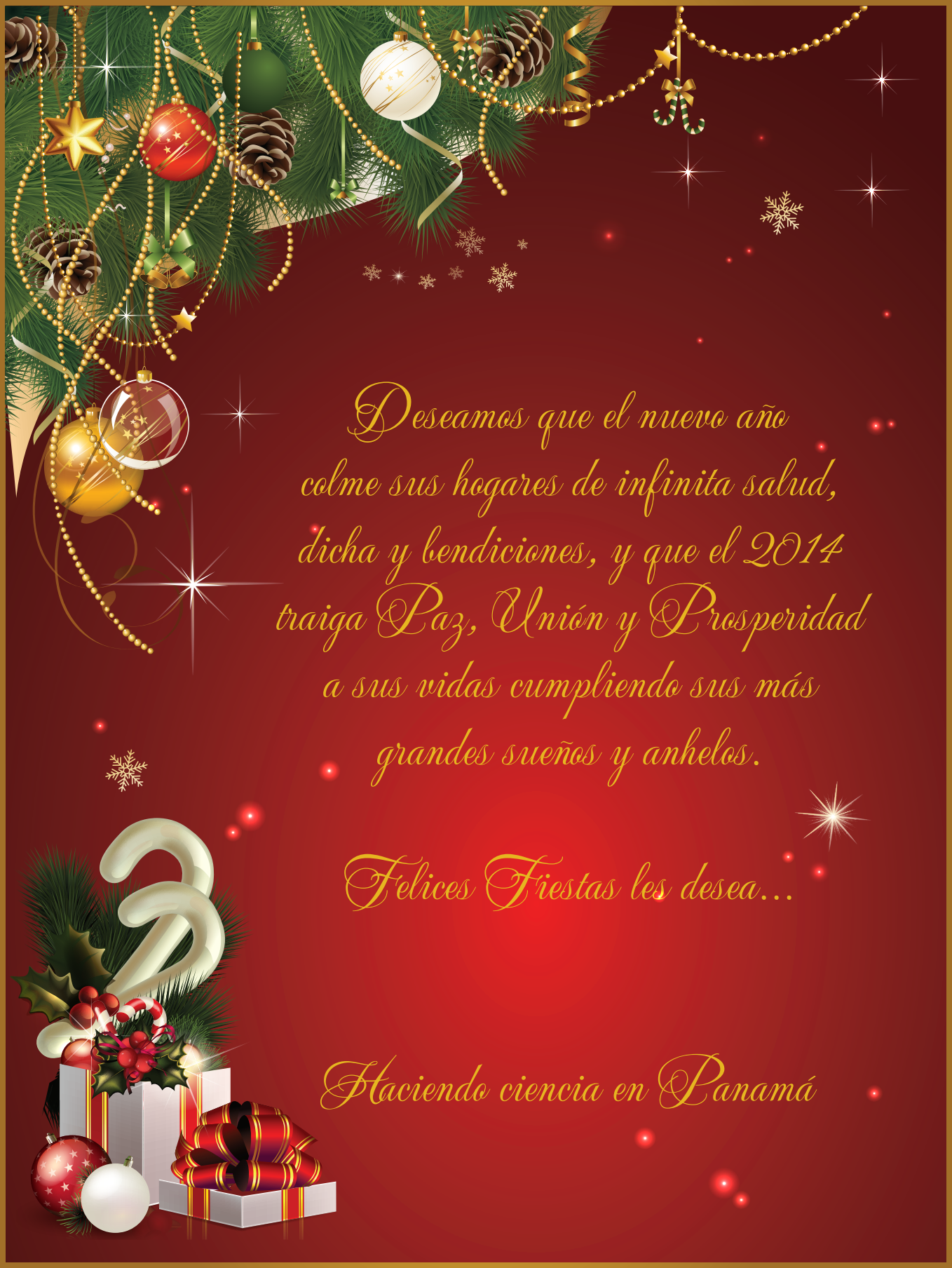
Prudent inquilines and proactive hosts: behavioral dynamics between an ant social parasite, Megalomyrmex symmetochus and its fungus-growing ant host, Sericomyrmex amabilis

G. Bruner, W. T. Wcislo, and Hermógenes Fernández-Marín.

Abstract

Ant social parasites evolve adaptive relationships with their hosts. Theoretically coevolution predicts strong selection to maximize fitness of the parasite that minimizes costs to its host, which potentially leads to the evolution of benign interactions. We studied the demographic and behavioral traits of the ant social parasite Megalomyrmex symmetochus (Solenopsidini), an agro-predator that feeds on larvae and fungal garden products of their host, Sericomyrmex amabilis (Attini). Based on demographic data from 15 parasitized colonies, the proportion of parasitic workers to those of the host is 1:2. Moreover, defensive prophylactic behaviors observed during infections with Metarhizium brunneum, a generalist entomopathogen, and Escovopsis, a specialized fungal-garden parasite, showed that Sericomyrmex amabilis works extensively to remove and control fungal infections, in contrast to M. symmetochus. M. symmetochus, however, performed intraspecific-allogrooming during infections with Escovopsis and M. brunneum, suggesting that they may recognize fungal pathogens and indirectly limit dispersion of spores. Our results indicate that M. symmetochus did not have a strong role in maintaining a hygienic nest. Key words: amelioration, coevolution, symbiosis, xenobiosis, social parasitism

G. Bruner, W. T. Wcislo and H. Fernández-Marín. Prudent inquilines and proactive hosts: behavioral dynamics between an ant social parasite, Megalomyrmex symmetochus and its fungus-growing ant host, Sericomyrmex amabilis. Insectes Sociaux 2014, In press.


Deseamos que el nuevo año
colme sus hogares de infinita salud,
dicha y bendiciones, y que el 2014
traiga Paz, Unión y Prosperidad
a sus vidas cumpliendo sus más
grandes sueños y anhelos.
Felices Fiestas les desea…
Haciendo ciencia en Panamá

Felicidades

La estudiante de doctorado Erika Guerrero estará trabajando en el proyecto entre INDICASAT y UTMB, Galveston en TDP43 en ALS el cual es financiado por la MDA por los próximos tres años. La Srta. Guerrero ha estado involucrada en la generación de los datos preliminares, mientras estuvo en Galveston.

El proyecto de Galápagos dirigido por el Dr. Luis Fernando De León fue galardonado con una beca de expedición del Earthwatch Instituto.

Larissa C. Dutari was awarded a travelling fellowship grant to attend the Latin-American Training Workshop on Molecular Epidemiology Applied to Infectious Diseases. This event is organized by the Institute of Tropical Medicine (ITM), Antwerp, Belgium and will be held at the Institute of Tropical Medicine "Alexander von Humboldt" (IMTAvH), Lima, Peru, from November the 25th to December the 6th of 2013.
30-abril 4, 2014.

La estudiante Nadir Planes participó del 8th LFD Workshop in Advanced Fluorescence Imaging and Dynamics dictado en la Universidad de California, Irvine desde el 21 de octubre al 25 de octubre 2012. Aplicó a la convocatoria internacional publica y recibió el student weiver (descuento de estudiante) para presentar un poster. El objetivo del taller fue dar a conocer los avances de los nuevos conceptos de las técnicas de fluorescencia de imagines e instrumentos. Recibió entrenamiento sobre las aplicaciones del software para el análisis de los datos junto con entrenamiento en los laboratorios.

El Dr. Jose R. Loaiza was honored with The Academy of Sciences for the Developing World (TWAS) and the Panamanian Association for the Advancement of Science (APANAC) 2013 Award for Young Investigator.

La Fundación Bill y Melinda Gates le otorgó a la estudiante Ciara Ordoñez el premio Global Travel Health. que se celebrará en el Keystone Resort, Keystone, Colorado, EE.UU. en marzo 30-abril 4, 2014.

La Dra. Catherina Caballero George, ha sido invitada a participar del "14vo TWAS-ROLAC Conferencia de Jóvenes Científicos" que se llevará a cabo en Cancún, México, a partir de diciembre 5 al 6 de 2013 en una asociación TWAS - ICSU ORPALC.

India has approved the Line of Credit (LOC) for $10 million dollars to SENACYT to develop Centre for Biodiversity and Drug Discovery at INDICASAT-AIP in PRISM in collaboration with India. LOC was recently approved by Cabinet on 26 Nov, 2013. The Scientists thank the Cabinet for their support for Science in Panama.

Mr. Alexander Hernandez and Mrs. Claudia Guerrero from SENACYT support the presentation during Cabinet under the leadership of National Secretary of Science, Technology and Innovation of Panama, Dr. Ruben Berrocal and thus making Panama as International hub for Science.

MEF team headed by Minister Mr. Frank de Lima and Vice Minister Gladys Cedeño Urrutia did great a job in supporting the future of science in Panama.

Team INDICASAT-AIP and SENACYT thank H.E. Yogeshwar Varma, Indian Ambassador and his team for their support in making the dream of developing this center and to foster collaboration between India and Panama to come true.

Mr. Alexander Hernandez

Dr. Rubén Berrocal

Mr. Frank de Lima

H.E. Yogeshwar Varma

Vice Minister Gladys Cedeño Urrutia

Mrs. Claudia Guerrero

Le damos la bienvenida al Nuevo Grupo de Estudiantes de PhD 2013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Conferencias

Dr. Dixit, Vicepresidente de Biocon expuso charla "New innovations in Biotechnology in Biocon- Biosimilars" el 15 de noviembre en las instalaciones de INDICASAT AIP.

MELO DONATION PHASE II BRAIN GRANT


INDICASAT-AIP, Methodist
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November


ACYT
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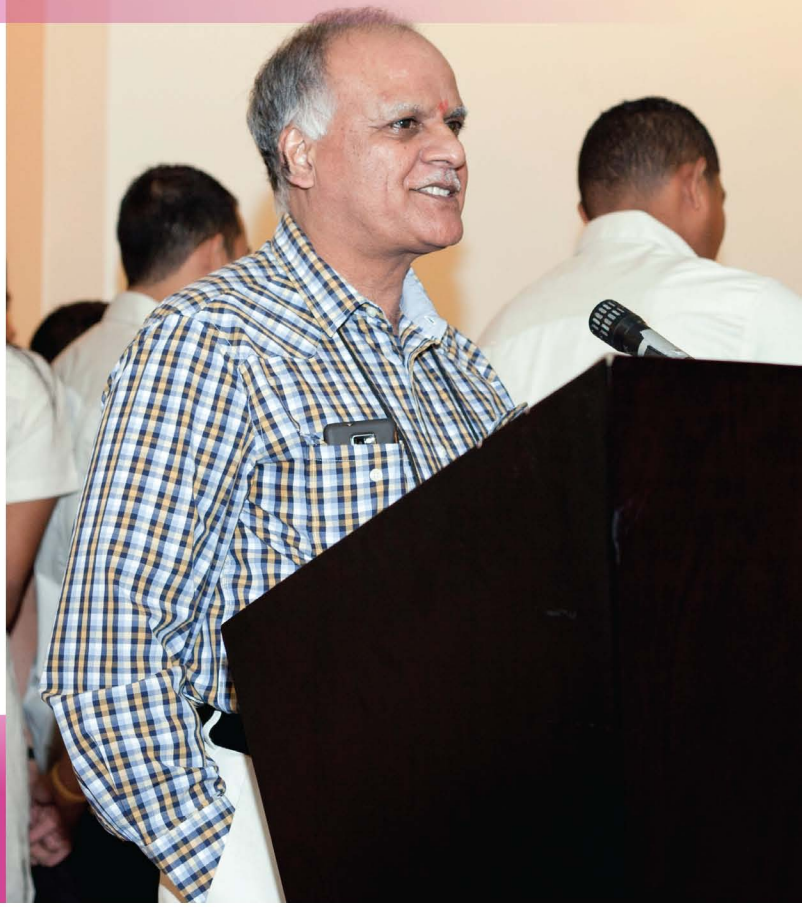
INDICASAT AIP FOUNDATION DAY
October 31, 2013

Dr. Rubén Berrocal highlighting Panama as an International Science Hub in the near future.



Dr. Ricardo Lleonart received leadership Award for his team work on the Leishmania Genome Research.

Dr. Marcelino Gutiérrez received leadership Award for his team work on Natural Product chemistry - new discoveries.

Mr. Carlos Restrepo received Award for his paper published in PLoS ONE.

Mr. Edgar Marín received Award for his paper published in International Journal of Nano - Medicine.

Dr. Rubén Berrocal received Award for his paper published in Journal of Alzheimer's Disease.


MODRIC

Vistazo


PREMIO
PREMIO

Visitas Recientes

Grupo de intercambio del Lafayette College, Pensilvania, EEUU, visitaron las instalaciones de INDICASAT AIP y discutieron el efecto de las costumbres, la cultura y como esto influye en la toma de decisiones.

Visitas Recientes

Los ganadores de la feria científica visitan las instalaciones de INDICASAT AIP.
Colegio San Felix, Provincia de Chiriquí, modalidad Video “Conservación del Ambiente”

Visitas Recientes

Visitas Recientes

La estudiante de medicina de la Universidad Latina, Sandra Trejos visitó las instalaciones de INDICASAT AIP junto con el Dr. Armando Durant, quien le mostró las investigaciones que se llevan a cabo y las diversas áreas que desarrollamos.


SENACYT
SECRETARÍA NACIONAL DE CIENCIA, TECNOLOGÍA E INNOVACIÓN
PANAMA AS AN INTERNATIONAL SCIENCE HUB
INDICASAT AIP