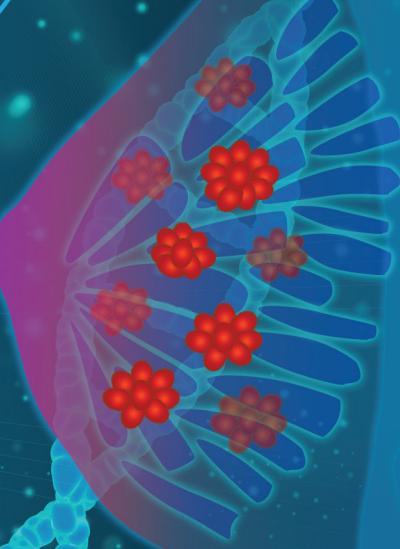


Making discoveries in Panama

INDICAT times

CARDIOMIOPATÍA DILATADA

En Pacientes con Mutación
en el gen *LMNA* Inducida por
el Tratamiento con Antraciclinas



CONTENIDO - CONTENT

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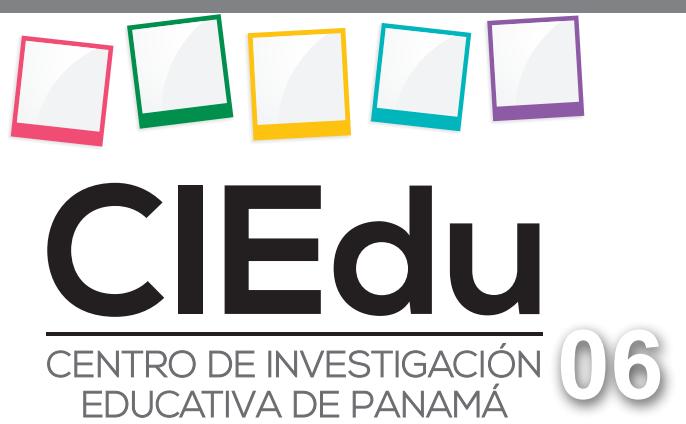
ES UNA REPRESENTACIÓN GRÁFICA DEL ARTÍCULO "CARDIOMIOPATÍA DILATADA EN PACIENTES CON MUTACIÓN EN EL GEN LMNA INDUCIDA POR EL TRATAMIENTO CON ANTRACICLINAS". / IT IS A GRAPHIC REPRESENTATION OF THE ARTICLE "DILATED CARDIOMYOPATHY IN PATIENTS WITH MUTATION IN THE LMNA GENE INDUCED BY ANTHRACYCLINE TREATMENT".

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DESARROLLO DE CARDIOMIOPATÍA DILATADA EN PACIENTES CON MUTACIÓN EN EL GEN LMNA INDUCIDA POR EL TRATAMIENTO CON ANTRACICLINAS - 4



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Desarrollo de

Cardiomiopatía Dilatada

en Pacientes con Mutación en el gen *LMNA* Inducida por el Tratamiento con Antraciclinas

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Las enfermedades cardiovasculares y el cáncer constituyen las dos principales causas de morbilidad y mortalidad en la República de Panamá, y a nivel mundial. Las investigaciones científicas en este campo son altamente necesarias a fin de entender los mecanismos bioquímicos y moleculares inherentes a estas patologías, lo cual permitirá determinar nuevas vías de tratamiento y cura de estas afecciones.

Las antraciclinas son sustancias químicas altamente efectivas utilizadas como agentes antineoplásicos, prescritas como medicamentos para el tratamiento de diversos tipos de cánceres, como lo es el cáncer de mama. Entre otros mecanismos, estas sustancias inhiben a la enzima topoisomerasa II impidiendo la replicación y transcripción del ADN en células

cancerígenas, lo cual limita ostensivamente la proliferación de estas células. No obstante, el uso de antraciclinas conlleva un riesgo de cardiotoxicidad en pacientes en tratamiento. Los distintos factores de riesgo descritos para la cardiotoxicidad inducida por el tratamiento con antraciclinas incluyen la edad, el sexo, la dosis, las infecciones, entre otras. Sin embargo, el estudio genético previo al uso de estas sustancias en pacientes no es considerado como un factor de riesgo en la actualidad.

Las investigaciones realizadas por nuestro equipo de investigación en Medicina Molecular aplicada a las enfermedades cardiovasculares, logró determinar por primera vez la existencia de una potencial predisposición genética a la inducción de cardiomiopatía dilatada debido al uso de antraciclinas en pacientes con cáncer de mama portadores de una mutación en el gen *LMNA*. El gen *LMNA* contiene la información genética conducente a la síntesis de la proteína lámina A/C. Estas proteínas estructurales filamentosas son constituyentes esenciales de la envoltura nuclear, las cuales interactúan tanto con la cromatina y proteínas integrales de la membrana nuclear.

La cardiomiopatía dilatada es una enfermedad que lleva al alargamiento y debilidad del músculo cardíaco, lo cual conduce a que el corazón no pueda bombear una cantidad adecua-

da de sangre al cuerpo llevando a la afectación de diferentes órganos que lo constituyen, como por ejemplo los pulmones. Esta patología lleva al desarrollo de arritmias, edemas, coágulos sanguíneos, o en el peor de los casos conducir a una muerte súbita.

En continuación a nuestros esfuerzos vinculados a esta investigación, en la actualidad estamos desarrollando estudios en torno a los mecanismos bioquímicos inherentes a la alteración en la proteína lámina A/C que predisponen a la cardiomiopatía dilatada en pacientes que reciben terapias cardiotóxicas.

Los resultados de este estudio Cardioncológico han sido publicados en la revista BMC Cardiovascular Disorders. Esta investigación fue realizada en INDICASAT AIP, con la colaboración de investigadores de la Universidad de Panamá, El Instituto Conmemorativo Gorgas, Houston Methodist Hospital (USA), The University of Texas Health Science Center (USA) y Georgia Institute of Technology (USA).

Agradecemos profundamente la participación de los pacientes que colaboraron en estas investigaciones, y a la Secretaría Nacional de Ciencia, Tecnología e Innovación (SENACYT) por haber financiado este proyecto de investigación.

Development of

Dilated Cardiomyopathy

in Patients with Mutation in the *LMNA* gene Induced by Anthracycline Treatment



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Cardiovascular diseases and cancer are the leading causes of morbidity and mortality in Panama, and at the global level. Scientific research on these diseases aimed at understanding the biochemical and molecular mechanisms of these pathologies, is highly necessary in order to determine new

strategies for their treatment and cure.

Anthracyclines are very effective antineoplastic agents prescribed for the treatment of different types of breast cancer and many others. The current assumptions indicate that anthracycline-induced cardiomyopathy is the result of complex multifactorial processes affecting cardiomyocytes such as through interactions with topoisomerase II enzyme, inhibiting DNA replication and transcription in cancer cells, this affecting the proliferation of these cells. However, the use of anthracycline carries a significant risk of cardiotoxicity in patients under treatment. The anthracyclines-induced cardiotoxicity risk factors include age, sex, cumulative and individual anthracyclines dose, infections, etc. Nevertheless, the genetic predisposition is not considered currently among the causes for development of cardiotoxicity.

The scientific investigations performed by our research group on Molecular Medicine and Cardiovascular Diseases, identifies for the first time the existence of a potential genetic predisposition for anthracyclines-induced dilated cardiomyopathy in breast cancer patients carrying a mutation in the *LMNA* gene. This gene holds the genetic information for the synthesis of lamin A/C protein. These structural proteins are important constituents of the nuclear membrane, and they interact with chromatin and membrane

proteins.

Dilated cardiomyopathy is a pathology that affects the heart muscle, causing that the heart to enable pumping blood efficiently. Symptoms of this disease include, legs and feet edema, chest pain, shortness of breath, fatigue, and arrhythmias.

Our continued efforts to undertake research with positive impact in this field, currently are aimed at furthering studies for understanding the biochemical mechanisms of dilated cardiomyopathy associated with the cardiotoxic therapies.

The results of this Cardioncology study were published in the journal BMC Cardiovascular Disorders. This research work was carried out at INDICASAT AIP, with the collaboration of researchers from the University of Panama, Gorgas Memorial Institute for Health Studies, Houston Methodist Hospital, The University of Texas Health Science Center (USA) y Georgia Institute of Technology (USA).

We are deeply indebted to the patients who participated in this study, and the National Secretary of Science and Technology of Panama (SENACYT) for funding this research project.

CIEdu y la Importancia de la Investigación para Mejorar la Educación en Panamá



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cundaria, menos a la post-secundaria, y aunque hay muchas universidades en Panamá ni una sale entre las mejores instituciones en ningún ranking regional o internacional. En adición, la inversión nacional en la investigación es extremadamente baja. La república dirige entre 0.1 y 0.2 por ciento de la producción interna bruta (PIB) a las actividades de investigación (UIS, 2018), o aproximadamente 20 veces menos que un país del OCDE típicamente invierte.

Un artículo publicado el año pasado por la Universidad Católica Santa María la Antigua (USMA) después de la conferencia internacional de LAURDS de la Unión Europea sobre *Perspectivas sobre la Cultura, Estrategias de Investigación y Estudios Doctorales en Latinoamérica* llevada a cabo en julio 2018, explora este dilema más profundamente y concluye que, en general, no hay una preparación adecuadamente para el futuro la juventud en Panamá. Esto amenaza las posibilidades de las personas para lograr el éxito, y también al desarrollo nacional y al crecimiento económico. El artículo argumenta que hay una necesidad urgente para invertir en la investigación y la educación superior como medida de enfrentar este problema y cita varias entidades

locales que están actualmente trabajando en actividades de investigación (Svenson, Bennett, De Gracia, De Leon, Psychoyos y Rao, 2018). Uno de los grupos mencionados es el recién lanzado proyecto público-privado Centro de Investigación Educativa (CIEdu).

CIEdu busca dirigirse a esta contradicción del éxito económico y la lucha educativa con un enfoque en la investigación educativa. Hay bastante literatura académica que indica que la educación es clave para avanzar el crecimiento y el desarrollo de una sociedad (ver como ejemplos OCDE/Hanushek y Woessmann, 2015 y los informes del UNESCO, 2019). Además, estudios muestran que la investigación es clave para avanzar la educación (ver como ejemplos Raudenbush, 2008 y Towne, Wise y Winters, T. (eds), 2004). Esto es el principio base detrás de CIEdu: que la investigación educativa sea crucial para mejorar los sistemas educativos y para hacerlos más equitativos. La misión de CIEdu es fomentar el estudio de la educación en Panamá y utilizarlo para influir la política y la práctica, y así elevar la educación de todos los niveles. CIEdu es el primer “think tank” (centro de pensamiento) de educación en el país dedicado

La República de Panamá tiene una de las economías más robustas de la región y del mundo y también uno de los sistemas educativos más débiles. El país ha estado creciendo anualmente 5-7% como promedio en las últimas décadas (Banco Mundial, 2019), pero la gran mayoría de sus estudiantes todavía se están desempeñando entre los más bajos en las evaluaciones internacionales estandarizadas. Solo alrededor de la mitad de la población relevante llega a la educación se-

al informar, educar e involucrar los académicos, educadores, políticos y el público general.

CIEdu, actualmente operando bajo los auspicios de INDICASAT en la Ciudad del Saber de Panamá, es una organización multifacética que provee:

- Producción de la investigación educativa
- Plataforma para publicaciones, datos e información sobre la educación en Panamá
- Conexión de investigadores y actores interdisciplinarios
- Capacitación de profesionales
- Comunicaciones y advocacy basadas en evidencia para promover los cambios educativos necesarios.

El centro efectúa todo esto a través de una serie de actividades que incluye las siguientes:

- Conducir investigaciones y producir publicaciones propias
- Mantener una base de datos comprehensivos de recursos relacionados con la educación en Panamá
- Convenir y participar en conferencias, seminarios y talleres
- Dirigir la formación y operación de una Asociación Nacional de Investigación Educativa
- Implementar un rango de eventos de entrenamiento y desarrollo de capacidades
- Diseminar varias clases de comunicaciones a través de distintos medios para informar e influir a la política y la práctica.

CIEdu trabaja con múltiples socios nacionales e internacionales que incluyen a INDICASAT, SENACYT, MEDUCA, ONGs educativas, el Banco Inter-American para el Desa-

rrollo (BID), las Naciones Unidas y otros para llevar a cabo su mandato. La Dra. Nadia De Leon, investigadora afiliada con INDICASAT y la USMA, es la investigadora principal dirigiendo la implementación, y la Dra. Nanette Svenson es la Directora Ejecutiva de CIEdu. La Dra. Svenson es una académica, autora y consultora con una trayectoria de experiencia de más de 20 años en los sectores de la educación y el desarrollo global que incluye trabajo con varias agencias de la ONU y otras organizaciones internacionales, distintos gobiernos, y universidades locales y extranjeras.

Entre las primeras tareas de CIEdu son (1) el lanzamiento de su sitio web, que incluye la base de datos de recursos sobre la educación en Panamá, programado para los finales de junio 2019, y (2) el desarrollo de una agenda nacional de investigación educativa.

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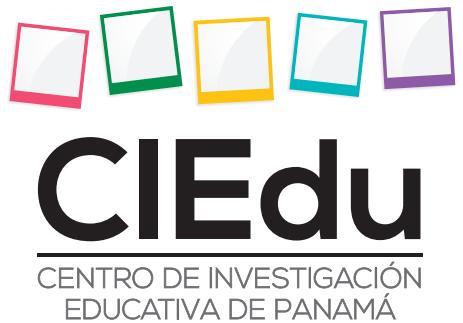
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CIEdu and the Importance of Research for Improving Education in Panama



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The Republic of Panama has one of the fastest growing economies in the region and in the world, yet also one of the weakest education systems. The country has been growing at around 5-7% annually on average over the past couple decades (World Bank, 2019), but the vast majority of its students still score among the lowest on international standardized tests. Only around half the relevant population cohort makes it to high school, much less post-secondary education, and while there are plenty of universities available, not one appears among the top institu-

tions in any international ranking. Added to this, national investment in research and development (R&D) is alarmingly low. Panama directs between 0.1 and 0.2 of its gross national product (GDP) to research activity (UIS, 2018), or about 20 times less than an OECD country typically invests.

An article published last year by Panama's Universidad Católica Santa María la Antigua (USMA) following the LAURDS International Conference on *Perspectives on Culture, Research Strategies and Doctoral Studies in Latin America* held in July 2018, explores this dilemma in more depth and concludes that most of Panama's youth is not being adequately prepared for the future. This threatens individuals' chances for success as well as national development and economic growth. The article makes the case for the urgent need to invest in research and higher education in Panama as a means of addressing this issue and cites several local entities currently working on education related R&D (Svenson, Bennett, De Gracia, De Leon, Psychoyos and Rao, 2018). One of the groups mentioned is the recently launched public-private Centro de Investigación Educativa (Center for Education Research,

CIEdu).

CIEdu aims to bridge a portion of Panama's economic success/education struggle gap with research. There is a significant body of academic literature indicating that education is key to advancing growth and development in societies around the world (see as examples OECD/Hanushek & Woessmann, 2015 and the UNESCO Global Education Monitoring and Education for All reports, 2019). There is also considerable study showing that research is key to advancing education (see as examples Raudenbush, 2008 and Towne, Wise & Winters, T. (eds), 2004). This is the guiding philosophy behind CIEdu: that education research is crucial for improving education systems and making them more equitable. CIEdu's mission is to further the study of education in Panama and utilize this study to further policy and practice directed toward improving education at all levels. CIEdu is the country's first education think tank, dedicated to informing, educating and engaging academics, practitioners, policymakers and the public at large.

CIEdu, currently operating under the auspices of INDICASAT in Panama's City of Knowledge, is a multi-faceted

organization that embodies the following roles:

- Producer of education research
- Platform for publications, data and information on education in Panama
- Connector of interdisciplinary researchers and practitioners
- Trainer of professionals
- Communicator and advocate of evidence-based analysis to push needed educational change.

The center carries out these functions through a series of activities that include:

- Conducting research and producing publications
- Maintaining a comprehensive online database of resources on education in Panama
- Convening and participating in conferences, seminars and workshops
- Leading the formation and operation of the National Association of Education Research
- Conducting a range of trainings and capacity development events
- Issuing various types of communications across diverse media to inform and influence policy and practice

Beyond INDICASAT, CIEdu is partnering with a multitude of national and international partners including SENACYT, MEDUCA, local education non-governmental organizations (NGOs), the Inter-American Development Bank (IDB), the United Nations (UN) and others in pursuit of its mandate. Dr. Nadia De Leon, an affiliated researcher with both INDICASAT and USMA, is the principal investigator leading the implementation, and Dr. Nanette Svenson is CIEdu's Executive Director. Dr. Svenson is a

seasoned scholar, author and consultant who comes to this position with an extensive background in education and development, having worked for the past 20 years with various UN agencies and international organizations, governments, and local and foreign universities.

Among CIEdu's first tasks are (1) the launch of its website, which will include a comprehensive database of resources on education in Panama, scheduled to take place at the end of June 2019; and (2) the development of a national education research agenda.

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INDICASAT-AIP

Crece en Ciencia y Sociedad.

Centro de Asuntos Académicos

El desarrollo académico de nuestros investigadores y representantes de la ciencia y la tecnología en Panamá ha sido marcadamente sostenido en las últimas décadas. Muchos de nuestros investigadores han obtenido experiencias en el extranjero, en laboratorios equipados con los últimos referentes, donde se reciben insumos a diario y hay oficinas especiales para aplicar a subvenciones y manejar fondos, presupuestos y proyectos.

Cuando estos investigadores regresan a Panamá lo hacen reconociendo que su trabajo incluye un aporte profesional en la construcción de la cultura científica y al desarrollo del Instituto como Asociación de Interés Público al servicio del país.

La comunidad científica y la sociedad civil han demostrado una notable voluntad para colaborar productivamente en conjunto con el estado. Hemos sido testigo y parte del alza y crecimiento de movimientos organizados en varios sectores: cultura, historia, nuevos negocios, ciencias y tecnología a través de la sociedad civil y fundaciones u organizaciones sin fines de lucro.

Este importante interés ha sido de

gran beneficio social y ha constituido una base para desarrollar redes y estrategias a largo plazo y lograr objetivos inmediatos. Nuestra guía, la ley 20 del 8 de agosto de 2018 sobre las asociaciones de interés, es muestra de que cuando los intereses público compartidos por un grupo de ciudadanos trabajan de forma exitosa en la comunidad, el apoyo del estado y las estructuras gubernamentales se vuelve sostenido y consecuente.

Por estas razones y en valía de su representación en la sociedad y el ambiente científico y sociocultural, el INDICASAT AIP, en busca de mejoramiento continuo, ha reestructurado el Centro de Asuntos Académicos y Colaboración a través la integración de nuevos programas y nuevos talentos.

Su misión se ha renovado acorde con las necesidades puntuales del entorno: *Apoyar la cultura colaborativa que promueve la investigación e innovación en Panamá.*

Nuestros objetivos son:

- 1) apoyar la investigación a través del desarrollo humano y académico.
- 2) identificar e involucrar a los interesados a lo largo de la cadena de valor de la investigación científica.
- 3) Supervisar los indicadores claves relacionados con las estrategias nacionales e internacionales (rendimiento

académico, estrategia de Ciencia, Tecnología e Innovación, Diplomacia científica, Objetivos de Desarrollo Sostenible.

El centro está liderado por el Doctor Ricardo Leonart, quien funge como Coordinador, La Doctora Marisín Peccio, como sub coordinadora. Kim Portmess dirige el área de Desarrollo y Divulgación, La licenciada Rita Marissa Giovani, es Directora Creativa y de Medios Digitales, La Licenciada Yamibel Díaz lleva la coordinación de eventos y contacto con medios de comunicación.

Los servicios y programas ofrecidos incluyen:

- Desarrollo académico:
 - a. Soporte y Fundamento en educación superior (Ph.D., Postdoc)
 - b. Orientación académica en todos los niveles.
 - 2. Colaboración y desarrollo
 - a. Creación de Capacidades
 - b. Comunicación y Divulgación Científica
 - c. Apoyo en la Gobernanza Institucional
 - 3. Protocolos e Investigaciones educativas
- Proyecto estratégico: el Centro está orgulloso de ser el anfitrión del proyecto “the Think Tank: Centro de Investigación educativa de Panamá.

INDICASAT AIP

Grows in Science and Society

Center for Academic Affairs

The academic development of our researchers and representatives of science and technology in Panama has been markedly sustained in recent decades. Many of our researchers have obtained experiences abroad, in laboratories equipped with the latest references, where supplies are received daily and there are special offices to apply for grants and manage funds, budgets and projects.

When these researchers return to Panama they do so recognizing that their work includes a professional contribution in the construction of scientific culture and the development of the Institute as a Public Interest Association at the service of the country.

The scientific community and civil society have demonstrated a remarkable will to collaborate productively with the state. We have witnessed and been a part of the rise and growth of organized movements in various sectors: culture, history, new business, science and technology through civil society and foundations or non-profit organizations.

This important interest has been of great social benefit and has formed a basis for developing long-term

networks and strategies and achieving immediate objectives. Our guide, the 20th law of August 20, 8, 2018, on associations of interest, shows that when public interests shared by a group of citizens work successfully in the community, state support and government structures are returns sustained and consistent.

For these reasons and in the value of its representation in society and the scientific and sociocultural environment, INDICASAT AIP in search of continuous improvement has restructured the Center for Academic Affairs and Collaboration through the integration of new programs and new talents.

Its mission has been renewed according to the specific needs of the environment:

Support the collaborative culture that promotes research and innovation in Panama.

Our objectives are:

- 1) Support research through human and academic development.
- 2) Identify and involve stakeholders throughout the value chain of scientific research.
- 3) Supervise the key indicators related to national and international strategies (academic performance, Science, Technology and Innovation strategy, Scientific Diplomacy, Sustainable

Development Goals.

The center is led by Dr. Ricardo Leonart, who serves as Coordinator, Dr. Marisin Pecchio, as sub coordinator. Kim Portmess directs the Development and Outreach area, Ms. Rita Marissa Giovani, is the Creative and Digital Media Director, Ms. Yamibel Díaz leads the coordination of events and contact with the mass media.

Within the services and programs that include:

- Academic development:
 - a. To Foundation and Support in Higher Education (Ph.D., Postdoc)
 - b. Academic orientation at all levels.
- Collaboration and development
 - a. Capacity Building
 - b. Communication and Outreach
 - c. Institutional Governance Support

3. Educational Protocols and Investigations

Strategic project: the Center is proud to host “the Think Tank: Educational Research Center of Panama.

|| PUBLICACIONES ||

Development of anthracycline-induced dilated cardiomyopathy due to mutation on *LMNA* gene in a breast cancer patient: a case report

BMC Cardiovascular Disorders (2019) 19:169



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Abstract:

Background: Anthracyclines are highly effective anticancer medication prescribed for the treatment of breast cancer. Nevertheless, the use of anthracyclines as chemotherapeutic agents involves a risk for development of cardiac toxicity which may cause restrictive and dilated cardiomyopathy. Currently, genetic predisposition is not considered as a risk factor for cardiotoxicity associated to the use of anthracyclines.

Case presentation: We report the case of a 37-years old Panamanian female patient diagnosed with breast cancer who developed clinical signs of severe heart failure after treatment with doxorubicin. A diagnosis of anthracycline induced cardiomyopathy was made and treatment was initiated accordingly. A whole exome sequencing study performed to the patient showed the presence of a missense mutation in *LMNA* gene, which codifies for lamin A/C. Our results points to a correlation between the *LMNA* variant and the anthracycline cardiotoxicity developed by the woman. Improvement of the clinical symptoms and the left ventricle ejection fraction was observed after proper treatment.

Conclusions: This case report suggests for the first time a potential genetic predisposition for anthracyclines induced cardiomyopathy in patients with mutations in *LMNA* gene. Perhaps chemotherapies accelerate or deliver the "second-hit" in the development of DCM in patients with genetic mutations. More data is needed to understand the contribution of *LMNA* variants that predispose to DCM in patients receiving cardiotoxic therapies.

Socioeconomic and demographic predictors of resident knowledge, attitude, and practice regarding arthropod-borne viruses in Panama

BMC Public Health (2018) 18:1261



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Abstract:

Background: We sought to identify if socioeconomic and demographic factors play a role in resident knowledge, attitude, and practice regarding Dengue, Chikungunya, and Zika in order to inform effective management procedures for disease prevention in Panama, a middle-income tropical country in Central America. All three are arthropod-borne viruses transmitted by Aedes mosquito vectors present in the focal region of Panama City, the largest city in Central America and an urban region of extreme socioeconomic polarization.

Methods: Between November 2017 and February 2018, we administered standardized, anonymous knowledge, attitude, and practice surveys to 263 residents split between two neighborhoods of high socioeconomic status (SES) and two neighborhoods of low SES. We then summed the knowledge, attitude, and practice scores respectively, and used linear and logistic regressions to quantify relationships with socioeconomic and demographic factors.

Results: Low-SES neighborhoods with high proportions of low income residents, residents over 70 years old had lower mean knowledge scores compared to other groups. Furthermore, residents in neighborhoods of low SES reported more mosquito biting relative to residents in neighborhoods of high SES, yet comparably lower level of concerns for disease transmission. Additionally, knowledge was lower for the more novel emergent threats of Chikungunya and Zika, compared to the endemic Dengue.

Conclusion: Findings suggest that low-SES neighborhoods with high proportions of low income, low education, and elderly residents should be targeted for outreach programs designed to prevent DENV, CHIKV, or ZIKV in Panama City. These outcomes support our initial hypotheses as lower relative knowledge and fewer practices related to the prevention of Dengue, Chikungunya, and Zika were found in low-SES neighborhoods. There is also a widespread lack of adequate knowledge regarding these diseases as well as low levels of concern in areas of highly reported mosquito biting. We provide suggestions for taking neighborhood socioeconomic status and specific aspects resident health literacy and attitude into account for creating more effective outreach campaigns as both endemic and novel arthropod-borne disease rates continue to increase throughout Latin America.

PUBLICACIONES

Maternal invasion history of *Aedes aegypti* and *Aedes albopictus* into the Isthmus of Panama: Implications for the control of emergent viral disease agents

PLOS ONE 2018;13(3):e0194874



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Abstract:

Despite an increase in dengue outbreaks and the arrival of chikungunya and Zika disease in Panama, studies on the demographic history of the invasive *Aedes* mosquitoes that are the principle vectors of these diseases are still lacking in this region. Here, we assess the genetic diversity of these mosquitoes in order to decipher their invasion histories into the Isthmus of Panama. DNA sequences from the mitochondrial cytochrome C oxidase I gene obtained from 30 localities in 10 provinces confirmed the presence of more than one mitochondrial haplogroup (i.e., maternal lineage) in each species. The invasion of *Aedes albopictus* was likely from temperate European countries, as the most frequent and widespread haplogroup in Panama harbored variants that are uncommon elsewhere in the Americas. Two infrequent and geographically restricted *Ae. albopictus* haplotypes appear to have subsequently invaded Panama from neighboring Costa Rica and the USA, respectively. In addition, we recovered two deeply divergent mitochondrial clades in Panamanian *Aedes aegypti*. The geographic origins of these clades is unknown, given that divergence in the mitochondrial genome is probably due to ancient population processes within the native range of *Ae. aegypti*, rather than due to its global expansion out of Africa. However, Panamanian *Ae. aegypti* mitochondrial sequences within the first clade were closely related to others from Colombia, Bolivia, Brazil, Mexico and the USA, suggesting two separate invasions from Western Hemisphere source populations. The pattern of increased genetic diversity in *Aedes* mosquitoes in Panama is likely facilitated by the numerous land and water inter-connections across the country, which allows them to enter via sea- and land-transportation from Europe, North, Central and South America. Our results here should be considered in disease mitigation programs if emergent arboviruses are to be effectively diminished in Panama through vector suppression.

The Panama Aging Research Initiative Longitudinal Study -- Lessons from the Field

MEDICC Review, April-July 2019, Vol 21, No 2-3



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Abstract:

The Panama Aging Research Initiative is a cohort study of 423 adults aged ≥ 65 years recruited from an outpatient geriatric department of Panama's largest public hospital, the Social Security Fund's Dr. Arnulfo Arias Madrid Hospital Complex (Complejo Hospitalario Dr. Arnulfo Arias Madrid de la Caja de Seguro Social). The study provides the first reports of modifiable and non-modifiable risk factors of cognitive impairment and dementia, as well as various health conditions common among older adults in Panama, including chronic illnesses, polypharmacy and rates of comorbidity. The initial study, conducted September 2012–May 2016, included a clinical interview; physical assessments of body mass index and handgrip strength; and cognitive testing, plus non-fasting blood draws for measurements of genetic (Apolipoprotein E genotype) and blood-based biological markers.

Information was collected regarding limitations in activities of daily living, symptoms of depression and fall incidents. A subsample of participants provided cerebrospinal fluid to measure proteins related to Alzheimer's disease; another subsample underwent ultrasonography and electroencephalography.

This report describes the general study design and highlights lessons learned and future directions. In particular, drawing on lessons learned from this clinical research, a community-based prospective cohort study is currently under way among older adults in Panama to validate a blood-based biomarker profile for detecting mild cognitive impairment and Alzheimer's disease, as well as risk factors for cognitive decline.

PUBLICACIONES

Historical and contemporary forces combine to shape patterns of genetic differentiation in two species of Mesoamerican *Anopheles* mosquitoes

Biological Journal of the Linnean Society, 2018, XX, 1-12



Jose R. Loaiza
Matthew J. Miller

α -Glucosidase inhibitors from a mangrove associated fungus, *Zasmidium* sp. strain EM5-10

BMC Chem. 2019;13(1):22



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Abstract:

Pleistocene environmental changes were important drivers of species- and population-level diversification in *Anopheles* mosquitoes. However, *Anopheles* species have different ecologies, so their response to Pleistocene climate oscillations should have differed. We investigate whether genetic diversification in *Anopheles punctimacula* s.s. (a forest specialist and secondary vector of *Plasmodium vivax*) and *Anopheles albimanus* (a habitat colonist and primary vector of *P. vivax* and *P. falciparum*) is due to: (1) historical population processes, (2) contemporary population processes or (3) a combination of both. Differences in the degree of refugial isolation during the Last Glacial Maximum (LGM) and the degree to which isolated populations evolved habitat niche differences appear to explain differences in the phylogeographical patterns between *A. punctimacula* s.s. and *A. albimanus* in Lower Middle America (Mesoamerica). Refugial isolation during the LGM and subsequent niche diversification shaped the phylogeographical history of *A. punctimacula* s.s. During the LGM, the genetic pool of this species was fragmented into extremely narrow and scattered habitat refugia, resulting in two discrete mitochondrial lineages. Subsequently, these lineages appear to have further evolved distinct niche preferences and diversified due to different climatic conditions between populations, which may have contributed to the lack of introgression or range overlap among mitochondrial lineages. While *A. albimanus* also experienced range contraction, recovery was more rapid, and we find no evidence of niche evolution among lineages. This appears to explain the broad mitochondrial introgression in this species. Greater resilience to climatic instability by *A. albimanus* might contribute to its principal transmission role for human *Plasmodium* parasites across the Neotropics.

Abstract:

Background: Mangroves plants and their endophytes represent a natural source of novel and bioactive compounds. In our ongoing research on mangrove endophytes from the Panamanian Pacific Coast, we have identified several bioactive endophytic fungi. From these organisms, an isolate belonging to the genus *Zasmidium* (Mycosphaerellaceae) showed 91.3% of inhibition against α -glucosidase enzyme *in vitro*.

Results: *Zasmidium* sp. strain EM5-10 was isolated from mature leaves of *Laguncularia racemosa*, and its crude extract showed good inhibition against α -glucosidase enzyme (91.3% of inhibition). Bioassay-guided fractionation of the crude extract led to obtaining two active fractions: L (tripalmitin) and M (Fungal Try-glycerides Mixture). Tripalmitin (3.75 μ M) showed better inhibitory activity than acarbose (positive control, IC_{50} 217.71 μ M). Kinetic analysis established that tripalmitin acted as a mixed inhibitor. Molecular docking and molecular dynamics simulations predicted that tripalmitin binds at the same site as acarbose and also to an allosteric site in the human intestinal α -glucosidase (PDB: 3TOP).

Conclusions: *Zasmidium* sp. strain EM5-10 represents a new source of bioactive substances that could possess beneficial properties for human health.

PUBLICACIONES

Application of matrix-assisted laser desorption/ionization mass spectrometry to identify species of Neotropical *Anopheles* vectors of malaria

Malaria Journal 2019;18(1):95



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Abstract:

Background: Malaria control in Panama is problematic due to the high diversity of morphologically similar *Anopheles* mosquito species, which makes identification of vectors of human *Plasmodium* challenging. Strategies by Panamanian health authorities to bring malaria under control targeting *Anopheles* vectors could be ineffective if they tackle a misidentified species.

Methods: A rapid mass spectrometry identification procedure was developed to accurately and timely sort out field-collected Neotropical *Anopheles* mosquitoes into vector and non-vector species. Matrix-assisted laser desorption/ionization (MALDI) mass spectra of highly-abundant proteins were generated from laboratory-reared mosquitoes using different extraction protocols, body parts, and sexes to minimize the amount of material from specimen vouchers needed and optimize the protocol for taxonomic identification. Subsequently, the mass spectra of field-collected Neotropical *Anopheles* mosquito species were classified using a combination of custom-made unsupervised (i.e., Principal component analysis—PCA) and supervised (i.e., Linear discriminant analysis—LDA) classification algorithms.

Results: Regardless of the protocol used or the mosquito species and sex, the legs contained the least intra-specific variability with enough well-preserved proteins to differentiate among distinct biological species, consistent with previous literature. After minimizing the amount of material needed from the voucher, one leg was enough to produce reliable spectra between specimens. Further, both PCA and LDA were able to classify up to 12 mosquito species, from different subgenera and seven geographically spread localities across Panama using mass spectra from one leg pair. LDA demonstrated high discriminatory power and consistency, with validation and cross-validation positive identification rates above 93% at the species level.

Conclusion: The selected sample processing procedure can be used to identify field-collected *Anopheles* species, including vectors of *Plasmodium*, in a short period of time, with a minimal amount of tissue and without the need of an expert mosquito taxonomist. This strategy to analyse protein spectra overcomes the drawbacks of working with out a reference library to classify unknown samples. Finally, this MALDI approach can aid ongoing malaria eradication efforts in Panama and other countries with large number of mosquito's species by improving vector surveillance in epidemic-prone sites such as indigenous Comarcas.

Analysis of the antiparasitic and anticancer activity of the coconut palm (*Cocos nucifera* L. ARECACEAE) from the natural reserve of Punta Patiño, Darién.

PLOS ONE. 2019;14(4):e0214193. doi: 10.1371/journal.pone.0214193



Tayler NM, Boya CA, Herrera L, Moy J, Ng M, Pineda L, Almanza A, Rosero S, Coronado LM, Correa R, Santamaría R, Caballero Z, Durant-Arribald AA, Tidgewell KJ, Balunas MJ, Gerwick WH, Spadafora A, Gutiérrez M, Spadafora C,

Abstract:

Cocos nucifera (C. nucifera) (the coconut palm tree) has been traditionally used to fight a number of human diseases, but only a few studies have tested its components against parasites such as those that cause malaria. In this study, C. nucifera samples were collected from a private natural reserve in Punta Patiño, Darien, Panama. The husk, leaves, pulp, and milk of C. nucifera were extracted and evaluated against the parasites that cause Chagas' disease or American trypanosomiasis (*Trypanosoma cruzi*), leishmaniasis (*Leishmania donovani*) and malaria (*Plasmodium falciparum*), as well as against a line of breast cancer cells. While there was no activity in the rest of the tests, five and fifteen-minute aqueous decoctions of leaves showed antiplasmoidal activity at 10% v/v concentration. Removal of some HPLC fractions resulted in loss of activity, pointing to the presence of synergy between the components of the decoction. Chemical molecules were separated and identified using an ultra-performance liquid chromatography (UPLC) approach coupled to tandem mass spectrometry (LC-MS/MS) using atmospheric pressure chemical ionization quadrupole-time of flight mass spectrometry (APCI-Q-TOF-MS) and molecular networking analysis, revealing the presence of compounds including polyphenol, flavone, sterol, fatty acid and chlorophyll families, among others.

PUBLICACIONES

Diverse novel phleboviruses in sandflies from the Panama Canal area, Central Panama

Journal of General Virology DOI 10.1099/jgv.0.001260



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Abstract:

The genus *Phlebovirus* (order Bunyavirales, family Phenuiviridae) comprises 57 viruses that are grouped into nine species complexes. Sandfly-transmitted phleboviruses are found in Europe, Africa and the Americas and are responsible for febrile illness and infections of the nervous system in humans. The aim of this study was to assess the genetic diversity of sandfly-transmitted phleboviruses in connected and isolated forest habitats throughout the Panama Canal area in Central Panama. In total, we collected 13 807 sandflies comprising eight phlebotomine species. We detected several strains pertaining to five previously unknown viruses showing maximum pairwise identities of 45–78 % to the RNA-dependent RNA polymerase genes of phleboviruses. Entire coding regions were directly sequenced from infected sandflies as virus isolation in cell culture was not successful. The viruses were tentatively named La Gloria virus (LAGV), Mona Grita virus (MOGV), Peña Blanca virus (PEBV), Tico virus (TICV) and Tres Almendras virus (TRAV). Inferred phylogenies and p-distance-based analyses revealed that PEBV groups with the Bujaru phlebovirus species complex, TRAV with the Candiru phlebovirus species complex and MOGV belongs to the proposed Icoaci phlebovirus species complex, whereas LAGV and TICV seem to be distant members of the Bujaru phlebovirus species complex. No specific vector or habitat association was found for any of the five viruses. Relative abundance of sandflies was similar over habitat types. Our study shows that blood-feeding insects originating from remote and biodiverse habitats harbour multiple previously unknown phleboviruses. These viruses should be included in future surveillance studies to assess their geographic distribution and to elucidate if these viruses cause symptoms of disease in animals or humans.

Caracterización fitoquímica y estudios comparativos de cuatro especies de *Cecropia* recolectadas en Panamá utilizando análisis de datos multivariados.

Sci Rep. 2019 Feb 11;9(1):1763. doi: 10.1038/s41598-018-38334-4.



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Abstract:

Las especies de plantas del género *Cecropia* (Urticaceae) se utilizan como medicina tradicional en América Latina y están disponibles comercialmente como complementos alimenticios. El objetivo de este estudio fue caracterizar y comparar los componentes fitoquímicos de cuatro especies de *Cecropia* recolectadas en Panamá. Las estructuras de 11 compuestos aislados de las hojas de *C. obtusifolia* se aclararon en base a espectrometría de masas de alta resolución (HRMS) y análisis espectroscópico de resonancia magnética nuclear (RMN); Los constituyentes polifenólicos de las hojas de las cuatro especies de *Cecropia* y los productos comerciales se caracterizaron mediante cromatografía líquida de alto rendimiento, detección de matriz de diodos, cuadrupolo, tiempo de vuelo, tandem espectrometría de masas de alta resolución (HPLC-DAD-QTOF). Cuarenta y siete compuestos fueron completamente identificados o tentativamente caracterizados. Treinta y nueve de estos no han sido reportados previamente para la especie bajo investigación. El análisis multivariado reveló que *C. obtusifolia* y *C. insignis* son las especies más relacionadas, mientras que *C. hispidissima* es la más segregada. Teniendo en cuenta la importancia de la descripción de nuevas entidades químicas y el creciente interés y uso de productos naturales, este estudio puede ser de gran ayuda para fines quimiotañómicos, la interpretación de propiedades medicinales y para la evaluación de la calidad de los suplementos herbales que contienen hojas de *Cecropia*.

PUBLICACIONES

High infestation of invasive Aedes mosquitoes in used-tyres along the local transport network of Panama.

Parasites and Vectors, 2019;12(1):264



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Loaiza JR.

Abstract:

Background: The long-distance dispersal of the invasive disease vectors *Aedes aegypti* and *Aedes albopictus* has introduced arthropod-borne viruses into new geographical regions, causing a significant medical and economic burden. The used-tire industry is an effective means of *Aedes* dispersal, yet studies to determine *Aedes* occurrence and the factors influencing their distribution along local transport networks are lacking. To assess infestation along the primary transport network of Panama we documented all existing garages that trade used tires on the highway and surveyed a subset for *Ae. aegypti* and *Ae. albopictus*. We also assess the ability of a mass spectrometry approach to classify mosquito eggs by comparing our findings to those based on traditional larval surveillance.

Results: Both *Aedes* species had a high infestation rate in garages trading used tires along the highways, providing a conduit for rapid dispersal across Panama. However, generalized linear models revealed that the presence of *Ae. aegypti* is associated with an increase in road density by a log-odds of 0.44 (0.73 ± 0.16 ; $P = 0.002$), while the presence of *Ae. albopictus* is associated with a decrease in road density by a log-odds of 0.36 (0.09 ± 0.63 ; $P = 0.008$). Identification of mosquito eggs by mass spectrometry depicted similar occurrence patterns for both *Aedes* species as that obtained with traditional rearing methods.

Antiparasitic Compounds from the Panamanian Marine Bacterium *Pseudomonas aeruginosa*

Natural Product Communications 2019; 14 (1), 31-32



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Abstract:

Fractionation of the ethyl acetate extract of the bacterium *Pseudomonas aeruginosa* led to the isolation of five compounds, cyclo-(L-Phe-L-Pro) (1), 3-heptyl- 3-hydroxy-1,2,3,4-tetrahydroquinoline-2,4-dione (2), 2-heptyl-4-hydroxyquinoline (3), 2-nonyl-4-hydroxyquinoline (4), and 1-phenazinecarboxylic acid (5).

The structures of compounds 1–5 were established by spectroscopic analyses. Compounds 2–4 produced inhibition on the growth of *Plasmodium falciparum*, with IC₅₀ values of 3.47, 2.57 and 2.79 µg/mL, respectively. Compounds 3–4 had activity against *Trypanosoma cruzi*, with IC₅₀ values of 3.66 and 3.99 µg/mL. Finally, all compounds were found inactive when tested against *Leishmania donovani* at 10 µg/mL.

PUBLICACIONES

Aedes mosquito infestation in socioeconomically contrasting neighborhoods of Panama City.

EcoHealth, 2019; 16(2):210-221.



Ari Whiteman
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Jose Loaiza

Abstract:

The global expansion and proliferation of *Aedes aegypti* and *Aedes albopictus* represents a growing public health threat due to their capacity to transmit a variety of arboviruses to humans, including dengue, chikungunya, and Zika. Particularly important in urban regions, where these species have evolved to breed in man-made containers and feed nearly exclusively on human hosts, the threat of vector-borne disease has risen in recent decades due to the growth of cities, progression of climate change, and increase in globalization. While the dynamics of *Aedes* populations in urban settings have been well studied in relation to ecological features of the landscape, relatively less is known about the relationship between neighborhood socioeconomic status and *Aedes* infestation. Here, we compare infestation levels of both *A. aegypti* and *A. albopictus* in four socioeconomically contrasting neighborhoods of urban Panama City, Panama. Our results indicate that infestation levels for both *Aedes* species vary between neighborhoods of contrasting socioeconomic status, being higher in neighborhoods having lower percentage of residents with bachelor degrees and lower monthly household income. Additionally, we find that proximity between socioeconomically contrasting neighborhoods can predict infestation levels by species, with *A. aegypti* increasing and *A. albopictus* decreasing with proximity between neighborhoods. These findings hold key implications for the control and prevention of dengue, chikungunya, and Zika in Panama, a region with ongoing arbovirus outbreaks and high economic inequity.

Biodegradation of the Allelopathic Chemical Pterostilbene by a *Sphingobium* sp. Strain from the Peanut Rhizosphere

Applied and Environmental Microbiology 2019, e02154-18



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Abstract:

Many plants produce allelopathic chemicals, such as stilbenes, to inhibit pathogenic fungi. The degradation of allelopathic compounds by bacteria associated with the plants would limit their effectiveness, but little is known about the extent of biodegradation or the bacteria involved. Screening of tissues and rhizosphere of peanut (*Arachis hypogaea*) plants revealed substantial enrichment of bacteria able to grow on resveratrol and pterostilbene, the most common stilbenes produced by the plants. Investigation of the catabolic pathway in *Sphingobium* sp. strain JS1018, isolated from the rhizosphere, indicated that the initial cleavage of pterostilbene was catalyzed by a carotenoid cleavage oxygenase (CCO), which led to the transient accumulation of 4-hydroxybenzaldehyde and 3,5-dimethoxybenzaldehyde. 4-Hydroxybenzaldehyde was subsequently used for the growth of the isolate, while 3,5-dimethoxybenzaldehyde was further converted to a dead-end metabolite with a molecular weight of 414 ($C_{22}H_{31}O_6$). The gene that encodes the initial oxygenase was identified in the genome of strain JS1018, and its function was confirmed by heterologous expression in *Escherichia coli*. This study reveals the biodegradation pathway of pterostilbene by plant-associated bacteria. The prevalence of such bacteria in the rhizosphere and plant tissues suggests a potential role of bacterial interference in plant allelopathy.

PUBLICACIONES

Forest disturbance and vector transmitted diseases in the lowland tropical rainforest of central Panama

Tropical Medicine & International Health, 2019 24(7): 849-861. doi. org/10.1111/tmi.13244.



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Abstract:

Objective To explore possible changes in the community attributes of haematophagous insects as a function of forest disturbance. We compare the patterns of diversity and abundance, plus the behavioural responses of three epidemiologically distinct vector assemblages across sites depicting various levels of forest cover.

Methods Over a 3-year period, we sampled mosquitoes, sandflies and biting-midges in forested habitats of central Panama. We placed CDC light traps in the forest canopy and in the understorey to gather blood-seeking females.

Results We collected 168 405 adult haematophagous dipterans in total, including 26 genera and 86 species. Pristine forest settings were always more taxonomically diverse than the disturbed forest sites, confirming that disturbance has a negative impact on species richness. Species of Phlebotominae and *Culicoides* were mainly classified as climax (i.e. forest specialist) or disturbance-generalist, which tend to decrease in abundance along with rising levels of disturbance. In contrast, a significant portion of mosquito species, including primary and secondary disease vectors, was classified as colonists (i.e. disturbed-areas specialists), which tend to increase in numbers towards more disturbed forest habitats. At pristine forest, the most prevalent species of Phlebotominae and *Culicoides* partitioned the vertical niche by being active at the forest canopy or in the understorey; yet this pattern was less clear in disturbed habitats. Most mosquito species were not vertically stratified in their habitat preference.

Conclusion We posit that entomological risk and related pathogen exposure to humans is higher in pristine forest scenarios for *Culicoides* and Phlebotominae transmitted diseases, whereas forest disturbance poses a higher entomological risk for mosquito-borne infections. This suggests that the Dilution Effect Hypothesis (DEH) does not apply in tropical rainforests where highly abundant, yet unrecognised insect vectors and neglected zoonotic diseases occur. Comprehensive, community level entomological surveillance is, therefore, the key for predicting potential disease spill over in scenarios of pristine forest intermixed with anthropogenic habitats. We suggest that changes in forest quality should also be considered when assessing arthropod-borne disease transmission risk.

Ultrasound-assisted extraction optimization and validation of an HPLC-DAD method for the quantification of polyphenols in leaf extracts of *Cecropia* species

SCIENTIFIC REPORTS | (2019) 9:2028



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Abstract:

Cecropia species are traditionally used in Latin American folk medicine and are available as food supplements with little information warranting their quality. The optimum conditions for the extraction of chlorogenic acid (CA), total flavonoids (TF) and flavonolignans (FL) from leaves of *Cecropia* species were determined using a fractional factorial design (FFD) and a central composite design (CCD). A reversed-phase high-performance liquid chromatographic method coupled to a diode array detector (HPLC-DAD) was validated for the quantification of CA, TF and FL, following the ICH guidelines. Quantitative and Principal Component Analysis (PCA) was also performed. The extraction-optimization methodology enabled us developing an appropriate extraction process with a time-efficient execution of experiments.

The experimental values agreed with those predicted, thus indicating suitability of the proposed model. The validation parameters for all chemical markers of the quantification method were satisfactory. The results revealed that the method had excellent selectivity, linearity, precision (repeatability and intermediate precision were below than 2 and 5%, respectively) and accuracy (98-102%). The limits of detection and quantification were at nanogram per milliliter (ng/mL) level.

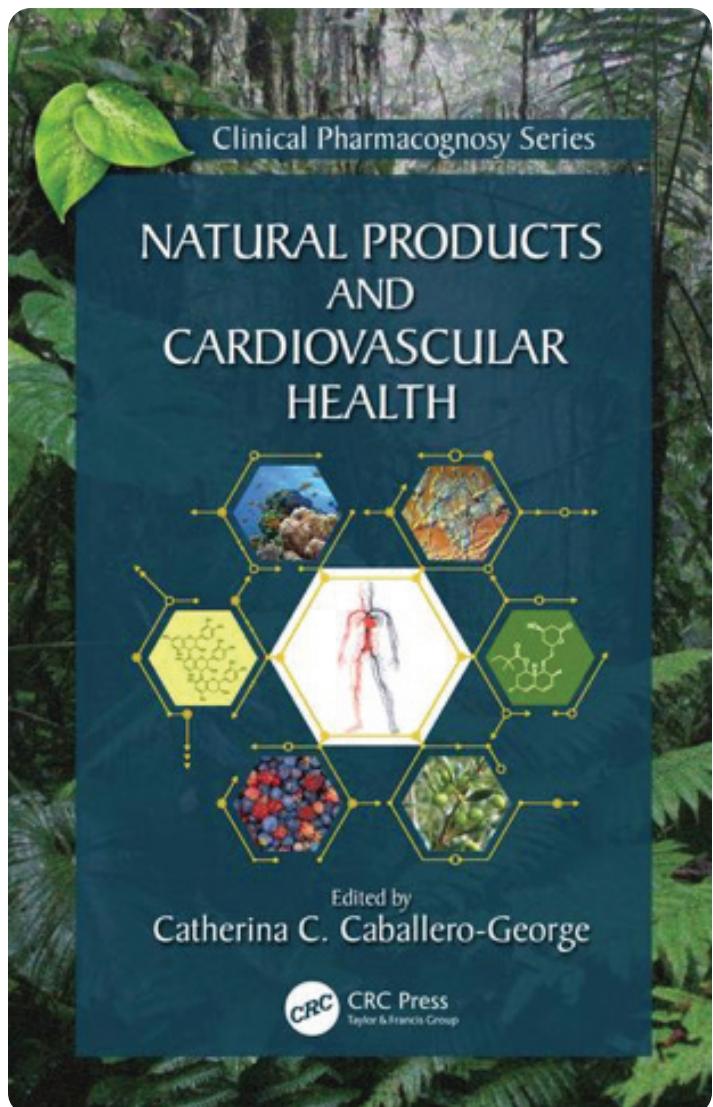
In conclusion, the simultaneous quantification of chemical markers using the proposed method is an appropriate approach for species discrimination and quality evaluation of *Cecropia* sp."

LIBRO:

PRODUCTOS NATURALES Y SALUD CARDIOVASCULAR. 1^A EDICION

CRC Press Published December 13, 2018
Reference - 222 Pages - 36 B/W Illustrations
ISBN 9781498789004 - CAT# K30326
Series: Clinical Pharmacognosy Series

Catherina Caballero George



Resumen

Este volumen único proporciona la información más reciente sobre los metabolitos secundarios obtenidos de organismos seleccionados (plantas o microorganismos) que tienen efectos beneficiosos en el tratamiento de enfermedades cardiovasculares y la capacidad de ofrecer protección contra su progreso. Se proporciona una descripción detallada de su fuente, química y mecanismo de acción, junto con los resultados de estudios clínicos. Aquí, se establece una conexión clara entre las estructuras químicas, los estudios *in vitro* y su importancia clínica. El tema es extenso y la audiencia obtiene una comprensión de las aplicaciones medicinales de estos grupos de metabolitos secundarios que tienen el potencial de mejorar la salud cardiovascular.

Características:

La información más reciente sobre metabolitos secundarios con efectos beneficiosos en el tratamiento de enfermedades cardiovasculares.

Escrito por un destacado equipo de autores, su trabajo proporciona nuevos conocimientos sobre los efectos beneficiosos de diferentes componentes presentes en productos vegetales bien conocidos, que evidencian sus impresionantes efectos cardiovasculares.

Este volumen analiza nuevos objetivos para detectar nuevos fármacos y la necesidad de obtener datos de estudios clínicos que utilizan productos naturales para analizar mejor la importancia de los datos experimentales *in vitro*.

Aquí el lector encontrará un volumen único y oportuno con un sabor internacional.

Este libro describe la fuente, la química y el mecanismo de acción de los productos naturales con el potencial de mejorar la salud cardiovascular.

PUBLICACIONES

Molecular validation of anthropophilic Phlebotominae sandflies (Diptera: Psychodidae) in Central Panama

Tropical Medicine & International Health 2019; 24(7): 849-861. doi. org/10.1111/tmi.13244.



Larissa Dutari
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Abstract:

Six Phlebotominae sand fly species are incriminated as biological vectors of human pathogens in Panama, but molecular corroboration is still needed. We aim at confirming the identity of Phlebotominae species documented as anthropophilic in Panama. Adult sandflies were collected from August 2010 to February 2012 in Central Panama using CDC light traps. Species confirmation was accomplished through molecular barcodes and allied sequences from GenBank. A total of 53,366 sand fly specimens representing 18 species were collected. Five species were validated molecularly as single phylogenetic clusters, but *Psychodopygus thula* depicted two genetically divergent lineages, which may be indicative of cryptic speciation.

Global variation in bacterial strains that cause tuberculosis disease: a systematic review and meta-analysis

BMC Medicine (2018) 16:196



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Simon I Hay

Abstract:

Background: The host, microbial, and environmental factors that contribute to variation in tuberculosis (TB) disease are incompletely understood. Accumulating evidence suggests that one driver of geographic variation in TB disease is the local ecology of mycobacterial genotypes or strains, and there is a need for a comprehensive and systematic synthesis of these data. The objectives of this study were to (1) map the global distribution of genotypes that cause TB disease and (2) examine whether any epidemiologically relevant clinical characteristics were associated with those genotypes.

Methods: We performed a systematic review of PubMed and Scopus to create a comprehensive dataset of human TB molecular epidemiology studies that used representative sampling techniques. The methods were developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We extracted and synthesized data from studies that reported prevalence of bacterial genotypes and from studies that reported clinical characteristics associated with those genotypes.

Results: The results of this study are twofold. First, we identified 206 studies for inclusion in the study, representing over 200,000 bacterial isolates collected over 27 years in 85 countries. We mapped the genotypes and found that, consistent with previously published maps, Euro-American lineage 4 and East Asian lineage 2 strains are widespread, and West African lineages 5 and 6 strains are geographically restricted. Second, 30 studies also reported transmission chains and 4 reported treatment failure associated with genotypes. We performed a meta-analysis and found substantial heterogeneity across studies. However, based on the data available, we found that lineage 2 strains may be associated with increased risk of transmission chains, while lineages 5 and 6 strains may be associated with reduced risk, compared with lineage 4 strains.

Conclusions: This study provides the most comprehensive systematic analysis of the evidence for diversity in bacterial strains that cause TB disease. The results show both geographic and epidemiological differences between strains, which could inform our understanding of the global burden of TB. Our findings also highlight the challenges of collecting the clinical data required to inform TB diagnosis and treatment. We urge future national TB programs and research efforts to prioritize and reinforce clinical data collection in study designs and results dissemination.

PUBLICACIONES

Dynamics and diversity of bacteria associated with the disease vectors *Aedes aegypti* and *Aedes albopictus*

Scientific Reports, 2019; 9:12160



Kelly L. Bennett
Carmelo Gómez-Martínez
Yamileth Chin
Kristin Saltonstall
W. Owen McMillan
Jose R. Rovira
Jose R. Loaiza

Abstract:

Aedes aegypti and *Aedes albopictus* develop in the same aquatic sites where they encounter microorganisms that influence their life history and capacity to transmit human arboviruses. Some bacteria such as *Wolbachia* are currently being considered for the control of Dengue, chikungunya and Zika. Yet little is known about the dynamics and diversity of *Aedes*-associated bacteria, including larval habitat features that shape their tempo-spatial distribution. We applied large-scale 16S rRNA amplicon sequencing to 960 adults and larvae of both *Ae. aegypti* and *Ae. albopictus* mosquitoes from 59 sampling sites widely distributed across nine provinces of Panama. We find both species share a limited, yet highly variable core microbiota, reflecting high stochasticity within their oviposition habitats. Despite sharing a large proportion of microbiota, *Ae. aegypti* harbours higher bacterial diversity than *Ae. albopictus*, primarily due to rarer bacterial groups at the larval stage. We find significant differences between the bacterial communities of larvae and adult mosquitoes, and among samples from metal and ceramic containers. However, we find little support for geography, water temperature and pH as predictors of bacterial associates. We report a low incidence of natural *Wolbachia* infection for both *Aedes* and its geographical distribution. This baseline information provides a foundation for studies on the functions and interactions of *Aedes*-associated bacteria with consequences for bio-control within panama.

VianniaTopes: a database of predicted immunogenic peptides for *Leishmania* (*Viannia*) species

Database, 2018, 1–12 doi: 10.1093/database/bay111 Database tool



Alejandro Llanes
Carlos Mario Restrepo
Ricardo Leonart

Abstract:

Leishmania is a protozoan parasite causing several disease presentations collectively known as leishmaniasis. Pathogenic species of *Leishmania* are divided into two subgenera, *L. (Leishmania)* and *L. (Viannia)*. Species belonging to the *Viannia* subgenus have only been reported in Central and South America. These species predominantly cause cutaneous leishmaniasis, but in some cases, parasites can migrate to the nasopharyngeal area and cause a highly disfiguring mucocutaneous presentation. Despite intensive efforts, no effective antileishmanial vaccine is available for use in humans, although a few candidates mainly designed for *L. (Leishmania)* species are now in clinical trials. After sequencing the genome of *Leishmania panamensis*, we noticed a high degree of sequence divergence among several orthologous proteins from both subgenera.

Consequently, some of the previously published candidates may not work properly for species of the *Viannia* subgenus. To help in vaccine design, we predicted CD4⁺ and CD8⁺ T cell epitopes in the theoretical proteomes of four strains belonging to the *Viannia* subgenus. Prediction was performed with at least two independent bioinformatics tools, using the most frequent human major histocompatibility complex (MHC) class I and class II alleles in the affected geographic area. Although predictions resulted in millions of peptides, relatively few of them were predicted to bind to several MHC alleles and can therefore be considered promiscuous epitopes. Comparison of our results to previous applications to species of the *Leishmania* subgenus confirmed that approximately half of the reported candidates are not present in *Viannia* proteins with a threshold of 80% sequence similarity and coverage. However, our prediction methodology was able to predict 70–100% of the candidates that could be found in *Viannia*. All the prediction data generated in this study are publicly available in an interactive database called VianniaTopes.

PUBLICACIONES

Habitat disturbance and the organization of bacterial communities in Neotropical hematophagous arthropods

Plos One 2019; 14(9): e0222145



Kelly L. Bennett
Alejandro Almanza
W. Owen McMillan
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Jorge S. Vinald
Luis Mejia
Kaitlin Driesse
Luis F. De Leo'n
Jose R. Loaiza

Abstract:

The microbiome plays a key role in the biology, ecology and evolution of arthropod vectors of human pathogens. Vector-bacterial interactions could alter disease transmission dynamics through modulating pathogen replication and/or vector fitness. Nonetheless, our understanding of the factors shaping the bacterial community in arthropod vectors is incomplete.

Using large-scale 16S amplicon sequencing, we examine how habitat disturbance structures the bacterial assemblages of field-collected whole-body hematophagous arthropods that vector human pathogens including mosquitoes (Culicidae), sand flies (Psychodidae), biting midges (Ceratopogonidae) and hard ticks (Ixodidae). We found that all comparisons of the bacterial community among species yielded statistically significant differences, but a difference was not observed between adults and nymphs of the hard tick, *Haemaphysalis juxtakochi*. While *Culicoides* species had the most distinct bacterial community among dipterans, tick species were composed of entirely different bacterial OTU's. We observed differences in the proportions of some bacterial types between pristine and disturbed habitats for *Coquillettidia* mosquitoes, *Culex* mosquitoes, and *Lutzomyia* sand flies, but their associations differed within and among arthropod assemblages. In contrast, habitat quality was a poor predictor of differences in bacterial classes for *Culicoides* biting midges and hard tick species. In general, similarities in the bacterial communities among hematophagous arthropods could be explained by their phylogenetic relatedness, although intraspecific variation seems influenced by habitat disturbance.

Pumilacidins from the Octocoral-Associated *Bacillus* sp. DT001 Display Anti-Proliferative Effects in *Plasmodium falciparum*

Molecules 2018; 23, 2179; doi:10.3390/



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Lorena M. Coronado
Laura M. Pineda
Héctor M. Guzmán
Pieter C. Dorrestein
Carmenza Spadafora
Marcelino Gutiérrez

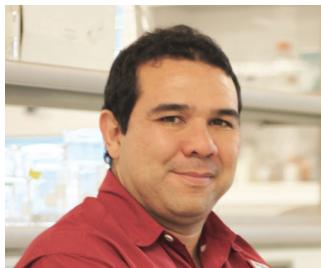
Abstract:

Chemical examination of the octocoral-associated *Bacillus* species (sp.) DT001 led to the isolation of pumilacidins A (1) and C (2). We investigated the effect of these compounds on the viability of *Plasmodium falciparum* and the mechanism of pumilacidin-induced death. The use of inhibitors of protein kinase C (PKC) and phosphoinositide 3-kinase (PI3K) was able to prevent the effects of pumilacidins A and C. The results indicated also that pumilacidins inhibit parasite growth via mitochondrial dysfunction and decreased cytosolic Ca^{2+} .

|| PUBLICACIONES ||

Agua Salud alphavirus defines a novel lineage of insect-specific alphaviruses discovered in the New World

Journal of General Virology. 2019; doi: 10.1099/jgv.0.001344



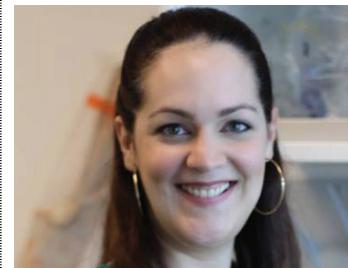
Kyra Hermanns
Marco Marklewitz
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Christian Drosten
Ronald P. van Rij
Sandra Junglen

Abstract:

The genus *Alphavirus* harbours mostly insect-transmitted viruses that cause severe disease in humans, livestock and wildlife. Thus far, only three alphaviruses with a host range restricted to insects have been found in mosquitoes from the Old World, namely Eilat virus (EILV), Taï Forest alphavirus (TALV) and Mwinilunga alphavirus (MWAV). In this study, we found a novel alphavirus in one *Culex declarator* mosquito sampled in Panama. The virus was isolated in C6/36 mosquito cells, and full genome sequencing revealed an 11 468 nt long genome with maximum pairwise nucleotide identity of 62.7 % to Sindbis virus. Phylogenetic analyses placed the virus as a solitary deep rooting lineage in a basal relationship to the Western equine encephalitis antigenic complex and to the clade comprising EILV, TALV and MWAV, indicating the detection of a novel alphavirus, tentatively named Agua Salud alphavirus (ASALV). No growth of ASALV was detected in vertebrate cell lines, including cell lines derived from ectothermic animals, and replication of ASALV was strongly impaired above 31 °C, suggesting that ASALV represents the first insect-restricted alphavirus of the New World.

The potential of invertebrate animal models for advancing science in the developing world

EMBO reports, 2019; Invertebrates, drugs and developing nations DOI 10.15252



Armando Castillo
Yila de la Guardia

Abstract:

Creating and expanding research and development (R&D) programs remains a challenge for developing and middle-income countries, but it is also a great potential for creating new industries, jobs and wealth. However, merely trying to catch up with the research infrastructure, scientific expertise and research output by developed nations is largely futile; fostering research requires different approaches.

Many Asian and Latin American countries have implemented national scholarship programmes to send students, junior and senior researchers abroad for scientific training in an effort to create qualified personnel so as to jumpstart local R&D upon their return. As a result, the publication rates of South American countries have doubled during the past decade, but still account for only 4% of the global publication volume [1], mainly owing to limited funding. It is therefore necessary to adopt additional, cost-efficient strategies to produce reliable data, within the funding constraints, that contribute to building a viable research infrastructure. In terms of biomedical research and drug discovery, this could involve investing into cheaper alternatives to rodent models for *in vivo* testing of drug candidates, such as invertebrate species, to decrease cost and time, and to stimulate new research areas and high-throughput (HTS) screening. Adopting research strategies based on HTS of invertebrate models, which are already benefiting research elsewhere, could thereby provide a boost for research in developing and middle-income countries.

PUBLICACIONES

Detecting space-time clusters of dengue fever in Panama after adjusting for vector surveillance data

Plos Neglected Tropical Diseases 2019; 13 (9): e0007266



Ari Whiteman
Michael R. Desjardins
Gilberto A. Eskildsen
Jose R. Loaiza

Abstract:

Long term surveillance of vectors and arboviruses is an integral aspect of disease prevention and control systems in countries affected by increasing risk. Yet, little effort has been made to adjust space-time risk estimation by integrating disease case counts with vector surveillance data, which may result in inaccurate risk projection when several vector species are present, and when little is known about their likely role in local transmission. Here, we integrate 13 years of dengue case surveillance and associated *Aedes* occurrence data across 462 localities in 63 districts to estimate the risk of infection in the Republic of Panama. Our exploratory space-time modelling approach detected the presence of five clusters, which varied by duration, relative risk, and spatial extent after incorporating vector species as covariates. The *Ae. aegypti* model contained the highest number of districts with more dengue cases than would be expected given baseline population levels, followed by the model accounting for both *Ae. aegypti* and *Ae. albopictus*. This implies that arbovirus case surveillance coupled with entomological surveillance can affect cluster detection and risk estimation, potentially improving efforts to understand outbreak dynamics at national scales.

Peridomestic small Indian mongoose: An invasive species posing as potential zoonotic risk for leptospirosis in the Caribbean

Acta Tropica 2019; 190:166-170



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Abstract:

In this study, we investigated *Leptospira* infection and exposure in small Indian mongoose (*Herpestes auropunctatus*), an invasive animal species, in two different sites in the Caribbean island of Saint Kitts. Overall a low seroprevalence (12/148; 8.1%; 95%CI: 3.7–12.5) was observed. Agglutinating antibodies to serovars Mankarso (3.4%), Copenhageni (2.7%), Icterohaemorrhagiae (1.4%), Bratislava (1.4%), Canicola (1.4%), Autumnalis (0.7%), Alexi (0.7%), Pomona (0.7%) and Grippotyphosa (0.7%) was observed on the microscopic agglutination test. The seroprevalence observed in mongooses trapped from peridomestic sites was significantly higher compared to the arid and less inhabited site ($p=0.0268$). The real time PCR targeting *lipL32* gene was positive for 9 out of 146 mongooses. Bacterial culture of kidneys resulted in two *Leptospira* isolates. Whole genome sequencing and analysis suggested that these isolates are closely related to *L. interrogans* serovar Copenhageni.

We observed mild to severe chronic renal lesions in 20.2% of mongooses in the absence of an antibody response or active infection. Our findings emphasize the need to investigate other infectious etiologies or atypical outcomes and potential chronic long-term impact of *Leptospira* infection in animals and people living in an endemic area. In addition, our data reinforces the need for including locally prevalent *Leptospira* isolates rather than representative members of a serogroup in the microscopic agglutination test panel in epidemiologic and diagnostic investigations. In conclusion, mongoose inhabiting the island are exposed to and harbor pathogenic *Leptospira* and hence may play a role in the transmission. The invasive nature of the species highlights their presence as a potential risk factor for this widespread zoonotic disease.

PUBLICACIONES

HLA Upregulation During Dengue Virus Infection Suppresses the Natural Killer Cell Response

Frontiers in Cellular and Infection Microbiology 2019;9:268



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Lisseth Saenz,
Ana B. Araúz,
Rosemary Vergara,
Eva Harris,
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Abstract:

Dengue virus (DENV) is the most prevalent mosquito-borne virus in the world and a major cause of morbidity in the tropics and subtropics. Upregulation of HLA class I molecules has long been considered a feature of DENV infection, yet this has not been evaluated in the setting of natural infection. Natural killer (NK) cells, an innate immune cell subset critical for mounting an early response to viral infection, are inhibited by self HLA class I, suggesting that upregulation of HLA class I during DENV infection could dampen the NK cell response. Here we addressed whether upregulation of HLA class I molecules occurs during *in vivo* DENV infection and, if so, whether this suppresses the NK cell response. We found that HLA class I expression was indeed upregulated during acute DENV infection across multiple cell lineages *in vivo*. To better understand the role of HLA class I upregulation, we infected primary human monocytes, a major target of DENV infection, *in vitro*. Upregulation of total HLA class I is dependent on active viral replication and is mediated in part by cytokines and other soluble factors induced by infection, while upregulation of HLA-E occurs in the presence of replication-incompetent virus. Importantly, blocking DENV-infected monocytes with a pan-HLA class I Fab nearly doubles the frequency of degranulating NK cells, while blocking HLA-E does not significantly improve the NK cell response. These findings demonstrate that upregulation of HLA class I during DENV infection suppresses the NK cell response, potentially contributing to disease pathogenesis.

Extracellular vesicles carrying lactate dehydrogenase induce suicide in increased population density of *Plasmodium falciparum* in vitro.

Sci Rep. 2019;9(1):5042. doi: 10.1038/s41598-019-41697-x.



Correa R, Coronado L, Caballero Z, Faral P, Robello C, Spadafora C,

Abstract:

Even with access to sufficient nutrients and atmosphere, *Plasmodium falciparum* can barely be cultured at maximum growth capacity *in vitro* conditions. Because of this behavior, it has been suggested that *P. falciparum* has self-regulatory mechanisms in response to density stress. Only recently has this process begun to be acknowledged and characteristics of a programmed cell death been assigned to the parasite at high parasitaemia *in vitro* cultures. In searching for death signals within the parasite community, we have found that extracellular vesicles (EVs) of *P. falciparum* from high parasitaemia cultures are able to induce programmed cell death processes in the population. A comparative proteomic analysis of EVs from low (EVL) and high (EVH) parasitaemia cultures was conducted, pointing to lactate dehydrogenase from *P. falciparum* (PfLDH) as the only parasite protein overexpressed in the later. Although the major function of *P. falciparum* lactate dehydrogenase (PfLDH) is the conversion of pyruvate to lactate, a key process in the production of energy in most living organisms, we investigated its possible role in the mechanism of parasite density control by intercellular signaling, given that PfLDH had already been listed as a component of extracellular vesicles of *P. falciparum*. In this study we present evidence of the EV-associated PfLDH regulation of parasite population by inducing apoptosis in highly parasitized cultures.

|| PUBLICACIONES ||

Optimización de la extracción asistida por ultrasonido y validación de un método HPLC-DAD para la cuantificación de polifenoles en extractos de hojas de especies de *Cecropia*.

Sci Rep. 2019 Feb 14;9(1):2028. doi: 10.1038/s41598-018-37607-2.



Rivera-Mondragón A
Broeckx G
Bijttebier S
Naessens T
Fransen E
Kiekens F
Caballero-George C
Vander Heyden Y
Apers S
Pieters L
Foubert K

Abstract:

Las especies de *Cecropia* se usan tradicionalmente en la medicina popular latinoamericana y están disponibles como complementos alimenticios con poca información que justifique su calidad. Las condiciones óptimas para la extracción de ácido clorogénico (CA), flavonoides totales (TF) y flavonolignanos (FL) de las hojas de especies de *Cecropia* se determinaron utilizando un diseño factorial fraccional (FFD) y un diseño compuesto central (CCD). Se validó un método de cromatografía líquida de alto rendimiento en fase inversa acoplado a un detector de matriz de diodos (HPLC-DAD) para la cuantificación de CA, TF y FL, siguiendo las pautas de ICH. También se realizó el Análisis Cuantitativo y de Componentes Principales (PCA). La metodología de extracción-optimización nos permitió desarrollar un proceso de extracción apropiado con una ejecución eficiente en el tiempo. Los valores experimentales coincidieron con los previstos, lo que indica la idoneidad del modelo propuesto. Los parámetros de validación para todos los marcadores químicos del método de cuantificación fueron satisfactorios. Los resultados revelaron que el método tenía una excelente selectividad, linealidad, precisión (la repetibilidad y la precisión intermedia estaban por debajo del 2 y 5%, respectivamente) y la precisión (98-102%). Los límites de detección y cuantificación fueron a nivel de nanogramos por millilitro (ng / mL). En conclusión, la cuantificación simultánea de marcadores químicos utilizando el método propuesto es un enfoque apropiado para la discriminación de especies y la evaluación de la calidad de *Cecropia* sp.

Iberoamerican Pharmacometrics Network Congress 2018 Report: Fostering Modeling and Simulation Approaches for Drug Development and Regulatory and Clinical Applications in Latin America

Journal: CPT: Pharmacometrics & Systems Pharmacology 2019;8(4):197-200



Manuel Ibarra, Teresa Costa, Paula Schaiquevich, Rodrigo Cristofoletti, Ignacio González, Nicte Fajardo-Robledo, Marcela Novoa, Marisín Pecchio, Ignacio Cortinez, Iñaki Trocóniz, and Elba Romero-Tejeda.

Abstract:

This report provides a brief description of the 2018 Red Iberoamericana de Farmacometría (RedIF) Congress that took place in Guadalajara (Mexico) on November 7-9, 2018. The meeting aimed to foster modeling and simulation (M&S) approaches for drug development, regulatory sciences, and clinical application in Latin America. The organizations that cosponsored the meeting were the following: University of Guadalajara, International Society of Pharmacometrics (ISoP), International Pharmaceutical Federation (FIP), Clinic of Chronic Diseases and Special Procedures (CECyPE), Zurich Pharma, Pharmet (Pharmometrica), Lixoft, and ICON.

PUBLICACIONES

100-year time series reveal little morphological change following impoundment and predator invasion in two Neotropical characids

Evolutionary Applications 2019;12(7):1385-1401



Ilke Geladi
Luis Fernando De León
Mark E. Torchin
Andrew P. Hendry
Rigoberto González
Diana M.T. Sharpe

Abstract:

Human activities are dramatically altering ecosystems worldwide, often resulting in shifts in selection regimes. In response, natural populations sometimes undergo rapid phenotypic changes, which, if adaptive, can increase their probability of persistence. However, in many instances, populations fail to undergo any phenotypic change, which might indicate a variety of possibilities, including maladaptation. In freshwater ecosystems, the impoundment of rivers and the introduction of exotic species are among the leading threats to native fishes. We examined how the construction of the Panama Canal, which formed Lake Gatun, and the subsequent invasion of the predatory *Cichla monoculus* influenced the morphology of two native fishes: *Astyanax ruberrimus* and *Roeboides* spp. Using a 100-year time series, we studied variation in overall body shape over time (before vs. after impoundment and invasion) as well as across space (between an invaded and an uninvaded reservoir). In addition, we examined variation in linear morphological traits associated with swim performance and predator detection/avoidance. Notwithstanding a few significant changes in particular traits in particular comparisons, we found only limited evidence for morphological change associated with these two stressors. Most observed changes were subtle, and tended to be site- and species-specific. The lack of a strong morphological response to these stressors, coupled with dramatic population declines in both species, suggests they may be maladapted to the anthropogenically perturbed environment of Lake Gatun, but direct measures of fitness would be needed to test this. In general, our results suggest that morphological responses to anthropogenic disturbances can be very limited and, when they do occur, are often complex and context-dependent.

Urbanization erodes niche segregation in Darwin's finches

Evolutionary Applications 2018;12(7):1329-1343



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Diana M. T. Sharpe
Kiyoko M. Gotanda
Joost A. M. Raeymaekers
Jaime A. Chaves
Andrew P. Hendry
Jeffrey Podos

Abstract:

Urbanization is influencing patterns of biological evolution in ways that are only beginning to be explored. One potential effect of urbanization is in modifying ecological resource distributions that underlie niche differences and that thus promote and maintain species diversification. Few studies have assessed such modifications, or their potential evolutionary consequences, in the context of ongoing adaptive radiation. We study this effect in Darwin's finches on the Galápagos Islands, by quantifying feeding preferences and diet niche partitioning across sites with different degrees of urbanization. We found higher finch density in urban sites and that feeding preferences and diets at urban sites skew heavily toward human food items. Furthermore, we show that finches at urban sites appear to be accustomed to the presence of people, compared with birds at sites with few people. In addition, we found that human behavior via the tendency to feed birds at non-urban but tourist sites is likely an important driver of finch preferences for human foods. Site differences in diet and feeding behavior have resulted in larger niche breadth within finch species and wider niche overlap between species at the urban sites. Both factors effectively minimize niche differences that would otherwise facilitate interspecies coexistence. These findings suggest that both human behavior and ongoing urbanization in Galápagos are starting to erode ecological differences that promote and maintain adaptive radiation in Darwin's finches. Smoothing of adaptive landscapes underlying diversification represents a potentially important yet underappreciated consequence of urbanization. Overall, our findings accentuate the fragility of the initial stages of adaptive radiation in Darwin's finches and raise concerns about the fate of the Galápagos ecosystems in the face of increasing urbanization.

PUBLICACIONES

Simplified Model to Survey Tuberculosis Transmission in Countries without Systematic Molecular Epidemiology Programs

Emerging Infectious Diseases -2019;25(3):507-514.



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Fermín Acosta
Laura Pérez-Lago
Dilcia Sambrano
Victoria Batista
Carolina De La Guardia
Estefanía Abascal
Álvaro Chiner-Oms
Iñaki Comas
Prudencio González
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Samantha Rosas
Patricia Muñoz
Amador Goodridge
Darío García de Viedma

Abstract:

Systematic molecular/genomic epidemiology studies for tuberculosis surveillance cannot be implemented in many countries. We selected Panama as a model for an alternative strategy. Mycobacterial interspersed repetitive unit-variable-number tandem-repeat (MIRU-VNTR) analysis revealed a high proportion (50%) of *Mycobacterium tuberculosis* isolates included in 6 clusters (A–F) in 2 provinces (Panama and Colon). Cluster A corresponded to the Beijing sublineage. Whole-genome sequencing (WGS) differentiated clusters due to active recent transmission, with low single-nucleotide polymorphism-based diversity (cluster C), from clusters involving long-term prevalent strains with higher diversity (clusters A, B). Prospective application in Panama of 3 tailored strain-specific PCRs targeting marker single-nucleotide polymorphisms identified from WGS data revealed that 31.4% of incident cases involved strains A–C and that the Beijing strain was highly represented and restricted mainly to Colon. Rational integration of MIRU-VNTR, WGS, and tailored strain-specific PCRs could be a new model for tuberculosis surveillance in countries without molecular/genomic epidemiology programs.

Environmental Conditions May Shape the Patterns of Genomic Variations in *Leishmania panamensis*

Genes 2019, 10, 838; doi:10.3390/genes10110838



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Alejandro Llanes
Eymi M. Cedeño
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José A. Suárez
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Abstract:

Due to the absence of transcriptional regulation of gene expression in *Leishmania* parasites, it is now well accepted that several forms of genomic variations modulate the levels of critical proteins through changes in gene dosage. We previously observed many of these variations in our reference laboratory strain of *L. panamensis* (PSC-1 strain), including chromosomes with an increased somy and the presence of a putative linear minichromosome derived from chromosome 34. Here, we compared the previously described genomic variations with those occurring after exposure of this strain to increasing concentrations of trivalent antimony (Sb^{III}), as well as those present in two geographically unrelated clinical isolates of *L. panamensis*. We observed changes in the somy of several chromosomes, amplifications of several chromosomal regions, and copy number variations in gene arrays after exposure to Sb^{III} . Occurrence of amplifications potentially beneficial for the Sb -resistant phenotype appears to be associated with the loss of other forms of amplification, such as the linear minichromosome. In contrast, we found no evidence of changes in somy or amplification of relatively large chromosomal regions in the clinical isolates. In these isolates, the predominant amplifications appear to be those that generate genes arrays; however, in many cases, the amplified arrays have a notably higher number of copies than those from the untreated and Sb -treated laboratory samples.

PUBLICACIONES

Treatment verification using Varian's dynalog files in the Monte Carlo system PRIMO

Radiation Oncology 2019; 23;14(1):67



Miguel Rodriguez
Lorenzo Brualla

Abstract:

Background: The PRIMO system is a computer software that allows the Monte Carlo simulation of linear accelerators and the estimation of the subsequent absorbed dose distributions in phantoms and computed tomographies. The aim of this work is to validate the methods incorporated in PRIMO to evaluate the deviations introduced in the dose distributions by errors in the positioning of the leaves of the multileaf collimator recorded in the dynalog files during patient treatment.

Methods: The reconstruction of treatment plans from Varian's dynalog files was implemented in the PRIMO system.

Dose distributions were estimated for volumetric-modulated arc therapy clinical cases of prostate and head&neck using the PRIMO fast Monte Carlo engine DPM. Accuracy of the implemented reconstruction methods was evaluated by comparing dose distributions obtained from the simulations of the plans imported from the treatment planning system with those obtained from the simulations of the plans reconstructed from the expected leaves positions recorded in the dynalog files. The impact on the dose of errors in the positions of the leaves was evaluated by comparing dose distributions estimated for plans reconstructed from expected leaves positions with dose distributions estimated from actual leaves positions. Gamma pass rate (GPR), a hereby introduced quantity named percentage of agreement (PA) and the percentage of voxels with a given systematic difference (α/Δ) were the quantities used for the comparisons. Errors were introduced in leaves positions in order to study the sensitivity of these quantities.

Results: A good agreement of the dose distributions obtained from the plan imported from the TPS and from the plan reconstructed from expected leaves positions was obtained. Not a significantly better agreement was obtained for an imported plan with an increased number of control points such as to approximately match the number of records in the dynalogs. When introduced errors were predominantly in one direction, the methods employed in this work were sensitive to dynalogs with root-mean-square errors (RMS) ≥ 0.2 mm. Nevertheless, when errors were in both directions, only RMS > 1.2 mm produced detectable deviations in the dose. The PA and the α/Δ showed more sensitive to errors in the leaves positions than the GPR.

Conclusions: Methods to verify the accuracy of the radiotherapy treatment from the information recorded in the Varian's dynalog files were implemented and verified in this work for the PRIMO system. Tolerance limits could be established based on the values of PA and α/Δ . GPR_{3,3} is not recommended as a solely evaluator of deviations introduced in the dose by errors captured in the dynalog files.

Matched Short-Term Depression and Recovery Encodes Interspike Interval at a Central Synapse

SCIENTIFIC REPORTS | (2018) 8:13629



Armando E. Castillo
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Jeremy E. Niven

Abstract:

Reversible decreases in synaptic strength, known as short-term depression (STD), are widespread in neural circuits. Various computational roles have been attributed to STD but these tend to focus upon the initial depression rather than the subsequent recovery. We studied the role of STD and recovery at an excitatory synapse between the fast extensor tibiae (FETi) and flexor tibiae (flexor) motor neurons in the desert locust (*Schistocerca gregaria*) by making paired intracellular recordings *in vivo*.

Over behaviorally relevant pre-synaptic spike frequencies, we found that this synapse undergoes matched frequency-dependent STD and recovery; higher frequency spikes that evoke stronger, faster STD also produce stronger, faster recovery. The precise matching of depression and recovery time constants at this synapse ensures that flexor excitatory post-synaptic potential (EPSP) amplitude encodes the presynaptic FETi interspike interval (ISI).

Computational modelling shows that this precise matching enables the FETi-flexor synapse to linearly encode the ISI in the EPSP amplitude, a coding strategy that may be widespread in neural circuits.

PUBLICACIONES

Identification of Major α -Glucosidase Inhibitors from Stem Bark of Panamanian Mangrove Plant *Pelliciera rhizophorae*

SCIENTIFIC REPORTS | (2018) 8:13629



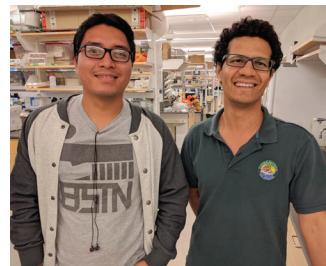
Lilia Cherigo
Sergio Martínez-Luis

Abstract:

In our continuous search for α -glucosidase inhibitors, three active pentacyclic triterpenes were isolated from stem bark samples of the Panamanian mangrove *Pelliciera rhizophorae* Triana & Planchon. These compounds were identified by both spectroscopic and spectrometric analysis. Of the isolated compounds, only betulinic acid has been previously isolated from *P. rhizophorae* leaves while both betulin (IC_{50} 2.09 μ M) and lupeol (IC_{50} 0.58 μ M) were isolated from this plant for the first time. All three pentacyclic triterpenes inhibited the α -glucosidase enzyme in a concentration-dependent manner, and their inhibitory activity was higher than that of the antidiabetic drug acarbose (IC_{50} 241.6 μ M). Kinetic analysis established that betulin and lupeol acted as competitive inhibitors. Finally, docking analysis suggested that all three triterpenes bind at the same site as acarbose does in the human intestinal α -glucosidase (PDB: 3TOP). This work contributes further evidence similar to previous studies that point out that the aerial parts of *P. rhizophorae* might be potential agents in controlling hyperglycemia in diabetic persons.

Mitogenomics of Central American weakly-electric fishes

Gene 686 (2019) 164-170



Celestino Aguilera
Matthew J. Miller
Jose R. Loaiza
Rüdiger Krahe
Luis F. De León

Abstract:

Electric fishes are a diverse group of freshwater organisms with the ability to generate electric organ discharges (EODs) that are used for communication and electrolocation. This group (ca. 200 species) has originated in South America, and six species colonized the Central American Isthmus. Here, we assembled the complete mitochondrial genomes (mitogenomes) for three Central American electric fishes (i.e. *Sternopygus dariensis*, *Brachyhypopomus occidentalis*, and *Apteronotus rostratus*), and, based on these data, explored their phylogenetic position among Gymnotiformes. The three mitogenomes show the same gene order, as reported for other fishes, with a size ranging from 16,631 to 17,093 bp. We uncovered a novel 60 bp intergenic spacer (IGS) located between the *COII* and *tRNA^{Lys}* genes, which appears to be unique to the Apteronotidae. Furthermore, phylogenetic relationships supported the traditional monophyly of Gymnotiformes, with the three species positioned within their respective family. In addition, the genus *Apteronotus* belongs to the early diverging lineage of the order. Finally, we found high sequence divergence (13%) between our *B. occidentalis* specimen and a sequence previously reported in GenBank, suggesting that the prior mitogenome of *B. occidentalis* represents a different South American species. Indeed, phylogenetic analyses using *Cytochrome b* gene across the genus placed the previously reported individual within *B. bennetti*. Our study provides novel mitogenome resources that will advance our understanding of the diversity and phylogenetic history of Neotropical fishes.

PUBLICACIONES

Tempo and mode of allopatric divergence in the weakly electric fish *Sternopygus dariensis* in the Isthmus of Panama

Scientific Reports (2019) 9:18828



Celestino Aguilar
Matthew J. Miller
Jose R. Loaiza
Rigoberto González
Rüdiger Krahe
Luis F. De León

Abstract:

Spatial isolation is one of the main drivers of allopatric speciation, but the extent to which spatially segregated populations accumulate genetic differences relevant to speciation is not always clear. We used data from ultraconserved elements (UCEs) and whole mitochondrial genomes (i.e., mitogenomes) to explore genetic variation among allopatric populations of the weakly electric fish *Sternopygus dariensis* across the Isthmus of Panama. We found strong genetic divergence between eastern and western populations of *S. dariensis*. Over 77% of the UCE loci examined were differentially fixed between populations, and these loci appear to be distributed across the species' genome. Population divergence occurred within the last 1.1 million years, perhaps due to global glaciation oscillations during the Pleistocene. Our results are consistent with a pattern of genetic differentiation under strict geographic isolation, and suggest the presence of incipient allopatric species within *S. dariensis*. Genetic divergence in *S. dariensis* likely occurred *in situ*, long after the closure of the Isthmus of Panama. Our study highlights the contribution of spatial isolation and vicariance to promoting rapid diversification in Neotropical freshwater fishes. The study of spatially-segregated populations within the Isthmus of Panama could reveal how genetic differences accumulate as allopatric speciation proceeds.

Fungus-Growing Ant's Microbial Interaction of *Streptomyces* sp. and *Escovopsis* sp. through Molecular Networking and MALDI Imaging

Natural Product Communications 2019; 14(1) 63 - 66



Cristopher A. Boya P.
Martin H. Christian
Hermógenes Fernández-Marín
Marcelino Gutiérrez

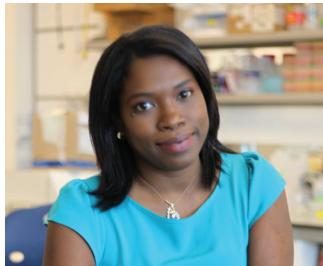
Abstract:

Microbes associated with fungus-growing ants represent a poorly explored source of natural products. In this study, we used mass spectrometry-based dereplication techniques for identifying a set of secondary metabolites produced during the microbial interaction between *Streptomyces* sp. (CB0028) and *Escovopsis* sp. (CBAcro424). Both microorganisms were isolated from the nest of the fungus-growing ant *Acromyrmex echinatior*. Through MALDI imaging and MS/MS molecular networking, we annotated the siderophores: desferrioxamine B (**1**), ferrioxamine B (**2**), ferrioxamine E (**3**) and the N-formylated peptide SCO-2138/SLI-2138 (**4**). MALDI imaging experiments suggest that siderophores occurred during the microbial interactions in the fungus-growing ants – microbes symbioses. This is the first report on the production of compounds **1-4** by bacteria associated with fungus-growing ants.

PUBLICACIONES

Image mean square displacement to study the lateral mobility of Angiotensin II type 1 and Endothelin 1 type A receptors on living cells.

Microscopy Research and Technique. 2019. doi: 10.1002/jemt.2342



Nadir Planes
Patrick P.M.L. Vanderheyden
Enrico Gratton
Catherina Caballero-George

Abstract:

The lateral mobility of membrane receptors provides insights into the molecular interactions of protein binding and the complex dynamic plasma membrane. The image mean square displacement (iMSD) analysis is a method used to extract qualitative and quantitative information of the protein diffusion law and infers how diffusion dynamic processes may change when the cellular environment is modified. The aim of the study was to describe the membrane diffusing properties of two G-protein-coupled receptors namely Angiotensin II type 1 (AT¹) and Endothelin 1 type A (ET^A) receptors and their corresponding receptor-ligand complexes in living cells using total internal reflection fluorescent microscopy and iMSD analysis. This study showed that both AT¹ and ET^A receptors displayed a mix of three modes of diffusion: free, confined, and partially confined. The confined mode was the predominant at the plasma membrane of living cells and was not affected by ligand binding. However, the local diffusivity and the confinement zone of AT¹ receptors were reduced by the binding of its antagonist losartan, and the long-range diffusion with the local diffusivity coefficient of ET^A receptors was reduced upon exposure to its antagonist BQ123. To the best of our knowledge, this is the first study addressing the protein diffusion laws of these two receptors on living cells using total internal reflection fluorescence microscopy and iMSD.

Temporally varying disruptive selection in the medium ground finch (*Geospiza fortis*).

Proc Biol Sci. 2019 Dec 4;286(1916):20192290.



Marc-Olivier Beausoleil , Luke O. Frishkoff , Leithen K. M'Gonigle , Joost A. M. Raeymaekers , Sarah A. Knutie , Luis F. De León , Sarah K. Huber , Jaime A. Chaves , Dale H. Clayton , Jennifer A. H. Koop , Jeffrey Podos , Diana M. T. Sharpe , Andrew P. Hendry† and Rowan D. H. Barrett

Abstract:

Disruptive natural selection within populations exploiting different resources is considered to be a major driver of adaptive radiation and the production of biodiversity. Fitness functions, which describe the relationships between trait variation and fitness, can help to illuminate how this disruptive selection leads to population differentiation. However, a single fitness function represents only a particular selection regime over a single specified time period (often a single season or a year), and therefore might not capture longer-term dynamics. Here, we build a series of annual fitness functions that quantify the relationships between phenotype and apparent survival. These functions are based on a 9-year mark-recapture dataset of over 600 medium ground finches (*Geospiza fortis*) within a population bimodal for beak size. We then relate changes in the shape of these functions to climate variables. We find that disruptive selection between small and large beak morphotypes, as reported previously for 2 years, is present throughout the study period, but that the intensity of this selection varies in association with the harshness of environment. In particular, we find that disruptive selection was strongest when precipitation was high during the dry season of the previous year. Our results shed light on climatic factors associated with disruptive selection in Darwin's finches, and highlight the role of temporally varying fitness functions in modulating the extent of population differentiation.

PUBLICACIONES

Number and brightness analysis to study spatio-temporal distribution of the angiotensin II AT¹ and the endothelin-1 ET^A receptors: Influence of ligand binding.

Biochim Biophys Acta Gen Subj. 2019 May;1863(5):917-924.



Nadir Planes
Michelle A. Digman
Patrick P.M.L. Vanderheyden
Enrico Grattan
Catherina Caballero-George

Abstract:

The angiotensin II AT₁ and the endothelin 1 ET_A receptors play a crucial role in the pathogenesis of cardiovascular diseases like hypertension, heart failure, stroke, pulmonary hypertension, and cardiac hypertrophy. Both receptors are members of the rhodopsin-like superfamily of G protein-coupled receptors which can exist as monomers, dimers, and higher order aggregates. Recently, oligomerization of these two receptors have been described by several biophysical methods based mainly on luminescence and fluorescence energy transfer. Since this oligomerization can occur either spontaneously or it can be induced by ligand-binding, the aim of this work was to address whether the oligomerization of these receptors occurs upon ligand-binding. For this purpose the Number and Brightness analysis, a method that allows the identification, localization, and quantification of protein aggregates in the plasma membrane of a single cell, was used. An advantage of this method is that it is not limited to certain dyes specially required for Fluorescence Resonance Energy Transfer measurements.

Our results showed that stably transfected angiotensin II AT₁ receptors and transiently transfected endothelin 1 ET_A receptors, were found as monomeric, dimeric, and tetrameric receptor aggregates. Interestingly, the binding of antihypertensive agents like losartan and BQ123, earlier suggested to be inverse agonists, significantly increased the proportion of monomers and reduced the occurrence of dimers on the cell membrane; while the known endothelin 1 ET_A antagonist sitaxentan did not influence the aggregation state of these receptors.

Amyotrophic lateral sclerosis-associated TDP-43 mutation Q331K prevents nuclear translocation of XRCC4-DNA ligase 4 complex and is linked to genome damage-mediated neuronal apoptosis

HUM MOL GENET. 2019;28(5):2459-2476. doi: 10.1093/hmg/ddz062



Guerrero EN
Mitra J, Wang H
Rangaswamy S
Hegde PM
Basu P
Rao KS
Hegde ML

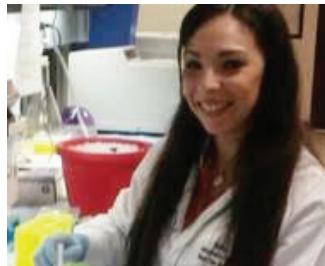
Abstract:

Dominant mutations in the RNA/DNA-binding protein TDP-43 have been linked to amyotrophic lateral sclerosis (ALS). Here, we screened genomic DNA extracted from spinal cord specimens of sporadic ALS patients for mutations in the TARDBP gene and identified a patient specimen with previously reported Q331K mutation. The patient spinal cord tissue with Q331K mutation showed accumulation of higher levels of DNA strand breaks and the DNA double-strand break (DSB) marker γH2AX, compared to age-matched controls, suggesting a role of the Q331K mutation in genome-damage accumulation. Using conditional SH-SY5Y lines ectopically expressing wild-type (WT) or Q331K-mutant TDP-43, we confirmed the increased cytosolic sequestration of the poly-ubiquitinated and aggregated form of mutant TDP-43, which correlated with increased genomic DNA strand breaks, activation of the DNA damage response factors phospho-ataxia-telangiectasia mutated (ATM), phospho-53BP1, γH2AX and neuronal apoptosis. We recently reported the involvement of WT TDP-43 in non-homologous end joining (NHEJ)-mediated DSB repair, where it acts as a scaffold for the recruitment of XRCC4-DNA ligase 4 complex. Here, the mutant TDP-43, due to its reduced interaction and enhanced cytosolic mislocalization, prevented the nuclear translocation of XRCC4-DNA ligase 4. Consistently, the mutant cells showed significantly reduced DNA strand break sealing activity and were sensitized to DNA-damaging drugs. In addition, the mutant cells showed elevated levels of reactive oxygen species, suggesting both dominant negative and loss-of-function effects of the mutation. Together, our study uncovered an association of sporadic Q331K mutation with persistent genome damage accumulation due to both damage induction and repair defects.

PUBLICACIONES

RT² PCR array screening reveals distinct perturbations in DNA damage response signaling in FUS-associated motor neuron disease.

Molecular Brain volume 12, Article number: 103 (2019)



Haibo Wang
Suganya Rangaswamy
Manohar Kodavati
Joy Mitra
Wenting Guo
Erika N. Guerrero
Ludo Van Den Bosch
Muralidhar L. Hegde

Abstract:

Amyotrophic lateral sclerosis (ALS) is a degenerative motor neuron disease that has been linked to defective DNA repair. Many familial ALS patients harbor autosomal dominant mutations in the gene encoding the RNA/DNA binding protein 'fused in sarcoma' (FUS) commonly inducing its cytoplasmic mislocalization. Recent reports from our group and others demonstrate a role of FUS in maintaining genome integrity and the DNA damage response (DDR). FUS interacts with many DDR proteins and may regulate their recruitment at damage sites. Given the role of FUS in RNA transactions, here we explore whether FUS also regulates the expression of DDR factors. We performed RT² PCR arrays for DNA repair and DDR signaling pathways in CRISPR/Cas9 FUS knockout (KO) and shRNA mediated FUS knockdown (KD) cells, which revealed significant (>2-fold) downregulation of BRCA1, DNA ligase 4, MSH complex and RAD23B. Importantly, similar perturbations in these factors were also consistent in motor neurons differentiated from an ALS patient-derived induced pluripotent stem cell (iPSC) line with a FUS-P525L mutation, as well as in postmortem spinal cord tissue of sporadic ALS patients with FUS pathology. BRCA1 depletion has been linked to neuronal DNA double-strand breaks (DSBs) accumulation and cognitive defects. The ubiquitin receptor RAD23 functions both in nucleotide excision repair and proteasomal protein clearance pathway and is thus linked to neurodegeneration. Together, our study suggests that the FUS pathology perturbs DDR signaling via both its direct role and the effect on the expression of DDR genes. This underscores an intricate connections between FUS, genome instability, and neurodegeneration.

Host-associated microbiomes drive structure and function of marine ecosystems

PLOS Biology 3000533 November 11, 2019



Laetitia G. E. Wilkins , Matthieu Leray , Aaron O'Dea, Benedict Yuen, Raquel S. Peixoto, Tiago J. Pereira, Holly M. Bik, David A. Coil, J. Emmett Duffy, Edward Allen Herre, Harilaos A. Lessios, Noelle M. Lucey, Luis C. Mejia, Douglas B. Rashner, Koty H. Sharp, Emilia M. Sogin, Robert W. Thacker, Rebecca Vega Thurber, William T. Wcislo, Elizabeth G. Wilbanks, Jonathan A. Eisen

Abstract:

The significance of symbioses between eukaryotic hosts and microbes extends from the organismal to the ecosystem level and underpins the health of Earth's most threatened marine ecosystems. Despite rapid growth in research on host-associated microbes, from individual microbial symbionts to host-associated consortia of significantly relevant taxa, little is known about their interactions with the vast majority of marine host species. We outline research priorities to strengthen our current knowledge of host–microbiome interactions and how they shape marine ecosystems. We argue that such advances in research will help predict responses of species, communities, and ecosystems to stressors driven by human activity and inform future management strategies.

Reproducible Molecular Networking Of Untargeted Mass Spectrometry Data Using GNPS.

Preprint submitted on 07.08.2019, 10:27 and posted on 08.08.2019, 14:42



Allegra T. Aron Emily Gentry Kerry L. McPhail Louis Felix Nothias Mélissa Nothias-Esposito Amina Bouslimani Daniel Petras Julia M. Gauglitz Nicole Sikora Fernando Vargas Justin J. J. van der Hooft Madeleine Ernst Kyo Bin Kang Christine M. Aceves Andrés Mauricio Caraballo-Rodríguez Irina Koester Kelly C. Weldon Samuel BERTRAND Catherine Roullier Kunyang Sun Richard M. Tehan Christopher A. Boya Christian Martin H. Marcelino Gutiérrez Aldo Moreno Ulloa Javier Andres Tejeda Mora Randy Mojica-Flores Johant Lakey-Beitia Victor Vásquez-Chaves Angela I. Calderón Nicole Tayler Robert A. Keyzers Fidele Tugizimana Nombuso Ndlovu Alexander A. Aksenov Alan K. Jarmusch Robin Schmid Andrew W. Truman Nuno Bandeira Mingxun Wang Pieter Dorrestein

Abstract:

Herein, we present a protocol for the use of Global Natural Products Social (GNPS) Molecular Networking, an interactive online chemistry-focused mass spectrometry data curation and analysis infrastructure. The goal of GNPS is to provide as much chemical insight for an untargeted tandem mass spectrometry data set as possible and to connect this chemical insight to the underlying biological questions a user wishes to address. This can be performed within one experiment or at the repository scale. GNPS not only serves as a public data repository for untargeted tandem mass spectrometry data with the sample information (metadata), it also captures community knowledge that is disseminated via living data across all public data. One of the main analysis tools used by the GNPS community is molecular networking. Molecular networking creates a structured data table that reflects the chemical space from tandem mass spectrometry experiments via computing the relationships of the tandem mass spectra through spectral similarity. This protocol provides step-by-step instructions for creating reproducible high-quality molecular networks. For training purposes, the reader is led through the protocol from recalling a public data set and its sample information to creating and interpreting a molecular network. Each data analysis job can be shared or cloned to disseminate the knowledge gained, thus propagating information that can lead to the discovery of molecules, metabolic pathways, and ecosystem/community interactions.

Carotenoids as Novel Therapeutic Molecules Against Neurodegenerative Disorders: Chemistry and Molecular Docking Analysis.

Int J Molecular Sciences 2019, 20(22), 5553



Johant Lakey
Jagadeesh Kumar
Hegde ML
Rao KS

Abstract:

Alzheimer's disease (AD) is the most devastating neurodegenerative disorder that affects the aging population worldwide. Endogenous and exogenous factors are involved in triggering this complex and multifactorial disease, whose hallmark is Amyloid- β (A β), formed by cleavage of amyloid precursor protein by β - and γ -secretase. While there is no definitive cure for AD to date, many neuroprotective natural products, such as polyphenol and carotenoid compounds, have shown promising preventive activity, as well as helping in slowing down disease progression. In this article, we focus on the chemistry as well as structure of carotenoid compounds and their neuroprotective activity against A β aggregation using molecular docking analysis. In addition to examining the most prevalent anti-amyloidogenic carotenoid lutein, we studied cryptocapsin, astaxanthin, fucoxanthin, and the apocarotenoid bixin. Our computational structure-based drug design analysis and molecular docking simulation revealed important interactions between carotenoids and A β via hydrogen bonding and van der Waals interactions, and shows that carotenoids are powerful anti-amyloidogenic molecules with a potential role in preventing AD, especially since most of them can cross the blood-brain barrier and are considered nutraceutical compounds. Our studies thus illuminate mechanistic insights on how carotenoids inhibit A β aggregation. The potential role of carotenoids as novel therapeutic molecules in treating AD and other neurodegenerative disorders are discussed.

PUBLICACIONES

A comparison of inducible, ontogenetic, and interspecific sources of variation in the foliar metabolome in tropical trees

PeerJ. 2019; doi:10.7717/peerj.7536



Brian E. Sedio
Armando Duran Archibald
Juan Camilo Rojas Echeverri
Chloé Debyser
Cristopher A. Boya
S. Joseph Wright

Abstract:

Plant interactions with other organisms are mediated by chemistry, yet chemistry varies among conspecific and within individual plants. The foliar metabolome—the suite of small-molecule metabolites found in the leaf—changes during leaf ontogeny and is influenced by the signaling molecule jasmonic acid. Species differences in secondary metabolites are thought to play an important ecological role by limiting the host ranges of herbivores and pathogens, and hence facilitating competitive coexistence among plant species in species-rich plant communities such as tropical forests. Yet it remains unclear how inducible and ontogenetic variation compare with interspecific variation, particularly in tropical trees. Here, we take advantage of novel methods to assemble mass spectra of all compounds in leaf extracts into molecular networks that quantify their chemical structural similarity in order to compare inducible and ontogenetic chemical variation to among-species variation in species-rich tropical tree genera. We ask (i) whether young and mature leaves differ chemically, (ii) whether jasmonic acid-inducible chemical variation differs between young and mature leaves, and (iii) whether interspecific exceeds intraspecific chemical variation for four species from four hyperdiverse tropical tree genera. We observed significant effects of the jasmonic acid treatment for three of eight combinations of species and ontogenetic stage evaluated. Three of the four species also exhibited large metabolomic differences with leaf ontogenetic stage. The profound effect of leaf ontogenetic stage on the foliar metabolome suggests a qualitative turnover in secondary chemistry with leaf ontogeny. We also quantified foliar metabolomes for 45 congeners of the four focal species. Chemical similarity was much greater within than between species for all four genera, even when within-species comparisons included leaves that differed in age and jasmonic acid treatment. Despite ontogenetic and inducible variation within species, chemical differences among congeneric species may be sufficient to partition niche space with respect to chemical defense.

Flavonoids from *Boldea purpurascens* inhibit proinflammatory cytokines (TNF- α and IL-6) and the expression of COX-2

Phytother Res. 2018 Sep;32(9):1750-1754. doi: 10.1002/ptr.6104.



D.M. González Mosquera
Y. Hernández Ortega
P.L. Fernández
Y. González
D. Doens
Y. Vander Heyden
K. Fouquet
L. Pieters

Abstract:

The flavonoids comprise a large class of plant metabolites distributed in food plants. These compounds have antioxidant, antitumor, antiallergic, and anti-inflammatory effects. The molecular mechanisms of their biological activities remain to be clearly understood. We investigated the *in vitro* anti-inflammatory potential of a flavonoid mixture and isolated compounds from the leaves of *Boldea purpurascens*. Our results provide direct evidence of the anti-inflammatory effects of the mixture, which are mediated by the inhibition of the proinflammatory cytokines tumor necrosis factor α and interleukin 6 as well as the modulation of the expression of cyclooxygenase 2.

|| PUBLICACIONES ||

Viscosin-like lipopeptides from frog skin bacteria inhibit *Aspergillus fumigatus* and *Batrachochytrium dendrobatidis* detected by imaging mass spectrometry and molecular networking

Sci Rep. 2019;9(1):3019



Christian Martin H.
Roberto Ibáñez
Louis-Félix Nothias
Cristopher A. Boya P.
Laura K. Reinert
Louise A. Rollins-Smith
Pieter C. Dorrestein
Marcelino Gutiérrez

Abstract:

Amphibian populations worldwide have declined and in some cases become extinct due to chytridiomycosis, a pandemic disease caused by the fungus *Batrachochytrium dendrobatidis*; however, some species have survived these fungal epidemics. Previous studies have suggested that the resistance of these species is due to the presence of cutaneous bacteria producing antifungal metabolites. As our understanding of these metabolites is still limited, we assessed the potential of such compounds against human-relevant fungi such as *Aspergillus*. In this work we isolated 201 bacterial strains from fifteen samples belonging to seven frog species collected in the highlands of Panama and tested them against *Aspergillus fumigatus*. Among the 29 bacterial isolates that exhibited antifungal activity, *Pseudomonas cichorii* showed the greatest inhibition. To visualize the distribution of compounds and identify them in the inhibition zone produced by *P. cichorii*, we employed MALDI imaging mass spectrometry (MALDI IMS) and MS/MS molecular networking. We identified viscosin and massetolides A, F, G and H in the inhibition zone. Furthermore, viscosin was isolated and evaluated in vitro against *A. fumigatus* and *B. dendrobatidis* showing MIC values of 62.50 µg/mL and 31.25 µg/mL, respectively. This is the first report of cyclic depsipeptides with antifungal activity isolated from frog cutaneous bacteria.

A multi-faceted genotoxic network of alpha-synuclein in the nucleus and mitochondria of dopaminergic neurons in Parkinson's disease: Emerging concepts and challenges.

Prog Neurobiol. 2019 Dec 18:101729. doi: 10.1016/j.pneurobio.2019.101729



Vasquez V.
Mitra J
Wang H
Hegde PM
Rao KS
Hegde ML

Abstract:

α -Synuclein is a hallmark amyloidogenic protein component of the Lewy bodies (LBs) that are found in dopaminergic neurons affected by Parkinson's disease (PD). Despite an enormous increase in emerging knowledge, the mechanism(s) of α -synuclein neurobiology and crosstalk among pathological events that are critical for PD progression remains enigmatic, creating a road-block for effective intervention strategies. One confounding question is about the potential link between α -synuclein toxicity and genome instability in PD. We previously reported that pro-oxidant metal ions, together with reactive oxygen species (ROS), act as a "double whammy" in dopaminergic neurons by not only inducing genome damage but also inhibiting their repair. Our recent studies identified a direct role for chromatin-bound, oxidized α -synuclein in the induction of DNA strand breaks, which raised the question of a paradoxical role for α -synuclein's DNA binding in neuroprotection versus neurotoxicity. Furthermore, recent advances in our understanding of α -synuclein mediated mitochondrial dysfunction, warrants revisiting the topics of α -synuclein pathophysiology in order to devise and assess the efficacy of α -synuclein-targeted interventions. In this review article, we discuss the multi-faceted neurotoxic role of α -synuclein in the nucleus and mitochondria with a particular emphasis on the role of α -synuclein in DNA damage/repair defects. We utilized a protein-DNA binding simulation to identify potential residues in α -synuclein that could mediate its binding to DNA and may be critical for its genotoxic functions. We also discuss the crosstalk of α -synuclein toxicity with the RNA binding protein, TDP-43. These emerging insights and paradigms may guide new drug targets and therapeutic modalities.

|| PUBLICACIONES ||

Thermo-Energetic study in blood Infected with *Plasmodium falciparum* radiated at 2.45 GHz.

EuMC 2019 (European Microwave Conference), 2019; doi:10.23919/EuMC.2019.8910930



Ng, K. D.
Plazaola, C.
González, G
Spadafora, C.
Zambrano, M.

Abstract:

Malaria is a disease that affects the world, caused by the parasite Plasmodium which resistance is emerging to medications that usually control it. Therefore, it is essential to seek alternative treatments like this one, our multidisciplinary work pursues, a variable radiofrequency energy at 2.45GHz to decrease the growth of parasitemia in blood. Experiments are carried on in vitro samples of blood infected with *Plasmodium falciparum* radiated in a microwave cavity controlling the rise of the temperature. The thermal properties of samples infected at different stages of the parasite are analyzed separately without using microwave radiation for thermal characterization. The energy absorbed by the infected sample is estimated using the specific heat of blood with *Plasmodium falciparum*. For thermo energetic control, radiation is applied in different duty cycles for a determined amount of energy observing an alteration which it is accentuated in energy radiation with more duty cycles and less power in watts. Our preliminary results show that thermo-energetic control system produce alterations in the growth of parasitemia levels. Furthermore, we confirm that using microwave radiation has a negative effect in the growth of *Plasmodium falciparum*. There is also, an increment of the specific heat as the parasitemia percentage increase in late stage parasites because in schizonts the *Plasmodium falciparum* changes the biophysical properties of the red blood cell. This thermo-energetic characterization could be transferred to in vivo samples, with the necessary adjustments for future applications.

LA UNIDAD DE FÍSICA E INGENIERÍA BIOMÉDICA DE INDICASAT-AIP ADQUIERE EQUIPOS SOFISTICADOS DE MMI (ALEMANIA) Y OLYMPUS (JAPÓN)



Doriana Dorta será la asistente de investigación a cargo del manejo de la operación de las pinzas ópticas y otras tecnologías de los nuevos equipos en INDICASAT-AIP.

El recientemente adquirido equipo comprende pinzas ópticas, un micromanipulador, un dispositivo de medición de nanofuerza y un selector de células. Las pinzas ópticas son capaces de detener nanopartículas con el uso de rayos láser. Los campos de fuerza generados por los láseres son capaces de ejercer una presión sobre las partículas, y usando dos rayos dirigidos al objeto desde dos direcciones exactamente opuestas, los dos láseres detienen y manipulan el objetivo entre los campos. Esto permite, entre otras cosas, la aplicación de fuerzas de tensión o de presión que pueden dar información exacta sobre las propiedades físicas de una nanopartícula. El CellXtor, otro de los aparatos instalados, puede marcar células individuales o partículas de interés y colectarlas,

una o muchas a la vez, para depositarlas en un pozillo o en un microtubo para su uso posterior. Uno de los primeros proyectos en usar la nueva tecnología utilizará las pinzas ópticas para medir la elasticidad de los glóbulos rojos sanos o infectados con el parásito de la malaria, *Plasmodium falciparum*. La caracterización de nanomateriales utiliza con frecuencia esta tecnología.

Este equipo fue adquirido a través de financiamiento competitivo de la Secretaría Nacional de Ciencia, Innovación y Tecnología de Panamá. Estará disponible para usuarios de cualquier institución que quieran realizar estudios utilizando esta tecnología. Doriana Dorta estará a cargo de servir a los usuarios de este equipamiento.

Nutrición y Cerebro

Centro de Asuntos Académicos

Si bien el cuerpo humano nunca dejará de maravillar e intrigar al sector científico y a la sociedad en general. Los recientes estudios y las capacidades desarrolladas por los investigadores nos han acercado más a conocer el desarrollo y el funcionamiento del cerebro que funge como centro de control del cuerpo para todos los seres humanos.

Profundizando en esta realidad, se han explorado diversas condiciones que afectan positiva o negativamente al cerebro y su funcionamiento. El interés creciente en las neurociencias ha catapultado la necesidad de obtener datos e información sobre los principales impulsos o variantes que afectan su desarrollo. En aquella búsqueda se destaca la relación entre la alimentación y el sano desenvolvimiento del cerebro.

Las cifras y los resultados no mienten, la dieta escogida conlleva efectos beneficiosos o adversos a la salud del cerebro. La preferencia por ciertos nutrientes impacta los procesos cognitivos e incluso el plano emocional. Puede o no provocar envejecimiento prematuro, diversas condiciones mentales y físicas a distintos niveles.

El impacto de la nutrición mantiene un rol relevante a lo largo de todo el ciclo de vida, es una figura decisiva durante las etapas de crecimiento: gestación, primera infancia, niñez y adolescencia.

El campo de investigación sobre esta importante materia es amplio y la necesidad de dar a conocer la capacidad de los nutrientes y su importante papel dentro nuestra salud física y mental es la principal motivación para instaurar, bajo nuestro planteamiento estratégico, un programa sobre Nutrición y el Cerebro.

Este programa se desarrolla bajo las perspectivas de colaboración y educación, especialmente dirigido a niños y niñas en la primera etapa de la adolescencia; busca constituir un producto de valor entre la población que empieza a definir un ritmo de vida propio, a tomar decisiones sobre qué y cómo comer y a practicar actividades físicas relevantes.

Para el desarrollo de este desafío, se inició con un proyecto Taller. INDICASAT solicitó la colaboración de uno de los líderes mundiales en Neu-

rociencias, IBRO (International Brain Research Organization), en el territorio panameño, bajo la visión de crecer en comunidad se unió con un aliado estratégico, Pacífica Salud, primer hospital en el país al afiliado del John Hopkins Medicine International.

El grupo hospitalario brindó al programa dos importantes exponentes como la Licenciada María José Martín quien desarrolló la sesión de Nutrición y Adolescencia y la Licenciada Luisa García, Nutricionista, quien expuso sobre la Aventura de los Nutrientes.

La Jornada de este primer proyecto fue dirigida a estudiantes adolescentes de colegios provenientes de áreas alrededor de la ciudad de Panamá. Zonas de alto riesgo social donde los chicos no han tenido la oportunidad de interactuar y experimentar la ciencia de la mano de científicos y médicos profesionales.

En la primera parte de la jornada, se inició con las palabras de introductorias del Director del Instituto, Dr. Jagannatha Rao, quien expuso sobre “El Entendimiento del Cerebro humano”, le siguió La Dra. Marisín Peccio quien habló sobre la visión



de Instituto sobre la nutrición de los panameños y se contó con el aporte de la Doctora Anilena Mejía, representante de la UNICEF, quien expuso a la audiencia, el rol de Organización en el desarrollo de los niños.

En la segunda parte de la jornada en sesión de la Doctora Martín, se introdujo el valor y la importancia de la nutrición en la etapa en la que los chicos viven, todo lo que significa para sus cuerpos los alimentos que reciben. La doctora María realizó varios ejercicios sobre las rutinas diarias para que los chicos aprendieran sobre cómo pueden rescatar nutrición de una amplia variedad de menús, también jugaron a armar platos basados en combinaciones saludables y hábitos para alimentar cuerpo y mente.

Por parte del Instituto, la sesión fue dirigida por el Dr. Armando Durant, investigador del Centro de Descubrimientos de Drogas y Biodiversidad quien acompañado de un grupo de sus mejores estudiantes universitarios, brindó una exposición dinámica sobre

las Frutas y los Vegetales presentes en el territorio nacional y su enorme valor nutricional. Durante la sesión, los estudiantes pudieron aprender sobre cada una de los cultivos que se realizan en Panamá. Desde su constitución nutricional, su variedad hasta las aplicaciones en cocina, medicina y vida diaria.

Cerrando la sesión de Charlas, La doctora Luisa García, expuso el camino que toman los nutrientes en el cuerpo y la mente y la labor que realizan en nuestros órganos, funciones y desarrollo. De una forma divertida en un contexto de aventuras y misiones, cada estudiante invitado reconoció el valor de la buena alimentación.

Luego de las sesiones los estudiantes recorrieron de la mano de los científicos, los laboratorios de INDICASAT durante 3 horas. Allí pudieron aprender de primera mano, el trabajo que se realiza en la Institución y lo que representa para el país. Los chicos, entusiasmados, hicieron todo tipo de preguntas, apreciaron experimentos y procedimientos estándares y conocieron la trayectoria de nuestros

científicos.

El resultado de la visita les permitió tener conciencia sobre las acciones que se llevan a cabo en los centros de investigación y desarrollo del Instituto, también les permitió visibilizar un camino dentro de la ciencia y sobre todo reconocer esa capacidad que todos tenemos de explorar y experimentar nuestro alrededor.

El Objetivo de INDICASAT, es elevar el alcance del programa durante una segunda etapa y llevar ciencia e innovación al campo de la nutrición. Con un especial énfasis en los recursos o cultivos que podemos encontrar en cada región del país como vegetales, frutos y granos.

La retroalimentación obtenida de los participantes y el desarrollo de la experiencia prometen el inicio de un compromiso a largo plazo a beneficio de la sociedad, especialmente del sector juvenil.

Nutrition and Brain

**Centro de Asuntos
Académicos**

Although the human body will never cease to amaze and intrigue the scientific sector and society in general. Recent studies and capabilities developed by researchers have brought us closer to knowing the functioning of the brain, control center for all human beings.

Going deeper into this reality, various conditions that positively or negatively affect the brain and its functioning have been explored. The growing interest in neurosciences has increased the need to obtain data and information on the main impulses or variants that affect its development. In that search, the relationship between food and healthy brain development stands out.

The facts and the results do not lie; the chosen diet has beneficial or adverse effects on brain health. The preference for certain nutrients impacts cognitive processes and even the emotional side. It may or may not cause premature aging, various mental and physical conditions at different levels.

The impact of nutrition maintains a relevant role throughout the entire life

cycle; it is a decisive figure during the growth stages: pregnancy, early childhood, childhood and adolescence.

The field of research on this important subject is wide and the need to publicize the capacity of nutrients and their important role in our physical and mental health is the main motivation to establish, under our strategic approach, a program on Nutrition and Brain.

This program is developed under the perspectives of collaboration and education, specially aimed at children in the first stage of adolescence; seeks to constitute a product of value among the population that begins to define a rhythm of their own life, to make decisions about what and how to eat and to practice relevant physical activities.

For the development, the Institute requested the collaboration of one of the world leaders in Neurosciences, IBRO (International Brain Research Organization). In the Panamanian territory, under the vision of growing in community, we joined with a strategic ally, Pacifica Salud, the first hospital in the country to the affiliate from

John Hopkins Medicine International.

The hospital group provided two important speakers for the program, such as Ms. María José Martín who developed the Nutrition and Adolescence session and Ms. Luisa García, Nutritionist, who presented on the Nutrient Adventure.

This first project was aimed at teenage students from schools in high social risk communities where children cannot interact and experience science with professional scientists and doctors.

In the first part of the day, The workshop began with introductory words from the Director of the Institute, Dr. Jagannatha Rao, who spoke on "The Understanding of the Human Brain", followed by Dr. Marisin Pecchio who spoke about the vision of the institute on the nutrition of Panamanians and the contribution of Dr. Anilena Mejia, UNICEF representative, who presented to the audience, the role of Organization in the development of children.

In the second part the session of Dr. Martin, the value and importance of



nutrition was introduced, health and all that means for their bodies the food they receive. Dr. Maria did several exercises on daily routines so that the children learned about how they can take nutrition from a wide variety of menus, they also played putting together dishes based on healthy combinations and habits to feed body and mind.

On behalf of the Institute, the session was directed by Dr. Armando Durant, a researcher at the Center for Drug and Biodiversity Discoveries who, accompanied by a group of his best university students, gave a dynamic exhibition on the Fruits and Vegetables present in the national territory and its enormous nutritional value. During the session, the students were able to learn about each of the crops that are cultivated in Panama. Crops nutritional constitution and the variety of applications in cooking, medicine and daily life.

Closing the session of talks, Dr. Luisa Garcia explained the path taken by nutrients in the body and mind and

the work they do in our organs, functions and development. In a fun way in a context of adventures and missions, each guest student recognized the value of good food.

After the sessions, the students toured the laboratories of INDICASAT for 3 hours. There they were able to learn from first hand, the work that is done in the institution and what it represents for the country. The students, excited, asked all kinds of questions, appreciated standard experiments and procedures and learned about the trajectory of our scientists.

The result of the visit allowed them to be aware of the actions that are carried out in the research and development centers of the Institute, it also allowed them to make visible a path within science and above all to recognize that capacity we all have to explore and experience around us.

The objective of INDICASAT AIP is to raise the scope of the program during a second stage and to bring science and innovation into nutrition

grounds. With a special emphasis on the natural resources and crops that we can find in each region of the country such as vegetables, fruits, and grains.

The feedback obtained from the participants and the whole experience promises the beginning of a long-term commitment to the benefit of the society, especially in young people.

3er Taller Anual sobre StartUps y Transferencia de Tecnología “Desarrollando una Economía Impulsada por la Innovación: Biodiversidad y Tecnología en la Estrategia de Desarrollo de Panamá”

12-13 de junio de 2019, Panamá, República de Panamá

Dra. Catherina Caballero-George
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Dr. Thomas Richardson,
Richardson & Choi.

El Instituto de Investigación Científica y Servicios de Alta Tecnología (INDICASAT-AIP), con el apoyo de la Secretaría de Ciencia, Tecnología e Innovación (SENACYT), el Ministerio del Medio Ambiente (MIAMBIENTE) y el Programa de las Naciones Unidas para el Desarrollo (PNUD), organizó el 3er. Taller anual sobre startups y transferencia de tecnología

“Desarrollo de una economía impulsada por la innovación: biodiversidad y tecnología en la estrategia de desarrollo de Panamá”, los días 12 y 13 de junio de 2019, en el Radisson Summit Hotel Golf & Spa, Paraíso, Panamá.

Este evento da continuidad al programa concebido e iniciado por INDICASAT-AIP en 2017 con el objetivo de crear y estimular las capacidades empresariales locales dentro de la academia. Este año se le dio un interés especial a la industria basada en la biodiversidad, dada la larga historia de científicos panameños que investigan el potencial medicinal de la biodiversidad de este país. Los temas específicos incluyeron: crear una estrategia de desarrollo económico impulsado por la innovación, la industria basada en la tecnología de la información y la comunicación en Panamá, estudio de caso de una institución emprendedora modelo de ciencias de la vida, estudio de caso de un Start Up basado en bioprospección y desafíos importantes en bioprospección en Panamá.

Para esta capacitación de dos días, estuvieron involucrados líderes empresariales con vasta experiencia en el sector académico de los Estados Unidos. El Dr. Thomas Richardson es presidente de una exitosa empresa

de consultoría especializada en la creación de nuevas empresas. Actualmente es el presidente del Institute for Life Sciences Entrepreneurship, un instituto de investigación sin fines de lucro, acelerador de negocios e incubadora de descubrimientos de ciencias de la vida para mejorar la salud humana, incluidos nuevos medicamentos, dispositivos y tecnologías transformadoras. El Dr. David Martin es el Director y Fundador de Martín Pharma Consulting, LLC, una empresa de consultoría de nicho enfocada en ayudar a las pequeñas empresas de biotecnología a desarrollar y ejecutar planes de desarrollo preclínicos, clínicos y reglamentarios estratégicamente sólidos. Es un científico de desarrollo experimentado en todas las fases del desarrollo de medicamentos y un exitoso agente de recaudación de fondos públicos y privados.

“Este taller anual es un excelente foro para líderes académicos, industriales y gubernamentales para compartir ideas y desarrollar estrategias para promover el desarrollo económico a través de la ciencia y la tecnología. El ecosistema panameño tiene tantos recursos únicos y me

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ha impresionado mucho el progreso durante los últimos 3 años hacia el desarrollo de objetivos comunes para capitalizar de manera responsable estos activos. Las continuas inversiones financieras en investigación básica y aplicada y el compromiso de los líderes del ecosistema presentan una oportunidad emocionante para el crecimiento económico y laboral. INDICASAT- AIP ha hecho un trabajo excepcional desarrollando esta serie de talleres” - dijo el Dr. Richardson.

Más de 40 personas que representan a más de 17 universidades, empresas e instituciones gubernamentales se registraron y hasta 100 espectadores siguieron este taller en el canal de YouTube de INDICASAT-AIP.

Entre los participantes se encontraban el Vicerrector de Investigación y Estudios de Posgrado de la Universidad Autónoma de Chiriquí, el Gerente de Asuntos Científicos del Instituto Smithsonian de Investigaciones Tropicales, así como el Director



Dr. David Martin,
Martin Pharma Consulting, LLC.

de Investigación del Instituto Gorgas Memorial de Estudios de Salud y el Director de Áreas Protegidas y Fauna del Ministerio del Medio Ambiente.

“El 3er Taller Anual en Start-ups y Transferencia de Tecnología fue un escaparate para el creciente movimiento empresarial de Panamá en el espacio de la biotecnología. Utilizando la biodiversidad que se encuentra en el ecosistema panameño, los científicos están buscando la próxima generación de tratamientos contra enfermedades que no solo se puedan usar localmente sino también a nivel mundial.” “Este movimiento está siendo impulsado por INDICASAT AIP, y la conferencia, organizada por la Dra. Catherine Cabellero-George, incluyó representantes locales de la academia y el gobierno, así como oradores internacionales con experiencia en negocios y descubrimiento de drogas. Dado el entusiasmo y la pasión de los asistentes, se debe esperar un progreso significativo en el cultivo y el desarrollo de oportunidades de negocios de biotecnología en los próximos años.” - señaló el Dr. Martin.

Los asistentes tuvieron la oportunidad de evaluar el evento. Entre los comentarios, se destacaron los siguientes:

“Me ayudó mucho a establecer alianzas con otras instituciones, a obtener

nuevas perspectivas a partir de las exposiciones y sobre todo permite que como grupo se presenten propuestas concretas a los entes tomadores de decisiones a nivel gubernamental y privado.”

“Considero que el taller fue un éxito. Los temas son una guía para afinar los elementos y criterios para un diagnóstico nacional sobre emprendimiento.

Los expositores tuvieron éxito ajustando el escenario de sus ponencias a la realidad local/nacional, para dar paso a la parte propositiva con los participantes...

Además, pienso que se debe buscar una estrategia para dejar plasmada, una visión de plan nacional de Bioprospección como un “proceso” sujeto a ser revisado y actualizado periódicamente.”



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3rd Annual Workshop on Startups and Technology Transfer “Developing an Innovation-Driven Economy: Biodiversity and Technology in Panamanian Development Strategy”

June 12-13, 2019, Panama, Republic of Panama

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Dr. Thomas Richardson,
Richardson & Choi.

The Institute of Scientific Research and High Technology Services (INDICASAT-AIP), with the support of the Secretariat of Science, Technology and Innovation (SENACYT), the Ministry of Environment (MINAMBIENTE) and the United Nations Development Program (UNDP), organized the 3rd Annual Workshop on Startups and Technology Transfer

“Developing an Innovation-Driven Economy: Biodiversity and Technology in Panamanian Development Strategy”, on June 12 and 13, 2019, at the Radisson Summit Hotel Golf & Spa, Paraiso, Panama.

This event gives continuity to the program conceived and initiated by INDICASAT AIP in 2017 with the aim of creating and stimulating local entrepreneurial capacities within the academia. This year a special interest was given to industry based on biodiversity, given the long history of Panamanian scientists investigating the medicinal potential of this country's biodiversity. Specific topics included: creating a strategy of economic development driven by innovation, information and communication technology based industry in Panama, case study of model life sciences entrepreneurial institution, case study of a Start Up based in bioprospection, and major challenges in bioprospection in Panama.

For this two-day training, entrepreneurial leaders with vast experience with academic sector of the United States were involved. Dr. Thomas Richardson is president of a successful consulting company specializing in the creation of startups. He is currently the president of the Institute

for Life Sciences Entrepreneurship, a non-profit research institute, business accelerator and incubator of life science discoveries to improve human health, including new medicines, devices and transformative technologies. Dr. David Martin is the Principal and Founder of Martin Pharma Consulting, LLC, a niche consulting company focused on assisting small biotech companies develop and execute strategically sound pre-clinical, clinical, and regulatory development plans. He is an experienced development scientist in all phases of drug development and a successful private and public fund raising agent.

“This annual workshop is an excellent forum for academic, industrial, and governmental leaders to share ideas and develop strategies to promote economic development through science and technology. The Panamanian ecosystem has so many unique resources and I have been very impressed by the progress over the past 3 years toward developing common goals to capitalize responsibly on these assets. Continued financial investments in basic

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and applied research and commitment from the leaders in the ecosystem present an exciting opportunity for economic and job growth. INDICASAT AIP has done an outstanding job developing this series of workshops” - said Dr. Richardson.

More than 40 people representing more than 17 universities, companies and government institutions were registered and up to 100 viewers followed this workshop on INDICASAT’s YouTube channel.

Among the participants were the Vice Chancellor for Research and Post-graduate Studies of the Autonomous University of Chiriquí, the Manager for Scientific Affairs of the Smithsonian Tropical Research Institute as well as the Research Director of the Gorgas Memorial Institute for Health Studies and the Director of Protected Areas and Wildlife of the Ministry of Environment.



Dr. David Martin,
Martin Pharma Consulting, LLC.

“The 3rd Taller Anual en Start-ups y Transferencia de Tecnología was a showcase for Pa-

nama’s growing entrepreneurial movement in the biotechnology space. Using the biodiversity found in the Panamanian ecosystem, scientists are looking for the next generation of treatments against diseases that can not only be used locally but also on the global stage.” “This movement is being fostered by INDICASAT AIP, and the conference, as organized by Dr. Catherina Cabellero-George, included local representatives from academia and government as well as international speakers with expertise in business and drug discovery. Given the enthusiasm and passion of the attendees, significant progress in cultivating and developing biotechnology business opportunities should be expected over the coming years.” – pointed out Dr. Martin.

The attendees had the opportunity to evaluate the event. Among the comments, the following were highlighted:

“It helped me a lot to establish alliances with other institutions, to obtain new perspectives from the presentations and above all it allows as a group to present concrete proposals to the decision-making entities at the governmental and private level.”

“I think the workshop was a success. The themes were a guide to refine the elements and criteria for a national diagnosis on entrepreneurship. The exhibitors were successful in adjusting the scenario of their presentations to the local / national reality, to give way to the proposition with the participants ... In addition, I think the aim should look for a strategy to capture, a vision of the National Bioprospecting plan as a “process” subject to review and update periodically.”



DÍA FAMILIAR INDICASAT-AIP 2019

La familia de todos los colaboradores del instituto asistieron al primer día familiar organizado por la administración, junto al equipo científico quienes siempre apoyan éstas iniciativas en pro de la educación y más aún de la familia. Investigadores de la talla de Luis Mejía, que investiga los hongos que atacan a la planta del café, José Loaiza cuya investigación se centra en los mosquitos y las enfermedades que transmiten, y Rolando Gittens quien compartió su investigación y las estructuras elaboradas en el taller de bioinformática, todos con un lenguaje amigable para sus pequeños oyentes, quienes felices y habidos de conocimiento hicieron múltiples preguntas que maravillaron a los investigadores y a sus padres.



SEMINARIO “GLOBAL BIODIVERSITY AND CONSERVATION OF FUNGI”



Por el Dr. David Minter de CABI UK.

Dr. Minter es el Presidente de la sociedad internacional para la conservación de Hongos y Presidente de la copa hongos, trufas y sus aliados el grupo especialista de la unión internacional para la conservación de la naturaleza (IUCN).



1ER TALLER DE ESTRATEGIAS DE CONSERVACIÓN PARA LOS HONGOS DE AMÉRICA LATINA Y EL CARIBE



El Dr. Luis Mejia da las palabras de bienvenida a todos los colegas de diferentes países al taller.



Apertura del taller por el Sr. Emilio Sempris, Ministro de Ambiente.



Palabras de bienvenida por el Dr. Jagannatha Rao, Director del INDICASAT AIP.



Información sobre el programa y desarrollo del taller por el Dr. Julio Mena, preside el grupo de conservación de los hongos de la asociación latinoamericana de Micología.

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El Dr. Julio Mena comparte antecedentes y la actualidad de la conservación de los hongos en América Latina y el Caribe.



El Lic. Darío Luque, Ministerio de Ambiente Panamá expone la legislación y conservación en Panamá.



Presentación de Matriz DAFO por país o región por Cecilia C. Carmaran, desde el 1er Taller Estrategia de Conservación para los Hongos de América Latina y el Caribe.



La situación actual de los aspectos relacionados con la conservación de los hongos en Brasil, por Luis F. P. Gusmão.



Situación de Chile en conservación de hongos por Daniela Torres, Fundación Funji.



Materias de trabajo DOFA conservación de Hongos en Colombia por Aida Vasco.

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Conservación de hongos en Costa Rica por Julieta Carranza.



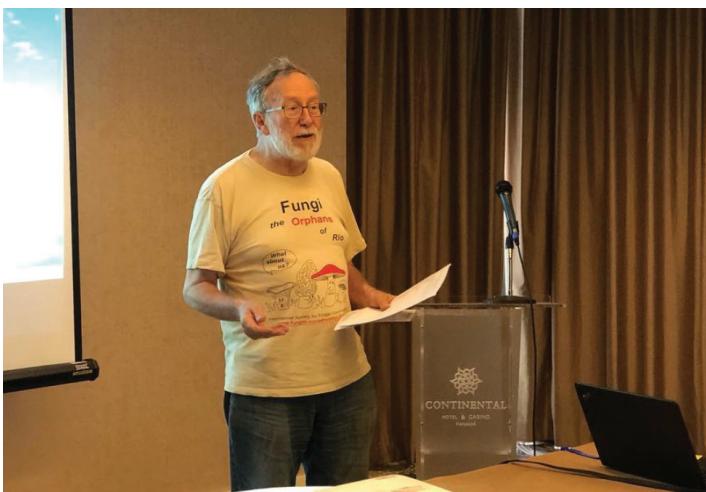
Matriz DAFO sobre la conservación de los Hongos en Cuba por Julio Mena, Instituto de Ecología y Sistemática, Cuba.



Estado de conservación de los hongos en el Ecuador por Paul Gamboa Trujillo, Universidad Central de Ecuador.



Estado de la conservación de hongos en Panamá por Luis Mejía, INDICASAT AIP, Panamá.



Presentación de la Matriz DAFO por región por David W. Minter, CABI



El equipo que analiza las debilidades y las amenazas está listo para presentarlas al grupo completo.

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El equipo que analiza las fortalezas y oportunidades está listo para presentarlas al grupo completo.



gira de campo para recolecta de hongos e identificación desde el Campana Parque nacional



Grupo completo de la gira de campo a Campana Parque nacional en le marco del 1er taller de estrategias de conservación para los hongos de América Latina y el Caribe.

“CELEBRANDO A LAS NIÑAS EN LA CIENCIA”



Como parte de la celebración del 11 de febrero, día internacional de la mujer y la niña en la ciencia, fecha instaurada por la Organización de las Naciones Unidas en 2015 para ayudar a aumentar la visibilidad del trabajo de las mujeres en STEAM (Ciencia, Tecnología, Ingeniería, Matemáticas y Arte). En base a esta importante fecha se desarrolló el taller “CELEBRANDO A LAS NIÑAS EN LA CIENCIA” dirigido a estudiantes de 6to grado con el fin de que conozcan la labor desarrollada por las mujeres en la ciencia en un contexto histórico con énfasis en el caso de Panamá y de promover el pensamiento científico e innovador en jóvenes de Panamá ayudando de esta forma a romper la brecha de género. Esta actividad se llevó a cabo el día 29 de marzo del 2019, en las instalaciones de INDICASAT- AIP. El evento contó con sesiones interactivas de biología, química, neurociencias y robótica.

En ésta primera entrega participaron 20 estudiantes de colegio y 2 profesores acompañantes.

CONFERENCIAS



Sesión interactiva de robótica con los chicos de Panamá-stem enseñando matemáticas con una caña de pescar



Sesión interactiva de robótica con los chicos de Panamá-stem enseñando matemáticas con una caña de pescar



Niñas de la Escuela Samaria Sinai.



Sesión interactiva de química por Andrea Burillo.



Sesión interactiva de biología, usamos la fresa para extraer el ADN de la fresa, por la Dra. Yisett González.



Sesión interactiva de biología, usamos la fresa para extraer el ADN de la fresa

CURSO DE BUENAS PRÁCTICAS CLÍNICAS



Grupo que participó junto a los Expositores del Instituto Pfizer para la Ciencia y la Investigación.



II SIMPOSIO DE BIODIVERSIDAD Y METAGENÓMICA



El Dr. Luis Fernando De León.



The electrosensory world of weakly electric fish,
por el Dr. Rüdiger Kramer.



Populations genomics and speciation in neotropical electric fishes, por el Dr. Carlos Arias



Dynamics and diversity of bacteria associated with the ecological competitors and disease vectors Aedes aegypti and Aedes albopictus, por Kelly Bennett.

SEMINARIO “BIOLOGY AND EVOLUTION OF RUST FUNGI WITH AN EMPHASIS ON HEMILEIA VASTATRIX (COFFEE RUST FUNGUS)

Dictado por la Dra. Mary Catherine Aime.



Dra. Mary Catherine Aime



Dra. Mary Catherine Aime



Dr. Luis Mejia



Dr. Luis Mejia

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NPS PANAMÁ 2019

II SIMPOSIO INTERNACIONAL SOBRE QUÍMICA, BIOLOGÍA Y
PROPIEDADES FARMACOLÓGICAS DE PRODUCTOS NATURALES,
EL IV SIMPOSIO IBEROAMERICANO DE INVESTIGACIÓN EN CÁNCER Y
EL IX SIMPOSIO IBEROAMERICANO SOBRE PLANTAS MEDICINALES.



Dr. Mauricio Caraballo, Universidad de California, San Diego, USA. Exponiendo la Plataforma global de redes moleculares comunitarias de productos naturales (GNPS)



Dr. Marcelino Gutiérrez da la bienvenida al NPS Panamá 2019



Dr. Mahabir Gupta da la bienvenida a los participantes del NPS Panamá 2019



Dr. William H. Gerwick abre la sección de conferencias con el tema: Anti-parasitic drug discovery in Panama.

CONFERENCIAS



Dra. Kerry L. McPhail expone el tema: *Natural products and metabolomics of south african tunicate-microbe consortia.*



Dr. Alfonso Mangoni, con el tema: *Challenges in the elucidation of stereochemistry of natural products.*



Entrega de la medalla Dr. Arturo Melo a la ciencia, al Dr. Mahabir Gupta en reconociendo por su extraordinaria labor en la ciencia de Panamá.



Entrega de placa de reconocimiento al Dr. Arturo San Feliciano por su trabajo y trayectoria en la ciencia.

CONFERENCIAS



Entrega de placa de reconociendo al Dr. João Ernesto Carvalho por su trabajo y trayectoria en la ciencia.



Entrega de placa de reconocimiento al Dr. Pieter C. Dorrestein por su trabajo y trayectoria en la ciencia.



Entrega de placa de reconocimiento al Dr. William H. Gerwick por su trabajo y trayectoria en la ciencia.

CONFERENCIAS



Dr. Daniel Petras da inicio a la segunda lectura corta con el tema: *Visualization of the chemical interaction of marine microbial Communities.*



Andres Tejada Mora expone el tema: *Untargeted metabolomic and molecular networking analysis of microorganisms from marine sediments of the Gulf of Mexico.*



Dr. Pieter C. Dorrestein inicia la plenaria de la tarde con el tema: *Global natural product social molecular networking - capturing and dissemination of knowledge by the community.*



Madeleine Ernst comparte el tema: *Digitizing chemoevolution: Chemical informs distance metrics for tandem mass spectrometry data.*



Dr. Norberto Peporine Lopes expone el tema: *Integrative metabolomics analysis of the brazilian biodiversity.*



Dra. Rachel Mata Expone el tema: *α -Glucosidases inhibitors from plants and fungi.*

CONFERENCIAS



Dra. Laura Grauso expone el tema: *Molecular networking based profiling of cytotoxic saponins from sea cucumber Holothuria atra.*



Librada Atencio, estudiante de doctorado expone el tema: *Genome mining of Pseudoalteromonas associated yo octocorals from Coiba National Park, Panama*



Dr. Luis Mejia expone el tema: *Exploring the chemical basis of microbiome mediated protection to diseases in the crop plant Coffea arabica.*



Dra. Lorena Coronado expone el tema: *Cytotoxic activity against breast cancer cells of local Justicia segunda vahl crude extract.*



Dr. Valdir Cechinel Filho con la plenaria: *Nature as a source of substances with therapeutic potential: state of the art and perspective.*



Dr. Arturo San Feliciano expone el tema: *Antineoplastic and antiparasitic agents with dual pharmacophores based on natural compounds.*

CONFERENCIAS



Dr. Mahabir Gupta expone el tema: *Biodiversity of Panama: untapped source of bioactive molecules.*



Dr. Matthias Hamburger con el tema: *HPLC-based activity profiling for pharmacologically and toxicologically relevant natural product-principles and recent examples.*



Dr. Rudolf Bauer expone el tema: *The role of the gut microbiome for the activity of herbal medicinal products.*



Dr. Sergio Martínez finaliza la sesión de la mañana con el tema: *Biological evaluation of some selected mangrove plants species of Panama.*



Sesión de póster en el NPS PANAMÁ 2019.

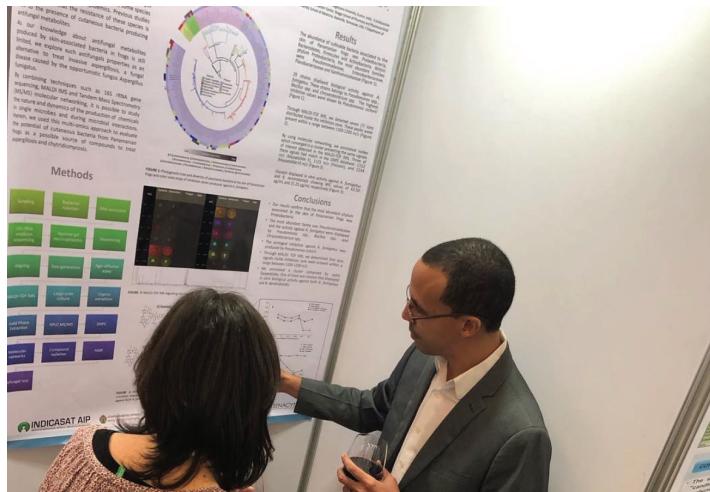
CONFERENCIAS



Sesión de póster en el NPS PANAMÁ 2019.



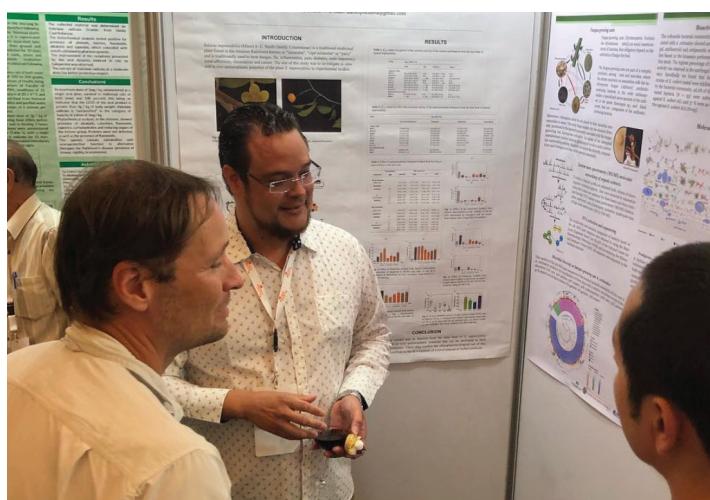
Sesión de póster en el NPS PANAMÁ 2019.



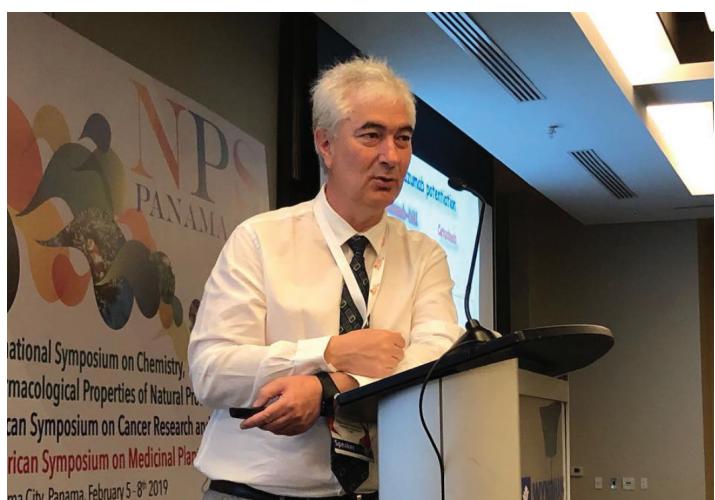
Sesión de póster en el NPS PANAMÁ 2019.



Sesión de póster en el NPS PANAMÁ 2019.



Dr. Valdir Cechinel Filho con la plenaria: *Nature as a source of substances with therapeutic potential: state of the art and perspective.*



Dr. Atanasio Pandiella con el tema: *Precision therapy in cancer.*

CONFERENCIAS



Dr. João Ernesto Carvalho Expone el tema: *Screening and development of anti-cancer drugs from plants.*



Dr. Jean-Lic Wolfender expone el tema: *Change of paradigm in pharmacognosy-prioritization of bioactive natural products using massive multi-informational molecular networks.*



Dr. Yoshinori Asakawa expone el tema: *Highlights in photochemistry of liverworts: biological activity.*



Dra. Ángela Calderon expone el tema: *Mass spectrometry-based strategies to assess bioactivities of natural products.*



Dra. Karin M. Monteiro expone el tema: *Ehrlich solid cancer model and laboratory animal suffering: can we get a better response from our mice?*



Dra. Susana A. Zacchino expone el tema: *Insights into the ability of natural products to inhibit planktonic fungi and eradicate biofilm communities, acting alone and in combination.*

CONFERENCIAS



Dr. Andrés Maurio Caraballo-Rodríguez expone el tema: *Molecular signatures for fungal garden-ant ecosystem.*



Dr. Marcelino Gutiérrez expone el tema: *Symbiotic microorganisms from Panama and their potential in drug discovery.*



Dr. Pawan K. Agrawal. Some contributions to natural product research.



Ganador en la categoría posters: 1er lugar Cristopher Boya.



Ganador en la categoría posters: 2do lugar, Christian Martin.



Ganador en la categoría posters: 3er lugar Erick Puertas.

CONFERENCIAS

Release of Special of
Communications [NPC]
Panama 2019



Ganador en la categoría posters: 3er lugar Johan Lakey.



Equipo de INDICASAT AIP que apoyó estos 4 días en el desarrollo del NPS PANAMÁ 2019.



Grupo de expositores del NPS PANAMÁ 2019.



NPS PANAMÁ 2019, Panorámica del grupo completo de participantes, expositores y asistentes.

PASA UN DÍA CON CIENTÍFICOS DE INDICASAT-AIP

Mgtr. Dilcia Sambrano
Lab Manager
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Los niños son curiosos por naturaleza y a esa edad todo lo que gira a su alrededor es impresionante. Es de allí la iniciativa de INDICASAT – AIP de que estos niños puedan conocer la labor que realizan los investigadores de nuestro Instituto. Este proyecto de Pasa un día con científicos, está diseñado para que nuestros investigadores en un lenguaje científico pero sencillo para la edad de estos niños, puedan ir introduciendo esa semillita del interés por la ciencia. La dinámica principal de esta visita fue que los estudiantes interactuaran con cada uno de los investigadores que se encontraban en las diferentes áreas donde los llevamos a recorrer. El recorrido inicio en el área de Neurociencias donde ellos pudieron preguntarles a los investigadores del área sus inquietudes sobre el cerebro y su funcionamiento. Uno de los lugares favoritos de nuestros pequeños visitantes fue el laboratorio de las abejas el cual pertenece al área de biodiversidad; Aquí pudieron aprender sobre las abejas y el proceso de la producción de miel y los diferentes tipos de abejas que viven dentro da un panal la forma como



conviven, lo que más les gusto es que cada una de esta abejas tiene una función importante para el funcionamiento del panal y lo relacionaron con la función de cada persona en la sociedad. Otro laboratorio de gran interés fue el de los mosquitos en donde los investigadores les explicaron los diferentes estadios de vida del mosquito. Además les hablaron de algunas enfermedades trasmitidas por los mosquitos presentes en nuestro país y como ellos podían ayudar a combatirlos en sus hogares y comunidades. En el laboratorio de parasitología tuvieron la oportunidad de observar placas en el microscopio de los diferentes estadios de los parásitos y aprender

con los investigadores de esta área las enfermedades causadas por estos organismos. Fue de mucha motivación para ellos todas las recomendaciones que les dieron los investigadores de cada área en la importancia del estudio para ser investigadores para ser profesionales.

El final de recorrido culmino con un taller de robótica para niños, diseñando con legos y circuito especializado de fácil armando en donde pusieron en práctica sus habilidades y compartieron con sus compañeros y con los investigadores del área de bioinformática. A través de la metodología de juego y el armado de modelos con estas piezas de lego, lograron

|| CONFERENCIAS ||

introducir a los niños en el mundo de la computación y la programación usando las computadoras. Logrando que comprendieran de manera práctica las ventajas del internet y las computadoras sus diferentes usos en la ciencia y en la robótica.

Al finalizar su visita compartieron un refrigerio con los investigadores del programa y nos hablaron de su experiencia y lo que más les había gustado del recorrido del laboratorio. Para su sorpresa se les tenía un incentivo a los niños que tuvieron una destacada participación a lo largo del recorrido. Se les entregó un sobre con un incentivo por su atención e interés en cada uno de los temas vistos en el laboratorio y a cada uno se le entregó un certificado de su visita.

Para INDICASAT AIP como instituto de formación académica es importante que la niñez panameña sea motivada al estudio y tenga modelos de ciencia a seguir en la sociedad lo que a futuro aumentaría número de investigadores en el país.



Estudiante destacada de la sección de preguntas y respuestas.



SPEND A DAY WITH INDICASAT-AIP SCIENTISTS

Mgtr. Dilcia Sambrano
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Children are curious by nature and at that age everything that revolves around them is impressive. This is the initiative of INDICASAT - AIP so that these children can learn about the work carried out by the researchers of our Institute. This project Spend a day with scientists, is designed so that our researchers in a scientific language but simple for the age of these children, can be introducing that little seed of interest in science.

The main dynamic of this visit was that students interact with each of the researchers who were in the different areas where we took them to tour. The tour began in the Neurosciences area where they were able to ask the researchers of the area their concerns about the brain and its functioning. One of the favorite places of our little visitors was the laboratory of the bees which belongs to the biodiversidad area; Here they were able to learn about bees and the process of honey production and the different types of bees that live inside a honeycomb the way they live together, what they liked most is that each of these bees has an important function for func-



Featured student of the questions and answers section.

tioning of the honeycomb and related to the role of each person in society. Another laboratory of great interest was that of the mosquitoes where the researchers explained the different stages of the mosquito's life. They also told them about some diseases transmitted by the mosquitoes present in our country and how they could help fight them in their homes and communities. In the parasitology laboratory they had the opportunity to observe plates in the microscope of the different stages of the parasites and learn with the researchers in this area the diseases caused by these organisms. It was very motivating for them all the recommendations

that the researchers of each area gave them in the importance of the study to be researchers to be professionals. The end of the tour culminated with a robotics workshop for children, designed with laymen and an easy-to-assemble specialized circuit where they put their skills into practice and shared with their colleagues and with researchers in the bioinformatics area. Through the game methodology and the assembly of models with these lego pieces, they managed to introduce children to the world of computing and programming using computers. Getting them to understand in a practical way the advantages of the internet and computers their different

uses in science and robotics.

At the end of their visit they shared a snack with the researchers of the program and told us about their experience and what they liked most about the laboratory tour.

To his surprise, there was an incentive for children who had an outstanding participation along the way. They were given an envelope with an incentive for their attention and interest in each of the topics seen in the laboratory and each one was given a certificate of their visit.

For INDICASAT AIP as an academic training institute it is important that Panamanian children are motivated to study and have science models to follow in society, which in the future would increase the number of researchers in the country.



Dr. Hermogenes Fernandez explains to children the importance of bees.



Seminario “Toxoplasmosis: Una enfermedad con graves implicaciones desde el punto de vista congénito y crónico”



Moderador: Dr. Xavier Sáez Llorens-Director del Departamento de infectología, Hospital del Niño José Renán Esquivel.



Lic. Mariangela Soberón, Investigadora asociada de INDICASAT-AIP “La toxoplasmosis congénita en Panamá, introducción y marco regulatorio”.



Dra. Zuleima Caballero, expone el tema: “Epidemiología y genética de Toxoplasmosis en Panamá. Un estudio integral del parásito en humanos, animales domésticos y silvestres”.



Dra. Rima Mcleod, Directora del Toxoplasmosis Center, Universidad de Chicago, con el tema: “Entendiendo y eliminando la Toxoplasmosis Congénita”.

Webinar En busca de un socio industrial



*Innovation-Driven Partnering Overview for Academics.
Por el Dr. Thomas P. Richardson*



*Dra. Catherina Caballero inicia la presentación del
Webinar - En busca de un socio industrial.*



*Dr. Thomas P. Richardson expone el tema:
Innovation-Driven Partnering Overview for Academics.*



*Dr. Thomas P. Richardson expone el tema:
Innovation-Driven Partnering Overview for Academics.*

Miembros del Sistema Nacional de Investigadores (SNI) 2018



Investigadores que son nuevos miembros del Sistema Nacional de Investigación (SNI).



Nuevos miembros Categoría de Estudiantes 2018 del Sistema Nacional de Investigación (SNI).



Investigadores de Cuarto Reingreso 2018, Miembros del Sistema Nacional de Investigadores (SNI)



Investigadores de Tercer Reingreso 2018, Miembros del Sistema Nacional de Investigadores (SNI)

ENTREGAN EL PREMIO L'ORÉAL-UNESCO “POR LAS MUJERES EN LA CIENCIA” EN PANAMÁ

FUNDACION LOREAL PARA LAS MUJERES EN LA CIENCIA

La Dra. Lorena Coronado, investigadora posdoctoral del Instituto de Investigaciones Científicas y Servicios de Alta Tecnología (INDICASAT AIP), recibió hoy el Premio Nacional L'Oréal-UNESCO “Por las Mujeres en la Ciencia” correspondiente al año 2018.

El Premio Nacional L'Oréal-UNESCO “Por las Mujeres en la Ciencia” es una iniciativa apoyada por la Secretaría Nacional de Ciencia, Tecnología e Innovación (SENACYT), que surgió en el marco del programa internacional L'Oréal-UNESCO “For Women in Science”, que ya ha recompensado la labor de más de dos mil mujeres científicas en unos 115 países.

La Dra. Coronado resultó ganadora con el proyecto “Diseño y prueba de aplicadores *in vitro* para el uso de energía electromagnética contra el parásito de la malaria” y recibirá B/. 10,000.00 para desarrollarlo.

El tratamiento de parásitos protozoarios, como el causante de la malaria, sigue siendo un reto mundial, pues causan más de un millón de muertes anualmente. Con este proyecto, la Dra. Coronado propone diseñar y estandarizar un dispositivo no invasivo y que

no requiera utilizar drogas, sino la energía electromagnética, para el tratamiento de la malaria. “Mi objetivo principal es lograr establecer un dispositivo aplicador de energía electromagnética que simule las condiciones del sistema real de una persona infectada por este parásito para, de esta forma, pasar a realizar las pruebas *in vivo*”, detalló la investigadora.

El periodo de postulación al Premio Nacional L'Oréal-UNESCO “Por las Mujeres en la Ciencia” de 2018 se inició el 30 de agosto y cerró el 12 de octubre de 2018. La adjudicación del Premio se realizó el pasado 23 de noviembre.

En la primera edición del Premio Nacional L'Oréal-UNESCO “Por las Mujeres en la Ciencia”, en 2017, se recibieron 11 postulaciones y se premiaron dos proyectos sobre Ciencias Biológicas, resultando ganadoras la Dra. María Beatriz Carreira (INDICASAT AIP) y la Dra. Laura Patiño (UNACHI).

Este año, se escogería un solo proyecto de investigación en el área de Física, Ingeniería o Informática. En total se recibieron 6 postulaciones, 5 de las cuales

fueron en el campo de la Ingeniería y una en el área de Física.

El Dr. Jorge A. Motta, Secretario Nacional de la SENACYT, señaló que *“con este galardón, la SENACYT busca reconocer el papel determinante de la mujer en las ciencias para el desarrollo de investigaciones que promuevan el avance económico, social y cultural de los países”*.

“La lista de desafíos es larga y variada, y la ciencia es el principal medio para lograr alcanzarlos. Preservar la biodiversidad, desentrañar los secretos de los genes, encontrar la cura para ciertas enfermedades, explorar el cosmos. La humanidad debe apoyarse sobre la máxima cantidad de espíritus brillantes y creativos, para hacer frente a los grandes desafíos del mañana”, señaló Anthony Ponsford, Presidente Director General de L'Oréal Centroamérica.

“En este contexto marcado por un sentimiento de urgencia, la ciencia debe movilizar todos los recursos intelectuales del planeta, de los cuales la mitad son mujeres. En cada continente, en todos los niveles, ellas dedican sus vidas

al avance del conocimiento para hacer progresar a la humanidad. Tengamos presente siempre que: el mundo necesita ciencia, la ciencia necesita mujeres, porque las mujeres científicas tienen el poder de cambiar el mundo”, agregó Ponsford.

Perfil de la Dra. Lorena Coronado

Lorena Coronado Vásquez estudió la Licenciatura en Biotecnología en Argentina. Realizó sus estudios de Doctorado en Biotecnología de la Universidad Acharya Nagarjuna dentro del programa de INDICASAT-IFARHU-SENACYT. Actualmente es Investigadora Postdoctoral en el Centro de Biología Celular y Molecular de Enfermedades de INDICASAT AIP. Desde el año 2009 estudia las interacciones de las ondas electromagnéticas en sistemas biológicos. Sus estudios de Doctorado se basaron en encontrar el mecanismo de acción de las microondas sobre el parásito causante de la malaria. La Dra. Coronado ha publicado más de 10 artículos en revistas científicas indexadas, ha participado en pasantías y congresos nacionales e internacionales, y es miembro del Sistema Nacional de Investigación (SNI).



Dra. Lorena Coronado-INDICASAT AIP, recibe el Premio L'OREAL 2018 de manos del Dr. Jorge Motta y el Sr. Anthony Ponsford.

|| VISTAZO ||

Feria Nacional de la Miel de Abeja de Panamá 2019





El domingo 14 de julio se llevó a cabo la primera feria de la miel de abeja de Panamá, totalmente gratuito para público de todas las edades, en el Centro Comercial Albrook Mall.

A esta primera entrega asistieron 140 apicultores provenientes de la provincia de Chiriquí, Colón, Coclé, Herrera, Veraguas, Panamá Oeste y de la Capital.

La gran variedad de miel y la diversidad de sabores que hubo para degustar fue cautivante, ya que cada región se caracterizó por su sabor particular. Además, la propuesta fue más amplia ya que presentaron productos para la venta como polen, jabones cosméticos, jalea real, bálsamo para labios, cremas faciales, galletas, cocadas, dulces, caramelos, tratamientos capilares y propóleo.

La actividad tuvo el propósito de promover la producción nacional de miel pura en el mercado panameño, y educar al consumidor con todos los beneficios que brinda la miel, ya que es un antioxidante natural, sirve para curar heridas, es rica en hierro, tiene propiedades antiinflamatorias, es rica en magnesio, potasio y calcio, estimula la producción de nuevas células dañadas, promueve la función cerebral entre otros.

On Sunday, July 14, the first honey bee fair in Panama was held, totally free for audiences of all ages, in the Albrook Mall.

This first installment was attended by 140 beekeepers from the province of Chiriquí, Colón, Coclé, Herrera, Veraguas, Panama Oeste and the Capital.

The great variety of honey and the diversity of flavors that were to taste was captivating, because each region was characterized by its particular flavor. In addition, the proposal was broader because they presented products for sale as pollen, cosmetic soaps, royal jelly, lip balm, facial creams, cookies, cocadas, cakes, candies, hair treatments and propolis.

The activity was intended to promote the national production of pure honey in the Panamanian market, and educate the consumer with all the benefits that honey offers, because it is a natural antioxidant, used to heal wounds, it is rich in iron, it has anti-inflammatory properties, it is rich in magnesium, potassium and calcium, stimulates the production of new damaged cells, promotes brain function among others.



Expo-Bioquímica 2018

Participación de INDICASAT-AIP como expositor dentro de la Primera Expo-Bioquímica 2019, realizada en la Universidad de Panamá. Iniciativa organizada por el Dr. Armando Durant con la finalidad de informar y educar en bioquímica, el impacto que tiene en la ciencia, la salud y la sociedad.

Es un espacio para motivar e inspirar a los estudiantes que llevan cursos de bioquímica en diversas carreras científicas a nivel de licenciatura, maestría y doctorado. Ha sido una oportunidad para conversar sobre el valor de la investigación científica que se realizan en Panamá.



Corte de cinta para dar inicio formal de la Expo-bioquímica 2018.



Dr. Armando Durant, Lic. Ileana Rodriguez y la Dra. Carmenza Spadafora.



Desde la Facultad de ciencias, en la escuela de Química participando como comunicadores de la ciencia que se hace en Panamá.



Lleno total en la primera Expo-bioquímica 2018, desde la Universidad de Panamá



Estudiantes exponiendo sus proyectos.



Estudiantes exponiendo sus proyectos.



Estudiantes exponiendo sus proyectos.



Dr. Rolando Gittens junto al Decano de la facultad de ciencias Magister Raúl Carranza y al Dr. Armando Durant.



Mucho interés por la investigación que realiza INDICASAT -AIP.



Estudiantes que asistieron a la Expo-Bioquímica 2018.

Kumbh Mela

2019-Prayagraj-India

El Kumbh Mela constituye la celebración religiosa de mayor importancia, y concurrencia, que se desarrolla en la India. Es un momento de una elevada entrega espiritual en donde millones de personas acuden tanto a fortalecer su fe.

Este año tuve la oportunidad de participar en el Kumbh Mela, en la ciudad Prayagraj, uno de los lugares más sagrados de toda India, y en donde se encuentra el Triveni Sangam, es decir, la confluencia de los tres ríos sagrados, El Ganges, el Yamuna y el místico río Saraswati. Es aquí, en Prayagraj, y como señala la tradición, donde cayó una de las gotas del néctar de la inmortalidad.

La hermosura del Triveni Sangam, en todos los sentidos, y su significado realmente son indescriptibles. Tuvimos la oportunidad de navegar por estas aguas, contemplar y vivir momentos que nos permitieron tener una visión profunda del yo espiritual que alberga el pueblo de la India.

Por otro lado, pudimos compartir un

Kumbh Mela representa one of the most important religious events that take place in India. It is a moment in which millions of people strengthen their faith.

This year I had the opportunity to attend the Kumbh Mela, held in Prayagraj, the most sacred of the Hindu cities, and where converge the Triveni Sangam, i.e., the Ganges, Yamuna and Saraswati rivers. According to the Indian tradition, drops of the nectar of immortality fell in this sacred place.

The beauty of the Triveni Sangam is certainly indescribable. We had the opportunity to share the deep spirituality that characterizes India. Moreover, we visited the Akshayavat, which is known as a sacred Indian tree. Kumbh Mela was for all of us who visited Prayagraj a time to dream, to grow in faith and to love.

Few years ago, Kumbh Mela was established by UNESCO as Intangible Cultural Heritage of Humanity. I want to acknowledge the people of India for inviting us to participate in



*Dr. Armando Durand
Archibald*



momento de elevada espiritualidad frente al Akshayavat, el cual es un árbol sagrado en la fe hinduista.

El festival Kumbh Mela fue para los asistentes un tiempo para reflexionar, compartir, desear, soñar, y de conocimiento de una de las culturas más antiguas del planeta como lo es la cultura india. Hace pocos años, el Kumbh Mela fue inscrito por la UNESCO como Patrimonio Cultural Inmaterial de la Humanidad, lo que da cuenta de su valor ya no solamente para el pueblo de la India, sino también para la humanidad. Deseo por este medio reconocer y agradecer al gobierno de la India y a INDICASAT AIP por la invitación a este evento.

Kumbh Mela 2019.



Primer encuentro Nacional de Desarrollo Sostenible



Inauguración del ENADES.

VISTAZO

-Institute of High Academic freedom
-High Academic freedom
-Patriotic feeling for Panama



Ciudad
del Saber



Dr. Jagannatha Rao, Director de INDICASAT AIP, inicia la última sesión del Primer encuentro Nacional de Desarrollo Sostenible, en su ultima sesión.



Francisco Garcia, Director de I+D



Vice rector de investigación y post grado de la Universidad de Panamá Dr. Jaime Gutierrez.



Dr. Axel Villalobos, Director del IDIAP.



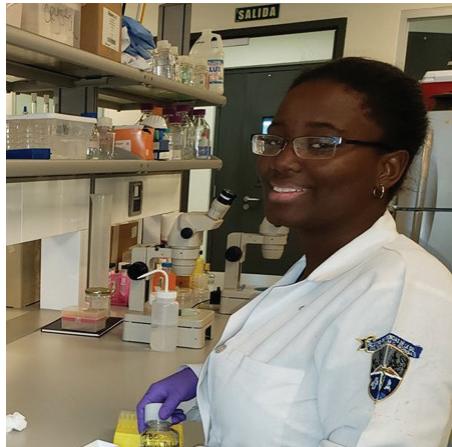
Dra. Oris Sanjur; Directora asociada administración científica-Smithsonian.



Dr. Juan Miguel Pascale, Sub Director General-Instituto Conmemorativo Gorgas.



► El Dr. Jose Loaiza investigador en INDICASAT-AIP y la Dra. Kelly Benneth presentan su más reciente trabajo sobre Genomica de mosquitos en SMBE 2019 en Manchester UK.



► Ariadne Campbell estudiante de Tesis en INDICASAT-AIP, dentro del grupo de investigación del Dr. Amador Goodridge, gano una beca del Washington Center por un período de 3 meses en Estados Unidos.



► Cristopher Boya, estudiante de doctorado en biotecnología en INDICASAT- AIP, expuso la pre-presentación de su tesis doctoral, seguido lo presentará en la India.



► Nadir Planes, estudiante de doctorado en biotecnología en INDICASAT-AIP, expuso la pre-presentación de su tesis doctoral, seguido lo presentará en la India.



► El Dr. Armando Durant investigador de INDICASAT-AIP ha recibido un reconocimiento por parte de la SENACYT, por la culminación del Proyecto de Cardiomiopatía Dilatada.



► La Dra. Idalina Cubilla y Maritza Rios, investigadoras adjuntas del INDICASAT- AIP presentaron los resultados de su investigación científica sobre la Nutrición y la Tuberculosis en Panamá, en ASN 2019 Baltimore, USA.



► Capacitación y actualización en equipos del laboratorio de diagnóstico de la tuberculosis en la provincia de Colón junto con el equipo de Tuberculosis del INDICASAT-AIP.



► Firma del Convenio Específico de Cooperación Educativo entre INDICASAT-AIP, Senacyt, IFARHU y la UTP, con la finalidad de apoyar el otorgamiento de becas para el Programa de Doctorado en Biociencia y Biotecnología que coordina la UTP e INDICASAT-AIP.



► La Dra. María Carreira fue seleccionada para el Programa de Entrenamiento Latinoamericano (LATP) como Becaria 2019 para asistir al curso “Iluminando el cerebro: El uso de la luz para comprender la función del sistema nervioso”. Del 26 de agosto al 13 de septiembre 2019 en Ciudad de México, México. Un total de quince estudiantes de toda América Latina fueron elegidos para participar en el curso.



► En representación de la pasada Expo Bioquímica 2018, el Dr. Armando Durant junto a una de sus estudiantes y co organizadora Bárbara Ruiz, hacen entrega de certificados en reconocimiento al apoyo recibido por INDICASAT-AIP.



► Dra. Yila De La Guardia es seleccionada como embajadora de eLife (2019-2020). El objetivo de este programa es unir a científicos de todas las regiones para trabajar juntos y “resolver” problemas en la ciencia.

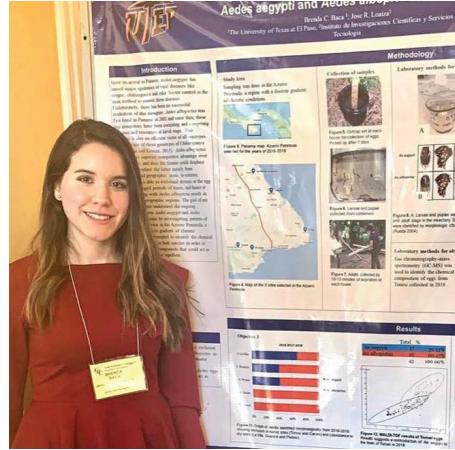


PANAMÁ LANZA EL PROYECTO BIOBANCO

► Por primera vez en casi 20 años, MIAMBIENTE lidera la inversión en investigaciones de descubrimiento de drogas y aprovechamiento científico de la biodiversidad panameña. Antes, la inversión había sido extranjera.



► Dra. Gabrielle Britton, fue galardonada con el premio “Mujer Destacada del Año”, por la Asociación Panameña de Ejecutivos de Empresas (APEDE)



- ▶ Brenda Bacca del mosquito Team, estudiante del programa Mhirt de INDI-CASAT-AIP y la Universidad de Texas, en el Paso presenta su investigación sobre mosquitos Aedes en Galveston.



- ▶ El Dr. Rao Jagannatha fue elegido miembro asesor del Comité TWAS (MAC) sobre Sistemas y Organismos Biológicos (2019-2020).

Científicas

Panameña realiza estudios para conocer los efectos del Alzheimer


ML | La investigadora panameña realizó estudios sobre la patogénesis de la enfermedad en Estados Unidos y desde 2008 dirige el Centro de Neurología Celular y Molecular, que aplica terapias alternativas con plantas contra la malaria y en formulación de productos naturales de la Pluma.

Investiga sobre la malaria

ML | La biogeógrafa Carmen Gómez realizó estudios sobre los efectos de la malaria en las personas de Estados Unidos y desde 2008 dirige el Centro de Neurología Celular y Molecular, que aplica terapias alternativas con plantas contra la malaria y en formulación de productos naturales de la Pluma.


ML | Dra. Carmen Gómez.

Logró premio internacional

ML | Sandra López Vergara obtuvo un premio en salud en las áreas de virología e inmunología en el congreso Commemorative Gor-gos observado en el 2014 premio internacional


ML | Sandra López Vergara.

Nuevas promesas

En un campo laboral, que en el pasado fue dominado por hombres, las mujeres buscan romper paradigmas y realizar investigaciones

GINA ASIAS RIVERA

En Commemorative Gor-gos observado en el 2014 premio internacional


ML | Gina Asias Rivera.

Cada año, el Instituto Smithsonian de Investigaciones Tropicales recibe cientos de pasantes.


ML | María Luisa Rodríguez.


ML | María Alejandra.

to jóvenes que presentan avances innovadores en un simposio internacional. La chiricana María Luisa Rodríguez, presentó su trabajo para detectar potas en muestras de suelo provenientes de zonas costeras. Según el STM es un proyecto interesante porque el tema es poco estudiado en los suelos tropicales, y es fundamental para el manejo agrícola.

ML | Marisol Ruiz.

En el laboratorio matrónico

Las científicas tienen una gran responsabilidad en el campo de las ciencias.

- ▶ El periódico Metro Libre destaca el trabajo de nuestras investigadoras la Dra. Gabrielle Britton, la Dra. Carmenza Spadafora y de nuestra investigadora adjunta la Dra. Sandra López, junto a varias mujeres profesionales exitosas de nuestro país.



▶ Agasajo para todas las mujeres que laboran en el instituto en el Día Internacional de la mujer 2019.



► Visita de Muhamad Talha Hajee, Embajador designado de Panamá en la India.



► Visita del Sr. Celestino Mariano Gallardo, Líder de la Comarca Ngäbe-Buglé.



► Ceremonia de la Academia Mundial de Ciencias en Trieste, Italia donde nuestro director el Dr. Jagannatha Rao es investido como el segundo miembro de Panamá.



► Dr. Sergio Martínez fue galardonado con el premio TWAS-APANAC para investigadores jóvenes, entregado por el Dr. Mahabir Gupta, el Dr. Jorge A. Motta y el Dr. Martín Candanedo en el marco del Acto de Reconocimiento a los Miembros del SNI.



► Participación de INDICASAT-AIP en la Expo Ambiente que se llevó a cabo del 23 al 25 de noviembre 2019, en el Centro de Conversaciones ATLAPA.



► Invitados al Conversatorio en Nuevas Vías No-invasivas de Diagnóstico Temprano en Enfermedades Crónicas y Degenerativas.



► Dr. Sergio Martínez, investigador de INDICASAT-AIP dictó curso de escritura de artículos a docentes y estudiantes de la Universidad Latina de Panamá, sede de Penonomé. Universidad Latina Penonome



► Jóvenes Diplomáticos visitan INDICASAT-AIP y reciben seminario sobre colaboración internacional y diplomacia científica.



► Dra. Carmenza Spadafora fue elegida como Jurado en la 2da Competencia de lanzamiento de ASTMH Innovations 2019. Organizada por la Sociedad Estadounidense de Medicina e Higiene Tropical.



► Dr. José Loaiza junto a su equipo Mosquito, aparecen dentro de la revista Copa Airlines en un artículo muy completo sobre las investigaciones que realizan.



► Dr. Hermógenes Fernández investigador de INDICASAT-AIP desde Altaplaza Mall, explica como la miel es un sustituto excelente a los medicamentos que alivian la tos y el dolor de garganta, además de ser más dulce que el azúcar y saludable.



► Dr. Luis Mejia, investigador de INDICASAT-AIP desde Altaplaza Mall, muestra el hongo que afecta el cacao y el efecto positivo al consumir chocolate oscuro o amargo sobre los niveles de estrés, estado de ánimo, la memoria e inflamación.



Dr. Rolando Gittens, ha sido invitado como copresidente de la sesión de Biodiversidad y Biotecnología en el marco de la “22^a Conferencia de Jóvenes Científicos TWAS LACREP / 1^a Conferencia Regional TYAN para América Latina y el Caribe”, la Academia Brasileña de Ciencias (BAS), el Socio Regional TWAS para América Latina y el Caribe (TWAS-LACREP), el TWAS Young Affiliates Network (TYAN) y el International Science Council (ISC) organizarán la conferencia “Ciencia en América Latina.

|| VISITAS RECIENTES ||



Visita del Ministerio de Ciencia y Tecnología de la República Popular de China, de Heilongjiang Bayi Agricultural University y del Institute of Oceanology, Chinese Academy of Sciences Academician, International Eurasian Academy.



Visita de Lhuana López-Segunda Secretaria de Carrera Diplomática y Consular, Juana Mudarra-Segunda Secretaria de Carrera Diplomática y Consular, Denisse Cabrera-Tercera Secretaria de Carrera Diplomática y Consular, funcionarias de la Carrera Diplomática, que tiene como objetivo conocer de primera mano el trabajo que realizamos y así puedan actuar como intermediarios y punto de contacto en la difusión del trabajo que desarrollamos en Panamá, además de nuestras aspiraciones y solicitudes de cooperación.

Grupo de Alemania encabezado por el Sr. Ben Cardoze Fabrega de la embajada de Alemania visitó indicasat para conocer las innovaciones en investigación y tecnología.

|| VISITAS RECIENTES ||



Visita de los jóvenes diplomáticos, futuros protectores y promotores de los intereses del estado, para la prosperidad, seguridad y justicia en el mundo.



Visita del H.S. YE DONGBAI, Director de Cooperación Internacional del MOST de la República Popular China a nuestro instituto.



Dr. Bai Chunli visita nuestras instalaciones con una delegación China junto al Dr. Jagannatha Rao





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