2nd International Conference on Global Challenges in Neglected Tropical Diseases

GCNTD 2018

June 25-27, 2018, The Condado Plaza Hilton, San Juan, Puerto Rico

"United to eradicate the global threat of Neglected Tropical Diseases"

Program

Organized by

Commission for Scientific Events and Formatives Activities
CAFEC

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2nd International Conference on Global Challenges in Neglected Tropical Diseases

June 25-27, 2018, The Condado Plaza Hilton, San Juan, Puerto Rico

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2nd International Conference on Global Challenges in Neglected Tropical Diseases (GCNTD 2018)

Welcome to GCNTD 2018. The aim of this knowledge convergence forum is to bring researchers and other participants from different world regions, where these diseases are prevalent, to interact with colleagues from North, South, Central America and the Caribbean basin. The objective is to bring discussion and knowledge exchange about new approaches for combating these diseases through treatment and prevention. In addition, the conference seeks elevating the awareness of neglected tropical diseases, particularly in Latin America and Caribbean. Also, this gathering will help stimulate the medicinal chemists from these countries to conduct research in the field by allowing them to have a platform for contacts between laboratories in academia, industry, health agencies and foundations in the Americas and other parts of the world. With the latter in mind, spaces for one to one meetings between participants will be made available throughout the three days of the event.

This conference was organized by Colegio de Químicos de Puerto Rico (CQPR) through the Commission for Scientific Events and Formatives Activities (CAFEC) with the help of other entities and academic institutions as acknowledged in this book. The CQPR is the Puerto Rico IUPAC National Adhering Organization (NAO).

The conference areas include:

•Biology and pathogenesis of the pathogens, diseases and hosts.

•Molecular targets-based and structure-based medicinal chemistry approach to maintain healthy drug-discovery pipelines.

•Monitoring, containment and treatment of drug resistant cases.

•Bench to bedside translational research to evaluate new drugs and drug combinations.

•Socioeconomic and public awareness programs in neglected tropical parasitic diseases.

•Opportunities to develop multidisciplinary programs and current funding opportunities.

•IUPAC CHEMRAWN session on low cost diagnostics.

•Research contributions and innovation from institutes and industry

2nd International Conference on Global Challenges in Neglected Tropical Diseases

June 25-27, 2018, The Condado Plaza Hilton, San Juan, Puerto Rico

GCNTD 2018 Organizing Committees

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Dr. Babu L. Tekwani - The University of Mississippi (btekwani@olemiss.edu) Dr. Rafael Balaña Fouce - University of León, León, Spain (rbalf@unileon.es) Dr. Néstor M. Carballeira - University of Puerto Rico, Río Piedras, PR (nestor.carballeira1@upr.edu) Dr. Adelfa E. Serrano Brizuela - University of Puerto Rico-School of Medicine (adelfa.serrano@upr.edu)

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Fund Raising Group

Carlos A. Tollinche, Néstor Carballeira, Roberto Cordero, Carlos Castañeda

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CAFEC

June 25, 2018

My heartiest welcoming to all of you for this 2nd International Conference on Global Challenges in Neglected Tropical Diseases being held in San Juan, Puerto Rico between June 25 and 27, 2018. We have put together a very exciting program for all of you, which we are sure that it will generate a lot of excitement and future research collaborations. The program has been successful in bringing together scientists from North America, the Caribbean, South America, and Europe to discuss present challenges in the field. We have also been able to bring representatives from the academia, industry, and private research laboratories assuring a complete perspective on the field. A total of 29 oral presentations as well as 23 poster presentations will be presented.

Interesting topics to be discussed at the meeting will include recent advances to treat Leishmaniasis by targeting important aspects such as parasite virulence, new drug targets, successful intervention with key metabolic mechanisms, new phenotypic models, and better detection methods for drug discovery. Chagas disease will also be heavily discussed in terms of new challenges for drug discovery and opportunities, new drug targets, and new possible solutions. Antimalarial drug discovery will also be discussed.

Since this meeting is taking place in a Caribbean island where mosquitoes are omnipresent, a considerable number of presentations will deal with Dengue and Zika. Interesting topics to be discussed include the incessant threat of Aedes-transmitted arboviruses, the state-of the art in the Zika epidemic, new methods to differentiate between Dengue and Zika, Zika and pregnancy, as well as how hurricane Maria affected the mosquito density in the island. We hope to finish with an interesting round table on the modern role of the Pharma Industry in drug discovery for Neglected Tropical Diseases emphasizing Central and Latin America.

We particularly welcome the support of the International Union of Pure and Applied Chemistry (IUPAC) that made possible the participation in this conference of three scientists from emerging countries, mainly from Latin America. We will be able to document the most significant new findings to be presented in this conference in IUPAC's official journal Pure and Applied Chemistry. Please feel free to talk to me about your possible participation in this exciting publication.

Once again, welcome to our beloved island of Puerto Rico and I am looking forward to meeting all of you during the conference.

Néstor M. Carballeira
Program Chair

2nd International Conference on Global Challenges in Neglected Tropical Diseases

Message from the International Union of Pure and Applied Chemistry

Greetings and a sincere welcome to all participants and guests from the International Union of Pure and Applied Chemistry (IUPAC) that endorses this 2nd International Conference on Global Challenges in Neglected Tropical Diseases taking place in San Juan, PR. This recognition is made possible because the scientific credentials and the representation of the PR Chemists Association (CQPR) in this international organization.

Briefly, the Union is a neutral and objective scientific organization, established in 1919, with a current governance of representatives from around 57 countries and jurisdictions. It provides a worldwide base of volunteers with the best skills and background, recruited by transparent and well-understood processes. In 2019, IUPAC celebrates its Centenary.

IUPAC's support of the conference is intended towards promoting a space for diversity, global regional representation under the principle of freedom, and the responsibility of scientists as per observance of the universality of science. In this manner, the aim is to craft and assure a place for openness, scientifically rewarding knowledge exchange that encourages networking and collaborations afterwards. For this reason, we have asked the organizers to allow for spaces for one to one meetings.

The main theme of the conference "United to eradicate the global threat of Neglected Tropical Diseases" reflects on the Union core values that focus on scientific excellence, communications, collaborations, diversity and inclusiveness guiding the organization's mission towards its efforts of serving / benefiting the humankind and the world. Moreover, the congress program incorporates many of the key components related to sustainability and the role of the chemical sciences in achieving Sustainable Development Goals set by the UN. For this reason, the scientific support from the appropriate bodies such as Division VII (Chemistry and Human Health) and ChemRAWN Committee (Chemistry Research Applied to World Needs) have granted financial support from IUPAC to support several Young Scientists through the sponsorship program for scientifically emerging regions.

We are sure that the broad exchange of knowledge, opinions, experience and opportunities for further collaborations allowed by the framework of the NTD's conference will help scientists and health professionals gather here to eradicate these diseases soon.

Next year marks the celebration of IUPAC's Centenary (https://iupac.org/100) and the International Year of the Periodic Table (http://www.iypt2019.org). An invitation is being extend to all the scientists to come and commemorate the Centenary milestone in Paris from July 5 – 12, 2019 in the 47th World Chemistry Congress. In addition, we encourage the scientific communities from all the world regions to join in the observance of both milestones by organizing your own activities in your respective countries

Together with the PRNAO-CQPR and the Organizing Committee, we hope you will enjoy this conference in this tropical setting that is distinguished for its great hospitality and make it an unforgettable, pleasant and lasting scientific experience.

On behalf of IUPAC

Carlos A. Tollinche, Ph.D.
IUPAC Bureau Member
Chair of ChemRAWN Committee

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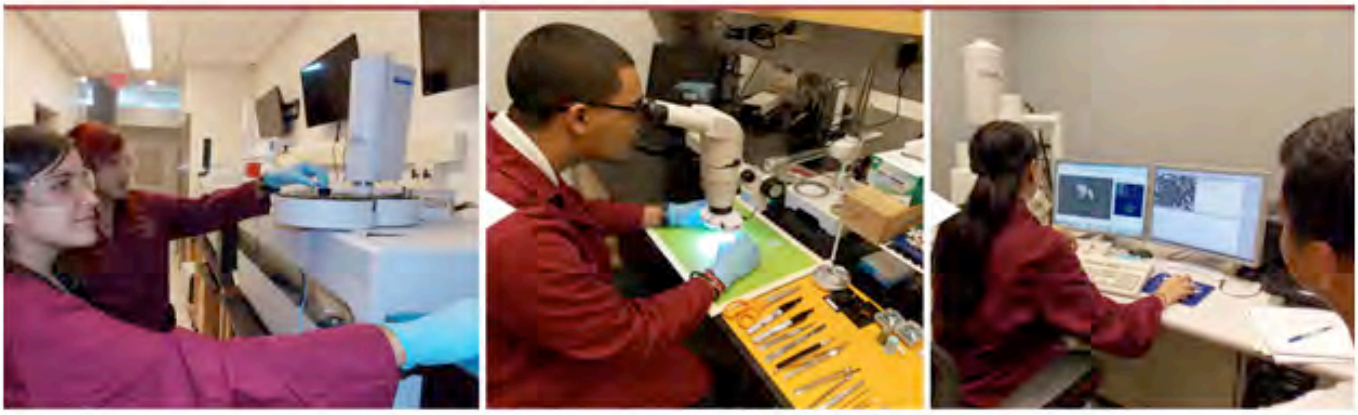

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2nd International Conference on Global Challenges in Neglected Tropical Diseases

CGNTD 2018 Venue

The Condado Plaza Hilton, San Juan, Puerto Rico

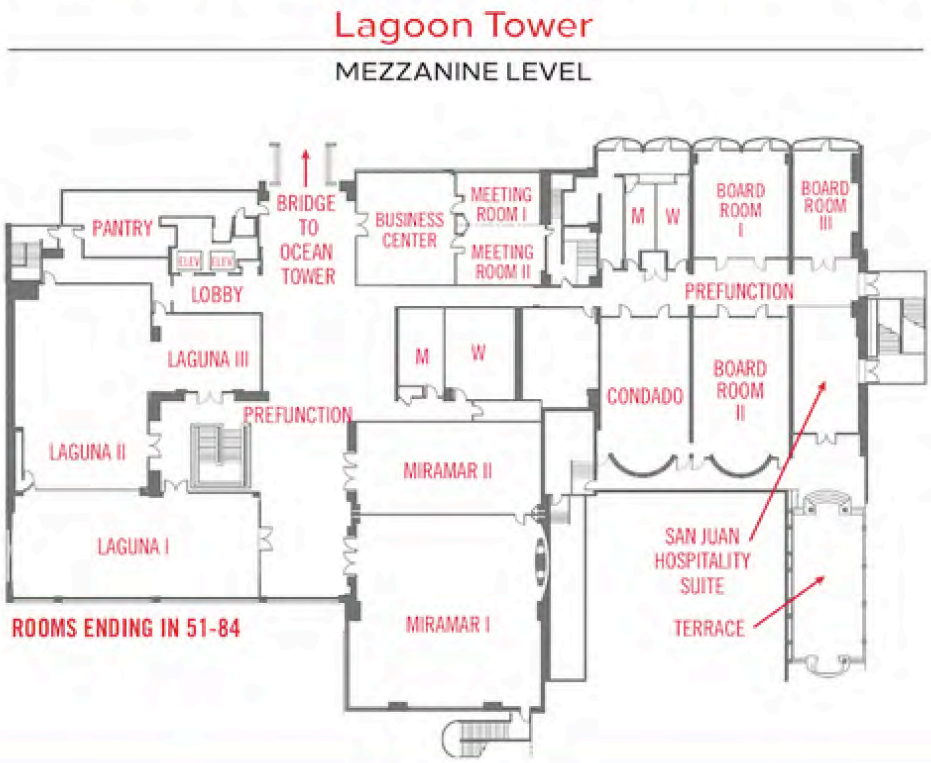
The GCNTD 2018 congress will take place at the **Condado Plaza Hilton Hotel** in San Juan, Puerto Rico. San Juan is the capital of Puerto Rico located at the northeastern part of the Island. The greater San Juan metro area has an approximate population of 1.3 millions.

The Condado Plaza Hilton, San Juan, Puerto Rico

Meeting Area: Lagoon Tower Mezzanine Level

GCNTD 2018 ROOMS:

Scientific Presentations – Miramar 1; Lunch – Miramar 2; Workshop – Condado Room



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GCNTD 2018 Program

Monday, June 25, 2018 – Miramar II

2:00 pm – 4:30 pm **Registration**

5:00 pm – 5:30 pm **Opening Ceremony**

5:30 pm – 6:15 pm **Keynote Speaker** *Dr. Raúl Castellanos - Presiding*
Rubén Santiago Nicholls, Panamerican Health Organization (PAHO), Washington, DC
"*PAHO's plan of action for the elimination of neglected infectious diseases and status of neglected infectious diseases in the Americas*"

6:30 pm – 7:15 pm **Keynote Speaker** *Dr. Laura C. Vicente - Presiding*
Timothy G. Geary, Director, Institute of Parasitology, McGill University, Montreal, Canada
"Evolving paradigms in anthelmintic discovery"

7:30 pm – 9:00 pm **Opening Reception**

Tuesday, June 26, 2018 – Miramar II

7:00 am – 8:30 pm **Continental Breakfast**

8:00 am – 4:30 pm **Registration**

8:30 am – 9:15 am **Keynote Speaker** *Dra. Rosa Mª Reguera - Presiding*
Stephen M. Beverley, Washington University, St. Louis, MO (USA)
"Leishmania RNA viruses and parasite virulence"

9:15 am – 9:40 am **Invited Speaker** *Dr. Néstor M. Carballeira - Presiding*
Rosa M. Reguera, Departamento de Ciencias Biomédicas, Universidad de León, León (SPAIN)
"A chronic bioluminescent model for experimental visceral Leishmaniasis"
(**CHEMRAWN**)

9:40 am – 9:55 am **Coffee Break**

Dr. Babu L. Tekwani – Presiding

9:55 am – 10:15 am **IUPAC Awardee**
Andrea Medeiros, Biochemistry Department, Faculty of Medicine and Institut Pasteur, Montevideo, Uruguay
"5-Substituted 3-chlorokenpaullone derivatives interfering thiol-redox metabolism of Leishmania"

10:15 am – 10:35 am
Néstor M. Carballeira, University of Puerto Rico, Río Piedras Campus, San Juan, PR
"Synthesis of novel brominated and chlorinated vinylic fatty acids as effective inhibitors of the Leishmania topoisomerase IB enzyme"

10:35 am – 10:55 am
Andrés Vacas-Oleas, Instituto de Salud Tropical, University of Navarra (ISTUN), Pamplona, Spain
"A trypanosomatid serine/threonine protein kinase involved in drug resistance and infectivity"

10:55 am – 11:15 am
Paul J. Koovits, Universidade Estadual de Campinas (UNICAMP), Brazil
"Anti-Kinetoplastids from the lead optimization Latin America (LOLA) consortium"

11:15 am – 12:00 pm **Keynote Speaker** *Dr. Rafael Balaña - Presiding*
Marc Ouellette, Laval University, Québec, Canada
"*Genomics of drug resistance in Leishmania leading to new drug targets"*

12:00 pm – 1:15 pm **Lunch and IUPAC Presentation – Miramar I**

1:30 pm – 2:15 pm **Keynote Speaker** *Dra. Adelfa Serrano - Presiding*
Rick L. Tarleton, University of Georgia, Athens, GA (USA)
"Chagas Disease: The real risks and possible solutions"

2:15 pm – 2:40 pm *Dr. Néstor M. Carballeira - Presiding*
Manu De Rycker, University of Dundee, Dundee (UK), and GSK (Spain)
"Chagas' disease drug discovery: challenges and opportunities"

2:40 pm – 3:00 pm **Coffee Break**

Dr. Néstor M. Carballeira – Presiding

3:00 pm – 3:20 pm
Eduardo J.E. Caro-Díaz, Scripps Institution of Oceanography, UCSD, USA
"*Gallinamide A analogues as potent and selective inhibitors of T. cruzi and potential therapeutic agents for Chagas disease"*

3:20 pm – 3:40 pm **IUPAC Awardee**
Jehad Almaliti, Faculty of Pharmacy, The University of Jordan, Amman, Jordan
"Novel and Selective epoxy-ketone based P. falciparum proteasome inhibitors: New antimalarial drug leads"

3:40 pm – 4:00 pm
Emilee E. Colón, University of Puerto Rico, Medical Sciences campus, San Juan, PR
"*Antimalarial drug discovery targeting Plasmodium glutathione S-transferase"*

4:00 pm – 6:00 pm **Poster Presentations – Foyer Miramar I**

P1 **Lourdes Garcia-Fragoso**, University of Puerto Rico School of Medicine, San Juan, PR
"Birth growth parameters in newborns with microcephaly secondary to congenital Zika virus syndrome"

P2 **Daniel W. Pérez-Ramos**, Inter American University of Puerto Rico, Bayamón Campus, PR
"*Entomological assessment on mosquito species: Estimation on the vector capacity potential of the malaria vector Anopheles vestitipennis*"

P3 **Idalí Martínez**, University of Puerto Rico Medical Sciences campus, San Juan, PR
"Secretome of monocytes-derived macrophages from patients with Chikungunya-induced Chronic arthralgia/arthritis"

P4 **Denisse Alequin-Torres**, Department of Chemistry, University of Puerto Rico, Río Piedras campus, San Juan, PR
"Synthesis of novel chlorinated and brominated haloallylated fatty acids with antileishmanial and antibacterial activity"

P5 **Harry G. Ramírez**, University of Puerto Rico, Río Piedras campus, San Juan, PR
"*Analysis of mosquito population during non-hurricane and hurricane season (2017)"*

P6 **Angélica K. de Jesús Sosa**, University of Puerto Rico, Medical Sciences campus, San Juan, PR
"*Plasmodium berghei abcg null mutants exhibits altered expression of antioxidant genes and changes in drug sensitivity"*

P7 **Rafael Balaña-Fouce**, Biomedical, University of León and Pharmacy, University of País Vasco, Spain *"Substituted 1,5-naphthyridine derivatives as novel antileishmanial agents"*
P8 **Rafael Balaña-Fouce**, Biomedical, University of León and CSIC, Madrid, Spain
"Fluorescent analogues of miltefosine as biomarkers for Leishmania presence in biological samples and as a tool for detection of sublethal miltefosine accumulation"
(**CHEMRAWN**)

P9 **José R. Muñiz González**, University of Puerto Rico, Medical Sciences campus, San Juan, PR
"*Analysis of non-linear growth functions to model Plasmodium berghei parasitemias"*

P10 **Mariana D. Padilla**, Ponce Health Sciences University**,** Ponce, PR
"Cannibalism in Aedes aegypti and Chironomus spp. larvae"

P11 **Kayra Rosado Ortiz**, Ponce Health Sciences University**,** Ponce, PR
"Competence in oviposition between Aedes mediovittatus and Aedes aegypti"

P12 **Alejandro J. Veintidós Feliú**, Ponce Health Sciences University**,** Ponce, PR
"The effects of different substrates on mosquito oviposition behavior: A field-based pilot study"

P13 **Christian Morales-Guzmán**, Department of Chemistry, University of Puerto Rico, Río Piedras campus, San Juan, PR
"Total synthesis and leishmanicidal evaluation of novel w-phenyl D6 fatty acids"

P14 **Alicia Schinini**, Departamento de Medicina Tropical, Universidad Nacional de Asunción, Paraguay
"Animal models in Chagas disease"

P15 **Gilberto A. Santiago**, Center for Disease Control and Prevention (CDC), San Juan, Puerto Rico, USA
"*Performance of the trioplex real time RT-PCR during the Zika epidemic in Puerto Rico*"
(**CHEMRAWN**)

P16 **Rosa Mª Reguera**, Biomedical Dept, University of León, Spain, and Freie Universität, Berlin, DE
"*Mannosylated polyglycerol nanoparticles as delivery systems in macrophages infected with Leishmania infantum*"

P17 **Shamika D. Mathis-Torres**, Inter American University of Puerto Rico, Bayamón Campus, PR
"*Assessment of Aedes aegypti in Puerto Rico using BGS-2 and CDC-UV traps*"

P18 **Rafael Balaña-Fouce**, Biomedical Department, Veterinary Medicine, University of León, Spain
"Potential anthelmintic activity of a certain series of new molecules (benzalphthalides and phtalazinones) against different phases of the gastrointestinal nematode Teladorsagia circumncincta"

P19 **Rafael Balaña-Fouce**, Biomedical Department, Veterinary Medicine, University of León, Spain
"Anthelmintic activity of synthetic amino alcohols on eggs and larvae of the gastrointestinal nematode Teladorsagia circumncincta"

P20 **Gabriela Matamoros,** Microbiology Research Institute, UNAH, Tegucigalpa, Honduras (**IUPAC**)
"Identification of SNPs associated with benzimidazole resistance in Ascaris lumbricoides and Trichuris trichiura recovered from humans in Honduras"

P21 **Jelissa Reynoso García**, Dept of Biology, Univ of Puerto Rico, Río Piedras campus, San Juan, PR
"*Paleomicrobiological studies show the presence of phytopathogenic fungi in coprolites revealing the diets of Ancient Caribbean cultures"*

P22 **Yazmary Meléndez-Contés**, Department of Chemistry, University of Puerto Rico, Río Piedras campus, San Juan, PR
"*Synthesis of a new series of 1,2,3-triazolyl fatty acids as potential novel Leishmania topoisomerase IB inhibitors"*

P23 **Alexandra Acevedo**, Institute of Neurobiology and Department of Anatomy & Neurobiology, University of Puerto Rico, Medical Sciences Campus
"Localization of pedal peptide 4-like immunoreactivity in the central nervous system of Biomphalaria glabrata, an intermediate host for schistosomiasis"

Wednesday, June 27, 2018 – Miramar II

7:00 am – 8:30 pm **Continental Breakfast**

8:00 am – 3:00 pm **Registration**

8:30 am – 9:15 am **Keynote Speaker** *Dr. Néstor M. Carballeira - Presiding*
Dale J. Kempf, Abbvie Pharmaceuticals, USA
"Pharma assisted drug discovery and development for neglected diseases"

9:15 am – 9:45 am **Plenary Speaker** *Dr. Rafael Balaña Fouce - Presiding*
Babu L. Tekwani, Division of Drug Discovery, Southern Research, Birmingham, AL, USA
"New phenotypic models for antimalarial and antileishmanial drug discovery"

9:45 am – 10:00 am **Coffee Break**

Dra. Luz A. Silva – Presiding

10:00 am – 10:20 am
Zillur Rahman, University of Puerto Rico, Río Piedras Campus, San Juan, PR
"Comparative genomics of apicomplexan"

10:20 am – 10:40 am
Robert Rodríguez González, Ponce Health Sciences University**,** Ponce, PR
"Environmental and sociodemographic factors after Hurricane Maria and its effect on mosquito density as a vector of diseases"

10:40 am – 11:00 am
Jason Pitts, Department of Biology, Baylor University, Waco, Texas (USA)
"Chemosensory mechanisms in disease-transmitting mosquitoes"

11:00 am – 11:20 am
Erick X. Pérez-Guzmán, University of Puerto Rico, Medical Sciences Campus San Juan**,** PR
"Previous immunity to Zika modulates Dengue infection pathogenesis and immune response in rhesus macaques"

11:20 am – 11:40 am
Manuel F. Lluberas, H.D. Hudson Manufacturing Company, USA
"*Integrated vector control: proven methods or miasmatic vapors*"

11:40 am – 12:00 pm
José Seguinot-Barbosa, Environmental Health, Medical Sciences, Univ. of Puerto Rico, San Juan, PR
"Geographical information systems (GIS): Application to the analysis of vectors borne diseases distribution in Puerto Rico" (**CHEMRAWN**)

12:00 pm – 1:15 pm **Lunch – Miramar I**

1:30 pm – 2:15 pm **Keynote Speaker** *Dra. Adelfa Serrano - Presiding*
Mariano García Blanco, UT Medical Branch/Duke, TX, USA
"RNA and immunity: A love-hate story about Dengue virus"

2:15 pm – 2:40 pm **Invited Speaker** *Dra. Adelfa Serrano - Presiding*
Roberto Barrera, Center for Disease Control (CDC), San Juan, PR
"Incessant threat of Aedes-transmitted arboviruses"

2:40 pm – 3:00 pm **Coffee Break**

Dr. Jason Pitts – Presiding

3:00 pm – 3:20 pm
Gabriela Paz-Bailey, *Center for Disease Control and Prevention (CDC), San Juan, Puerto Rico, USA*
"The Zika epidemic: risk to offspring and sexual transmission"

3:20 pm – 3:40 pm
Marianyoly Ortiz, Puerto Rico Science, Technology, and Research Trust and CDC, San Juan, PR
"Integrated vector management after two hurricanes"

3:40 pm – 4:00 pm
Juan C. Orengo, Ponce Health Sciences University**,** Ponce, PR
"Larval diversity of mosquitoes (Diptera: Culicidae) in the southern of Puerto Rico"

4:00 pm – 4:20 pm
Freddy A. Medina, *Center for Disease Control and Prevention (CDC), San Juan, Puerto Rico, USA*
"A MAC-ELISA that can differentiate dengue and Zika infections" (**CHEMRAWN**)

4:20 pm – 4:45 pm **Invited Speaker**
Carmen D. Zorrilla, *Maternal Infant Studies Center (CEMI), San Juan, Puerto Rico*
"Zika in Pregnancy"

4:45 pm – 5:30 pm

Dr. Carlos Tollinche – Presiding

Round Table Discussion – Dr. Dale Robinson, Dr. Manu De Rycker, Dr. Timothy G. Geary, Dr. Paul J. Koovits

"*Modern Role of the Pharma Industry in Drug Discovery for Neglected Tropical Diseases Emphasizing Central and Latin America*"

5:30 pm **Closing Remarks – Miramar II**

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- Isolators
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- Titrations
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- Heavy Metals
- Conductivity
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- pH measures
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  - HEPA Filters
- Purified Water

KEYNOTE SPEAKERS

Keynote Speaker

PAHO's Plan of Action for the Elimination of Neglected Infectious Diseases and currents status of Neglected Infectious Diseases in the Americas

Rubén Santiago Nicholls

Regional Neglected Infectious Diseases Program, Vector-borne, Neglected and Tropical Diseases Unit, Department of communicable Diseases and Environmental Determinants of Health, Pan American Health Organization, 525 23rd street NW, Washington DC 20037, USA E-mail: nicholls@paho.org

Collectively the Neglected Tropical Diseases, known in the Americas as the Neglected Infectious Diseases (NID), impose a considerable burden of disease on the poor and marginalized populations in Latin America and the Caribbean. They also create a significant social and financial burden because they contribute to and are also consequence of poverty. The social (lack of proper housing, education, lack of access to water and sanitation, etc.) and environmental determinants of health play an important role in perpetuating the transmission of the NID, and thus the cycle of poverty and disease.
In September 2016 PAHO's Directing Council, through Resolution CD55.R9, approved the "*Plan of action for the elimination of neglected infectious diseases and post-elimination actions 2016-2022*". Its aims are to eliminate, by 2022, 8 diseases, schistosomiasis, lymphatic filariasis, onchocerciasis, trachoma, leprosy teniosis/cysticercosis, Chagas disease and human rabies transmitted by dogs; to reduce the burden of 5 diseases, fascioliasis, soil-transmitted helminthiases, leishmaniasis (cutaneous and visceral), cystic echinococcosis and plague; and to assess the regional situation of brucellosis, Buruli ulcer, ectoparasitic infections (e.g., lice, scabies, tungiasis), selected fungal infections, myiasis, strongyloidiasis, venomous snake bite and arthropod bite poisonings, and yaws. The plan also aims to reduce the risk of recrudescence or reintroduction of diseases in the post-elimination phase. The plan proposes interprogrammatic and intersectoral interventions in 6 lines of action including innovative and intensified disease management; preventive chemotherapy, integrated vector management, veterinary public health/One Health approach, intersectoral approaches to reduce the risk of NID transmission and innovative approaches supported by operational research.

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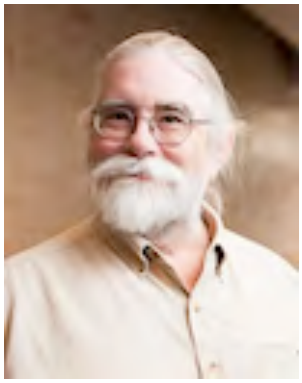
June 25-27, 2018, The Condado Plaza Hilton, San Juan, Puerto Rico

Keynote Speaker



Evolving Paradigms in Anthelmintic Discovery

Timothy Geary

Institute of Parasitology, McGill University, 21111 Lakeshore Road, Ste-Anne-de-Bellevue QC Canada, timothy.g.geary@mcgill.ca

Current chemotherapeutic strategies for the control of human helminth infections are targeted to the elimination of filariases, schistosomiasis and soil-transmitted helminths (STH) as public health threats. All drug-based programmes are sub-optimal, with issues of inadequate efficacy and potential drug resistance of foremost concern. The discovery of new drugs that can fill important therapeutic gaps rests on 3 primary concepts: repurposing of existing approved or near-approval compounds, including combinations; phenotypic whole organism screens; and mechanism-based (target- and structure-based) high-throughput screens. Challenges common to all 3 approaches include demanding target product profiles (including high efficacy with one or a few doses, breadth of spectrum and very high therapeutic indices), the difficulties of maintaining appropriate stages of the target parasites in culture, the need to use animal models of uncertain predictive value, and the limited return on investment in markets currently dominated by donated and inexpensive drugs. Nonetheless, a number of candidate compounds have been identified from each strategy, although the further development and distribution of any of them cannot be guaranteed. Critical to success in these endeavors is the ability to enlist scientists and regulators from disease endemic areas to lead the drug discovery and development process in ways that provide tangible benefits to the populations most affected by these pathogens.

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Keynote Speaker

Leishmania RNA Viruses and Parasite Virulence

Stephen M. Beverley

Department of Molecular Microbiology, Washington University School of Medicine, St. Louis MO 63105 USA

Leishmania in South America often bear the dsRNA *Leishmaniavirus* (LRV1). Like most Totiviruses, LRV1 is neither shed nor infectious, and thus may be viewed as a persistent endobiont. Perspectives on the importance of protozoal viruses changed upon discovery that *L. guyanensis* LRV1 is associated with hypervirulence and increased metastasis in animal models, the latter being a hallmark of the more severe forms of leishmaniasis (Ives *et al. Science* 2011). We have been pursuing this observation intensively as a new paradigm of protozoal virulence. For *Leishmania* we developed RNA interference tools for reproducibly generating isogenic lines lacking LRV1s (Brettmann *et al PNAS* 2016). This has allowed extension of findings with *L. guyanensis* to *L. braziliensis*, the predominant agent of mucocutaneous leishmaniasis (MCL). An important question is the contribution of LRV1 with *Leishmania* pathogenicity in human infections, where disease manifestations differ greatly from those seen in murine models, which is complicated by several factors. Recently we showed that the presence of LRV1 was associated with increased relapse and/or treatment failures in human *L. braziliensis*-infected patients treated with pentavalent antimonials in Peru and Bolivia, as well as in *L. guyanensis* infections treated with pentamidine (Adauai *et al* & Bourreau *et al. J. Inf. Dis* 2016). The association of LRV1 with clinical drug treatment failure could serve to guide more effective treatment of tegumentary disease caused by *Leishmania* sp.

We have embarked on a systematic survey of known and new viruses in *Leishmania* as well as their monoxenous insect trypanosomatid relatives, using a wide range of methods including next-gen RNA sequencing. This has greatly expanded our knowledge of the *Leishmania* virome with the discovery of multiple new viruses. The properties, evolution and potential contributions of these to virulence and biology will be discussed.

Acknowledgements: We thank our colleagues and many collaborators for provision of strains and/or discussions.

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Keynote Speaker

Genomics of Drug Resistance in Leishmania Leading to New Drug Targets

Marc Ouellette

Université Laval. Québec, Canada, Marc.Ouellette@crchul.ulaval.ca

Resistance in Leishmania is often due to gene copy number variations (CNVs) and to point mutations. Next generation sequencing (NGS) of Leishmania cells selected for resistance to anti-leishmania drugs has allowed the detection of a plethora of resistance mechanisms. The generation of drug resistant mutants can be rate limiting and we are developing a number of gain and loss of function genomic screens coupled to NGS for expediting the discovery of drug targets and resistance mechanisms in Leishmania. One screen is Cos-Seq combining cosmid functional cloning and NGS that we used both for promastigotes and amastigotes. This technique was used with known drugs but also with GSK Open resource compounds. Cos-seq revealed a number of known and novel resistance mechanisms and potential drug targets. We optimized the use of chemical mutagenesis coupled to NGS for both gain and loss of function while selecting for resistance to miltefosine and paromomycin. The role of an essential kinase in paromomycin resistance was studied thoroughly. A loss of function screen based on CRISPR-Cas is still in development and preliminary data suggests that this technique will be an helpful complement to the other more mature screens.

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Keynote Speaker

Chagas Disease: The Real Risks and Possible Solutions

Rick L. Tarleton

Center for Tropical & Emerging Global Diseases, Coverdell Center for Biomedical Research
University of Georgia, Athens, GA 30602 USA

Chagas disease is the highest impact parasitic disease in the Americas, yet remains virtually unknown and untreated, despite the fact that the infection is curable, and the global problem of Chagas disease is manageable. In short, Chagas is a solvable problem. This presentation will present the challenges that Chagas disease presents, why it will not be eradicated but how it could be eliminated as a human health problem. The presentation will include discussion of the challenges of vaccine design for this infection and recent disappointing and promising results in drug discovery.

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Keynote Speaker

Pharma Assisted Drug Discovery and Development for Neglected Diseases

Dale Kempf

AbbVie, North Chicago, IL, USA, dale.j.kempf@abbvie.com

Over one billion people suffer from one or more neglected tropical diseases (NTDs), including various parasitic diseases, tuberculosis and malaria. Recent efforts have resulted in renewed research toward the development of new therapies for these diseases, which have generally been neglected from drug development in the past. With vast expertise and resources in drug discovery and development, the biopharmaceutical industry can be a key partner for not-for-profit groups that focus on NTD drug development. This presentation will provide examples of the NTD program at AbbVie, a collaborative effort between R&D and Corporate Responsibility teams in which more than 400 scientists commit a portion of their time to supporting NTD projects. The intersection of Pharma capabilities and various partners' needs, spanning from early discovery through preclinical and clinical studies on promising candidates, provides high-quality scientific support, energizes and motivates participating scientists, and speeds the identification of new therapies for those most in need. In particular, a project focused on a new potential therapy for onchocerciasis and lymphatic filariasis will be highlighted.

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Keynote Speaker

RNA and Immunity: A Love-Hate Story about Dengue Virus

Mariano A. Garcia-Blanco

Department of Biochemistry and Molecular Biology, University of Texas Medical Branch, Galveston, Texas USA
Programme in Emerging Infectious Diseases, Duke-NUS Medical School, Singapore
maragarc@utmb.edu

RNAs are key tools and targets in the battles between pathogens and their hosts. This is most evident in infections caused by RNA viruses. Among these we focus on flaviviruses, which encompass human pathogens such as dengue, West Nile, yellow fever, and Zika viruses. In this talk we show how dengue and Zika viruses use many tools to counter the immune responses of their hosts. Among these is the subgenomic flaviviral RNA (sfRNA), a non-coding RNA that interacts with host RNA binding proteins to cripple the innate immune system of the human host and the mosquito vector. We will present examples that elucidate the mechanisms by which this non-coding RNA interferes with human and mosquito immune mechanisms, enhances viral fitness and increases epidemic potential.

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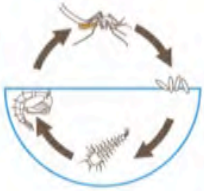
In 2016, Puerto Rico registered **38,058** confirmed cases of Zika, dengue, and chikungunya.

Aedes aegypti is the vector that transmits those diseases.



This mosquito needs containers with accumulated water to complete its life cycle.

One of the easiest ways to reduce diseases carried by *Aedes aegypti* is by reducing mosquito breeding sites.

PLENARY SPEAKER

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Plenary Speaker

New Phenotypic Models for Antimalarial and Antileishmanial Drug Discovery

Babu L. Tekwani

Division of Drug Discovery, Southern Research, Birmingham AL USA

Malaria and leishmaniasis continue to be the major global health challenge due to significant mortality and morbidity attributable to these diseases. The choice of therapies currently available for the treatment of these infectious diseases is highly limited and several of these may eventually be lost or compromised due to drug resistance. Continuous emergence of drug resistance underscores the need for identification of new drugs; indeed, the building and continuous augmentation of an armamentarium of multiple drugs is necessary to cope with the problem of further development of resistance. Molecular targets-based screening followed by evaluation of the compounds libraries through *in vitro* phenotypic models and *in vivo* animal models are the hallmarks of new drug discovery. The whole parasite cell culture-based phenotypic models have attracted significant attention due to recent development of advanced tools for cell imaging and technologies for generation of transgenic cell lines of the pathogens. New phenotypic cell-based models have been developed for *Leishmania donov*ani and *Plasmodium berghei/falciparum*. The parasite-rescue and transformation model was developed for the THP1 macrophage-internalized *L. donovani* amastigotes. The transgenic cell lines of *L. donovani* were developed with stable constitutive expression of mCherry and Citrine fluorescent reporter genes. Staining of the malaria parasites with LDS-751, a fluorescent cell-permeant nucleic acid stain, was developed for parasitemia analysis in blood samples from *P. berghei* infected mice and for *in vitro P. falci*parum cultures. The new phenotypic models offer significant advantages regarding selectivity, throughput and application for compounds' library screening with additional utility for evaluation of virulence of the pathogens.

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Periodic Table of Younger Chemists

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2019 has been declared as the International Year of the Periodic Table.This is also the time when IUPAC is turning 100!

As part of the celebration of IUPAC100, IUPAC and the International Younger Chemists Network (IYCN) announces the creation of a **'Periodic Table of Younger Chemists'.**

Beginning in July 2018 and ending in July 2019 at the World Chemistry Congress and IUPAC General Assembly, we will honor a diverse group of 118 outstanding younger chemists from around the world who embody the mission and core values of IUPAC. The resulting periodic table will highlight the diversity of careers, creativity, and dedication of the young chemists leading us into the next century. See details here: https://iupac.org/100/pt-of-chemist/.

Winners will be profiled on the IUPAC100 website and will receive a certificate from IUPAC. Elements of the Periodic Table of Younger Chemists will be revealed over time in order of scientific discovery (see Wikipedia). Approximately eight elements will be revealed each month beginning in July 2018 with the final elements being awarded at the IUPAC General Assembly and World Chemistry Congress in Paris, France in July, 2019.

Nominations are now being accepted. The deadline for nominations for the first 8 elements Copper, Lead, Gold, Silver, Iron, Carbon, Tin and Sulfur is 11 June 2018 at 5:00 EDT (UTC 21:00). Nominations received but not selected for the first group of elements will carry over for consideration for other elements. For criteria and to submit your nomination follow the link below:

https://iupac.org/100/pt-of-chemist/

For more activities associated with IUPAC100 and the Periodic Table of Chemical Elements see

https://iupac.org/100/

http://iupac.org/cms/wp-content/uploads/2017/12/IYPT-Prospectus_20171209.pdf

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INVITED SPEAKERS

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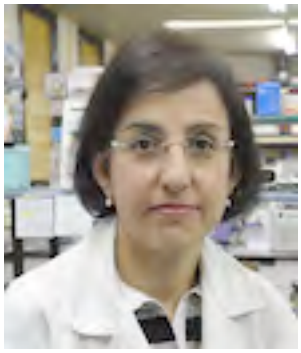
Invited Speaker



A Chronic Bioluminescent Model for Experimental Visceral Leishmaniasis

Alvarez R, Gutierrez MC, Punzón C, Pérez-Pertejo MY, Balaña-Fouce R, Fresno M, Reguera R

[1]Centro de Biología Molecular Severo Ochoa (UAM, CSIC), Madrid, [2]Departamento de Ciencias Biomédicas; Universidad de León, León (SPAIN), rmregt@unileon.es

Visceral leishmaniasis is a neglected disease that poses a significant threat to impoverished human populations of low-income countries. Due to the unavailability of vaccines, pharmacological treatment is the only approach to control the disease that otherwise can be lethal. To date, drug management in endemic regions is based on combinations of a handful of old-fashion and mostly unsafe drugs, where the emergence of resistant strains is an additional problem. To accelerate the discovery of new drug entities, many existing gaps from the early discovery of a compound to its public release, should be filled. One of these gaps is the need of a rapid go/no-go testing system for compound based on robust preclinical models.

Here, we propose a new long-term model of murine visceral leishmaniasis using *in vivo* bioluminescent imaging. For this purpose, a red-shifted bioluminescent *Leishmania infantum* strain was engineered that permitted the *in vivo* appraisal of the disease preventing unnecessary animal bloodshed. The convenience of this platform was evidenced with mice infected with the transgenic *L. infantum* strain treated with a standard schedule of miltefosine – the unique oral drug available against *Leishmania* parasites – used as proof of concept. Radiance detected by a CCD camera and parasite load in the target organs was compared showing a good correlation. Our findings provide a robust and reproducible tool for drug discovery in a chronic model of murine visceral leishmaniasis. Work supported by MINECO SAF2017-83575-R

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Invited Speaker

Incessant Threat of *Aedes*-Transmitted Arboviruses

Roberto Barrera

Center for Disease Control (CDC), 1324 Calle Canada, San Juan, Puerto Rico 00920.
rbarrera@cdc.gov

Dengue viruses (DENV 1-4), and more recently chikungunya (CHIKV) and Zika (ZIKV) viruses continue causing rampant outbreaks throughout the Americas. There are no effective treatments or vaccines against these arboviral diseases, and controlling the mosquito vectors is the only possible way to prevent infection. Human infections caused by these viruses are mediated by the bite of infected *Aedes aegypti* mosquitoes. This cosmopolitan mosquito species, originally from Africa, inhabits houses and surrounding areas closely associated with people. This mosquito uses containers with water to complete its immature development. Many of those containers are linked to deficient public services, such as lack or unreliable piped-water supply (water storage in unsafe vessels), infrequent or inexistent domestic garbage collection (trash containers), and lack of sewerage (unsealed septic tanks). People in most tropical countries are also fully exposed to bites from this mosquito because of a lack of window and door screens or air-conditioned; such as they exist in developed countries. Effective control of this mosquito has been limited by the lack of efficient devices to monitor adult mosquito density and therefore lack of evaluation of the effectiveness of existing vector control technology. Similarly, there has been a lack of precise entomological indicators of risk (e.g., critical mosquito density) to guide Vector Control Programs (VCP). Newer, more efficient devices for vector surveillance and control suggest that vector control can achieve a greater impact on disease prevention than before if VCPs would test and use them.

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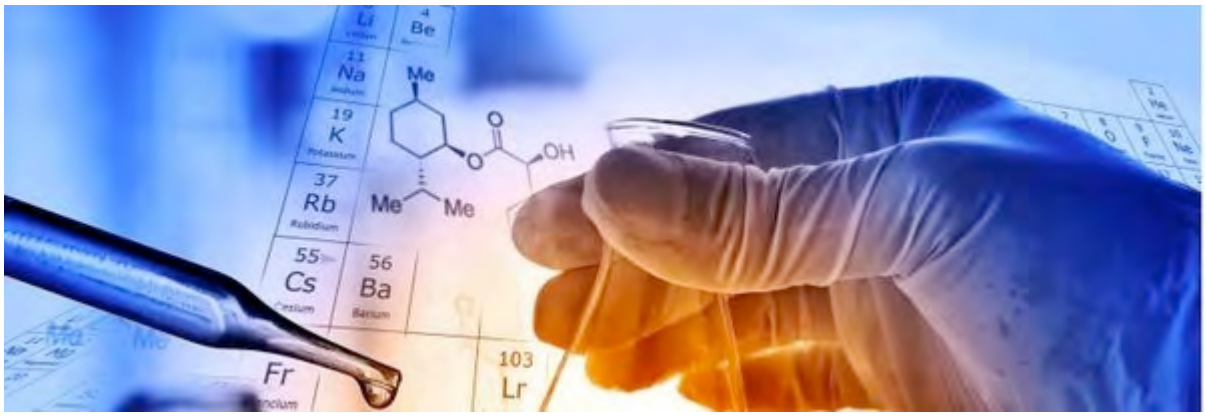
Invited Speaker

Zika in Pregnancy: An Update

Carmen D. Zorrilla, MD

Maternal Infant studies center (CEMI) PO Box 365067, SJ, 00936 carmen.zorrilla@upr.edu

For the past 2 years we encountered a new and serious epidemic that disproportionately affected fetuses and infants. The Zika virus (ZIKV) infection, often unnoticed, was capable of severe brain birth anomalies, neurologic damage on adults and multiple other disorders and manifestations yet to be described. Unfortunately, this pandemic will not be a single historical event. We have witnessed the re-appearance of many other epidemics in recent years. Globally more than half a million cases were reported. Among the challenges of ZIKV are: the difficulties with testing and diagnosis, the need for preventive and/or therapeutic vaccines, the need for therapies, the need to characterize the short and long-term impact on infants and children, the need to develop and implement vector control measures that are safe and sustained and the need to involve communities. Continuous testing during pregnancy is essential in endemic areas, to be able to identify mothers and exposed fetuses and infants. Despite decreasing numbers, the threat still exists. The official reported number of pregnant women with laboratory evidence of possible ZKV infection in Puerto Rico reached 3,300 cases in 2016 and early 2017, the largest number in the US. A population-based birth defects analysis demonstrated an increase in the prevalence of birth defects potentially related to ZIKV. The prevalence increased 20-fold in territories with local transmission (PR included). Health services need to incorporate prevention and testing for ZIKV not just among pregnant women who might be the most vulnerable at present, but men and children need to be able to be tested particularly in areas of ongoing ZIKV transmission. Care to pregnant women with ZIKV diagnosis need to include a multidisciplinary approach with Obstetricians, Pediatricians, experts in Maternal-Fetal Medicine (MFM) and Imaging (Ultrasound), mental health professionals and family empowerment strategies. The sense of urgency still exists to prevent additional morbidity and to guarantee the health of the next generation.



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ABSTRACTS

ORAL PRESENTATIONS

Abstracts Oral Presentations

5-Substituted 3-Chlorokenpaullone Derivatives Interfering Thiol-Redox Metabolism of Leishmania

Andrea Medeiros[1,2], Diego Benítez[2], Oliver Orban[3], Vinicius C. Ferreira[4], Camila I. de Oliveira[4], Conrad Kunick[3], Marcelo A. Comini[2]

[1]Departamento de Bioquímica, Facultad de Medicina, UdelaR, Uruguay, [2]Redox Biology of Trypanosomes Laboratory, Institut Pasteur de Montevideo, Uruguay, [3]Technische Universität Braunschweig, Institut für Medizinische und Pharmazeutische Chemie, Germany [4]IGM-FIOCRUZ, Brazil amedeiro@fmed.edu.uy

Leishmaniasis is an important disease that involve disfiguring (muco)cutaneous to fatal visceral infections for which the current treatment is far from optimal. The discovery of novel drug candidates is a priority due to the limited number and efficacy of the current treatment options. We employed a target-based strategy to identify and optimize the paullone scaffold (7,12-dihydroindolo[3,2-*d*][1]benzazepin-6(5*H*)-ones) as inhibitor of trypanothione synthetase (TryS), an enzyme unique and indispensable to kinetoplastids. TryS synthesizes N^1,N^8-bis(glutathionyl)spermidine, (trypanothione), the major redox cofactor of kinetoplastids, from spermidine and glutathione at expenses of ATP energy. The screening of N^5-substituted 3-chlorokenpaullones, against TryS, revealed several derivatives with potent enzyme inhibitory activity. Several hits exhibited a complex inhibition mode of *Leishmania infantum* TryS and on-target effect in cell-based assays. Importantly, most of them showed a wide spectrum anti-leishmanial activity (EC_{50} 0.1 - 1.6 µM and selectivity index >30) against the clinically relevant form of parasites from *L. braziliensis* and *L. infantum* species. We found that substitutions at the N^5-acetamide position of 3-chlorokenpaullones modulate the anti-TryS and biological activity. In addition, *in vivo* studies using a murine model of cutaneous leishmaniasis testing the therapeutic efficacy of KuRK259 are in progress

We acknowledged to Dr. H. Castro for the kindness in providing WT and TrySKO *L. infatum* cell lines and to F. Carrión for the technical assistance in the compound binding studies

Synthesis of Novel Brominated and Chlorinated Vinylic Fatty Acids as Effective Inhibitors of the *Leishmania* Topoisomerase IB Enzyme

Néstor M. Carballeira[1], Denisse Alequín[1], Leilani Lotti Díaz[1], Rosa M. Reguera[2], Yolanda Pérez-Pertejo[2], Rubén Carbajo-Andrés[2], and Rafael Balaña- Fouce[2]

[1]Department of Chemistry, University of Puerto Rico, Río Piedras campus, 17 Ave. Universidad STE 1701San Juan, PR (USA) 00925-2537; [2]Department of Biomedical Sciences, University of León, Campus de Vegazana, s/n 24071, León, Spain. E-mail: nestor.carballeira1@upr.edu

Many marine derived fatty acids, mainly from sponges, possess vinylic halogenated moieties (bromo or chloro) but their assessment as antileishmanial candidates remains elusive even though many of these halogenated compounds display cytotoxic properties. In this work, we undertook the first total synthesis of a novel series of 2-allyl-3-halo-2-nonadecenoic acids, which preferentially inhibit the *Leishmania* DNA topoisomerase IB enzyme (*L*TopIB), enzymes that are validated targets for the development of antiparasitic drugs. The synthesis of the new halogenated compounds was possible by means of a palladium catalyzed haloallylation of the 2-nonadecynoic acid using either allyl bromide or allyl chloride in the presence of $PdCl_2(PhCN)_2$ in hexane. Among the new halogenated synthetic compounds, the 2-allyl-3-bromo-2-nonadecenoic acid proved to be quite inhibitory of *L*TopIB with an EC_{50} = 7 μM. This enhanced inhibition could be rationalized in terms of a halogen bond between the acid and amino acids at the active site of the enzyme. The brominated analog displayed preferential cytotoxicity towards *L. infantum* amastigotes with an EC_{50} = 2.5 μM. The total synthesis of this novel series of fatty acids, their topoisomerase IB inhibitory activities as well as their antileishmanial potential against *Leishmania infantum* amastigotes and promastigotes will be presented and discussed.

A Trypanosomatid Serine/Threonine Protein Kinase Involved in Drug Resistance and Infectivity

Andrés Vacas-Oleas[1], Celia Fernández-Rubio[1], Miriam Algarabel-Olona[1], José Peña Guerrero[1], Esther Larrea Leoz[1], Fabio Rocha Formiga[2], Alfonso T. García-Sosa[3], Paul Nguewa[1*].

[1]*Instituto de Salud Tropical University of Navarra (ISTUN). Department of Microbiology and Parasitology. IdiSNA, Instituto de Investigación Sanitaria de Navarra. Pamplona, Spain.*
[2] *Gonçalo Moniz Research Center, Oswaldo Cruz Foundation (FIOCRUZ/BA), Salvador, Brazil.*
[3] *Institute of Chemistry, University of Tartu, Ravila 14a, Tartu 50411. Estonia.*
**panguewa@unav.es*

More than 350 million people worldwide are at risk of contracting Leishmaniasis, a vector-borne disease caused by intracellular parasites from the genus *Leishmania*. Currently, there is not an adequate vaccine, and a growing incidence of drug resistance reduces the efficiency of current treatment strategies. Thus, the generation of new antileishmanial drugs has become a priority. Our group has identified a Ser/Thr kinase in parasites. It is conserved and constitutively expressed in *Leishmania* spp. and *Trypanosoma* spp. To evaluate its implication in *L. major* biology, we generated overexpressing parasites. *In vitro* assays using murine peritoneal macrophages and *in vivo* infections in BALB/c mice revealed these transgenic parasites displayed reduced infectivity. Additionally, cytokines analysis showed that mice infected with overexpressing parasites produced a beneficial inhibition of the Th2 response that allowed them to control the disease. On the other hand, a predicted structure for the Ser/Thr kinase was generated. Subsequently, this structure was used for *in silico* docking studies and we discovered that several drugs may bind to the protein. These results were confirmed as overexpressing parasites showed higher EC_{50} values compared to that of the control treated with such drugs. Thus, our data suggest that this newly discovered kinase may not only be involved in *Leishmania* infectivity, but also in drug resistance.

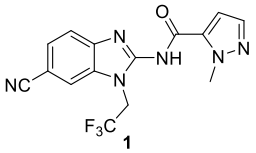
Anti-Kinetoplastids from the Lead Optimization Latin America (LOLA) Consortium

Koovits, P.;* Dessoy, M.;* Martinez, P.;* Rezende, C.;* Ferreira, R.;* Maes, L.;[#] Calljon, G.;[#] Matheeussen, A.;[#] Kratz, J.;[§] Mowbray, C.;[§] Dias, L. C.*

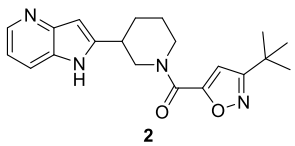
**Universidade Estadual de Campinas (UNICAMP), SP, Brazil. koovits@iqm.unicamp.br*
[#]LMPH, University of Antwerp, Belgium; [§]Drugs for Neglected Diseases initiative (DNDi)

Chagas disease and leishmaniasis are part of a group neglected diseases caused by the kinetoplastid parasites. Combined, they contribute to over 60,000 deaths per annum as well as leaving around 450 million people at risk worldwide. Current medicines suffer from severe toxicity, long treatment regimes, prohibitive costs and invasive administration procedures. As such there is large unmet need for new, affordable, and safe medicines.

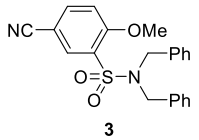
As part of our collaboration with the Drugs for Neglected Diseases Initiative (DND*i*), we have been examining new chemical series, identified through high-throughput screening, as potential leads for drug discovery programs. Through this partnership, we have identified several new series (Figure 1) with activity against *T. cruzi* and *L. infantum*. This presentation will discuss the latest results of our lead optimization programs as part of our ongoing attempts to develop clinical candidates for Chagas disease and leishmaniasis.



1
T. cruzi IC_{50} = 712 nM
Selectivity = 18



2
T. cruzi IC_{50} = 2.2 M
Selectivity = >30



3
L. Inf. IC_{50} = 220 nM
Selectivity = >200

Chagas' Disease Drug Discovery; Challenges and Opportunities

Manu De Rycker on behalf of the DDU/GSK Kinetoplastid Drug Discovery Team [(a,b)]

(a) Drug Discovery Unit, University of Dundee, Dundee, UK. Email: m.derycker@dundee.ac.uk
(b) Kinetoplastid Discovery Performance Unit (DPU), GSK, Tres Cantos, Spain

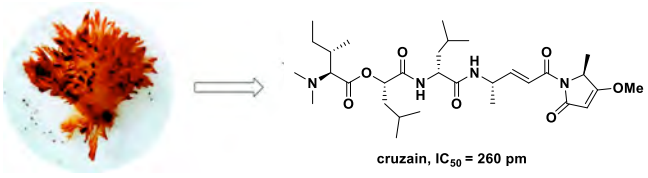
Chagas' disease has a significant impact in Latin America and beyond. Current treatments are inadequate due to adverse side effects that result in treatment discontinuation. The Drug Discovery Unit at the University of Dundee and the Kinetoplastid DPU at GSK are working together to discover new pre-clinical candidates for Chagas' disease with a better safety profile. A key challenge is the poor understanding of the drug discovery path and the properties required for new Chagas' disease drugs. Through mouse efficacy studies with multiple new compound series, we have identified three key factors: compound mode of action, parasite localisation and compound distribution. We have carried out a series of experiments, both *in vitro* and *in vivo*, to address these points and based on the outcome, we have re-defined our Chagas' drug discovery cascade. We have achieved promising *in vivo* efficacy results with combination therapy, demonstrating the usefulness of this approach to overcome some of the key challenges in Chagas' drug discovery.

Gallinamide A Analogues as Potent and Selective Inhibitors of *T. Cruzi* and Potential Therapeutic Agents for Chagas Disease

Paul Bourdeau, Bailey Miller, Eduardo J.E. Caro-Diaz, Jehad Almaliti, Jeremiah D. Momper, Jair Siquiera-Neto, James McKerrow, William Gerwick

Center for Marine Biotechnology and Biomedicine, *Scripps Institution of Oceanography, University of California, San Diego, La Jolla, CA*

Based on the structural and functional similarities between chathepsin L and cruzain, gallinamide A, a marine natural product isolated from cyanobacteria collected from Panama, was assayed against the amastigote stage of *T. Cruzi*. Gallinamide A showed remarkable activity in a cell-based assay infecting C2C12 mouse myoblast cell line (IC_{50} = 14.7 nm) and also showed inhibitory activity against recombinant cruzain at sub-nanomolar concentrations (IC_{50} = 0.26 nm). Furthermore, no cytotoxicity to the host murine cells was observed at concentrations up to 10 μM. Given its biological profile *in vitro*, a set of analogues were synthesized to describe its structure-activity-relationship and increase the compound's metabolic stability and solubility for *in vivo* evaluation. We have evaluated these synthetic analogs *in vitro* and confirmed their activity both to the parasite and biochemical target. Additionally, we have investigated their pharmacokinetic stability in plasma and a Snap-PK model. Preliminary results indicate a good distribution profile as well as good half-life *in vivo*.



Novel and Selective epoxy-ketone based P. Falciparum Proteasome inhibitors: New antimalarial Drug Leads

Jehad Almaliti,* Gregory M. LaMonte, Sabine Ottilie, Anthony J. O'Donoghue, Elizabeth A. Winzeler, William H. Gerwick

Department of Pharmaceutical Sciences, Faculty of Pharmacy, The University of Jordan, Amman 11942, Jordan. J.almlaiti@Ju.edu.jo

Naturally derived chemical compounds are the foundation of much of our pharmacopeia, especially in antiproliferative and anti-infective drug classes. Here, we report that a naturally derived molecule called carmaphycin B is a potent inhibitor against both the asexual and sexual blood stages of malaria infection. These studies were validated using in vitro inhibition assays with proteasomes isolated from *Plasmodium falciparum*. As carmaphycin B is too toxic to mammalian cells, we synthesized a series of novel chemical analogs that reduce host cell toxicity while maintaining blood-stage and gametocytocidal antimalarial activity and proteasome inhibition. This series of ~100 analogues contain some compounds that have shown selectivity for inhibition of *P. falciparum* over the human HepG2 cells with selectivity difference of more than 2000 folds. The synthesized compounds contain non-natural amino acids with D-amino acids at the P3 position. This study describes the most promising new class of antimalarial compound known in the literature that inhibits *P. falciparum* with negligible toxicity to human cells.

Antimalarial Drug Discovery Targeting *Plasmodium* Glutathione S-Transferase

Emilee E. Colón-Lorenzo[1], Daisy D. Colón-López[2], Alexis G. Cotto Rosario[3], Sara Delgado[4], Abel J. Baerga Ortiz[1], Ingrid Montes[4], Jose G. Ortiz[1], Jürgen Bosch[2,5], Adelfa E. Serrano[1]

[1]University of Puerto Rico-Medical Sciences Campus, San Juan, PR; [2]Johns Hopkins School of Public Health, Baltimore, MD; [3]University of Puerto Rico-Cayey Campus, Cayey, PR; [3]University of Puerto Rico-Río Piedras Campus, San Juan, PR; [4]Case Western Reserve University, Cleveland, OH. emilee.colon@upr.edu

Development of multidrug resistance to commonly used drugs, including Artemisinin and derivatives, continues to represent a real challenge for malaria control. The long-term goal of our research is to identify, validate, and eventually transfer antimalarial compounds to the pipeline. Our approach is based on structure-based *in silico* screening of 4,900,000 small compounds against an identified target protein, glutathione S-transferase, which was genetically validated to be crucial for parasite development in the asexual stages. Comparative modeling was used to generate a 3D structural model of *P. berghei* GST (pbGST). The pbGST 3D model was used to perform *in silico* screening of two libraries: ChEMBL-NTD archive and ChemBridge library. Virtual library hits were visually inspected for the G and H pbGST binding sites. A total of 61 compounds were identified as potential pbGST inhibitors. Five identified small compounds displayed *in vitro* antimalarial activity with EC_{50} ranging from 0.5 to 3μM. Initial toxicological evaluation of the compounds revealed lack of hemolytic activity and no mammalian cytotoxicity as tested in a mammalian lung fibroblast. Chemical modification to one compound improved the antimalarial activity. Analysis of GST inhibition using protein parasite extract revealed a concentration dependent inhibition in some compounds. Five novel lead compounds that inhibit malaria parasite growth were identified representing potential antimalarial candidates for further development.

This research was supported by the Puerto Rico Science, Technology and Research Trust; NIMHHD grants 8G12MD007600 and U54MD007600

Comparative Genomics of Apicomplexa

Zillur Rahman and Steven E Massey

University of Puerto Rico, Department of Biology, Rio Piedras campus, San Juan, PR
md.rahman@upr.edu

Apicomplexa are obligate intracellular parasites, many of which are responsible for diseases in human and other animals including malaria. They have small genomes, and have lost some distinct pathways which may contribute to pathogenicity and drug resistance. A comparative and phylogenomic analysis of 43 apicomplexa was conducted in the context of cellular, molecular, metabolic and evolutionary processes. Phylogenomic alignment was constructed by concatenating 522 genes from the core genome. We found significantly distinct relationships among hierarchical clusters of distance of phylogenomic, pairwise shared genes and pathways where only plasmodiums were found congruent among all the clusters. The number of some pathways varies substantially in different species, but some pathways remain almost same, with 41 pathways found in all species examined. We have found significant correlations between proteome size and pathways in these organisms for metabolic pathways and informational genes. This data is consistent with the idea that information content of a genome exerts a selective pressure on genes necessary for genetic fidelity.

Environmental and Sociodemographic Factors After Hurricane María and its Effect on Mosquito Density as a Vector of Diseases

Robert Rodríguez-Gonzalez, Luisa M. Morales, Mayra E. Roubert, Vivian Green, and Juan C. Orengo.

Public Health Program, Ponce Health Sciences University, Ponce, Puerto Rico.
rorodriguez13@stu.psm.edu

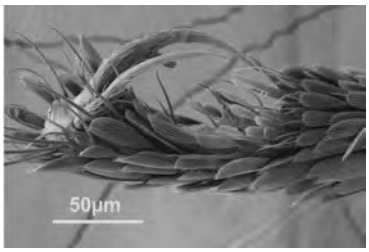
In Puerto Rico, the environmental and sociodemographic factors were altered after the atmospheric event Hurricane María. Our objectives: 1) Evaluate the environmental and climatic factors related to the density and distribution of mosquitoes. 2) Evaluate the social vulnerability indexes related to the distribution of mosquitoes. An ecoepidemiology substudy in Coamo, Juana Díaz, Ponce, Peñuelas and Villalba was performed to evaluate the type of mosquito, the environment and climatic factors. It was observed that when the wind speed increases the frequency of mosquitoes decreases ($r = -0.8263$) ($P<0.05$). In extreme temperature and pressures the distribution of mosquitoes was lower, however, precipitations led to an increase in mosquitoes. Through social vulnerability indexes it was observed that urban areas with per capita income $12,338 – $20,996 mosquito distribution was higher than areas with low level incomes, higher unemployment and less education. Regardless of the social stratum, the density and distribution of mosquitoes affect equally. Therefore, understanding environmental, climatic and sociodemographic factors before, during and after an atmospheric event leads to knowing the distribution of mosquitoes and being able to carry out interventions and vector control.

Chemosensory Mechanisms in Disease-Transmitting Mosquitoes

Jason Pitts

Baylor University, Dept. of Biology, Waco, Texas, USA. jason_pitts@baylor.edu

Our lab investigates the sensory neuronal basis for behaviors in disease-transmitting arthropods, especially mosquito vectors of arboviruses like Dengue and Zika. Of particular interest are the pathways that contribute to chemical- and temperature-oriented behaviors such as host seeking, nectar feeding and oviposition site selection. We have recently used RNA sequencing to quantify transcript expression in contact chemosensory organs, including the tarsi and labella, of vector species. Our analysis indicates that subsets of transmembrane receptors and downstream effector molecules display marked sex-biased expression. Comparative imaging of tarsi using scanning electron microscopy has revealed sexual dimorphism in ultrastructures, including putative chemosensilla. These studies are beginning to illuminate the structural and molecular mechanisms that are likely to underlie observed behavioral distinctions between the sexes. Moreover, we speculate that these mechanisms may also contribute to conspecific recognition and could be exploited for novel surveillance or control strategies.



Previous Immunity to Zika Modulates Dengue Infection Pathogenesis and Immune Response in Rhesus Macaques

Erick X. Pérez-Guzmán, Petraleigh Pantoja, Alexandra Ortiz-Rosa, Crisanta Serrano-Collazo, Idia V. Rodríguez, Luis Giavedoni, Vida Hodara, Lorna Cruz, Teresa Arana, Melween I. Martínez, Laura M. Parodi, Mariah A. Hassert, James D. Brien, Amelia K. Pinto, Laura J. White, Aravinda de Silva, Carlos A. Sariol

Department of Microbiology and Medical Zoology, University of Puerto Rico-Medical Sciences Campus, San Juan, Puerto Rico 00936, USA. erick.perez3@upr.edu

Recent Zika virus (ZIKV) outbreak in Dengue (DENV) endemic regions has raised concerns about their cross-immunological interactions and implications of this for development of severe clinical manifestations. During the ZIKV epidemic, part of the population naïve to DENV like newborns, DENV-naïve children/adults and travelers could be exposed to ZIKV before DENV. Eventually, herd immunity will reduce ZIKV transmission allowing DENV to re-emerge and potentially infect the ZIKV-immune population. The role of a short and long-term ZIKV pre-existing immunity in the outcome of a subsequent DENV infection remains unclear. Our hypothesis is that ZIKV pre-existing immunity will not enhance DENV pathogenesis, but modulates DENV-elicited immune response to induce protection in rhesus macaques. The experimental design is based on the infection of 14 rhesus macaques with DENV. Cohort 1 [ZIKV-10mo(N=4)] and 2 [ZIKV-2mo(N=6)] were exposed to ZIKV 10 and 2 months, respectively, before DENV infection, and cohort 3 [Naïve(N=4)] was naïve to ZIKV. qRT-PCR results show that ZIKV-immunity does not contribute to an increase of DENV viremia, but a tendency to clear the viremia earlier in comparison to naïve macaques. In accordance, cytokine and T-cell functional profile of ZIKV-10mo showed higher levels of cytokines/chemokines/markers involved in the activation of cellular immune response, while Naïve showed a more pro-inflammatory profile. Furthermore, the neutralizing antibody response of ZIKV-10mo against DENV was significantly higher than Naïve, in contrast to ZIKV-2mo. In conclusion, during a DENV infection, long-term previous immunity to ZIKV could positively modulate the immune response to induce protection.

This research was supported by: NIHODP40OD012217, 2U42OD021458-15, R25GM061838.

Integrated Vector Control: Proven Methods or Miasmatic Vapors

Manuel F. Lluberas MS IDHA

H.D. Hudson Manufacturing Company, USA lluberas@hdhudson.com; lluberasm@gmail.com

Dr. Ronald Ross earned the Nobel Prize in the early years of the 19th Century after confirming malaria was transmitted by a mosquito. Decades later, after heavy losses, environmental sanitation and larval source management (LSM) eliminated the mosquito and paved the way for the opening of the Panama Canal. In 1925, Israel Kligler eradicated malaria from Palestine using LSM and Fred Soper eradicated the malaria vector from over 55K km^2 in northern Brazil using LSM. The USA and Puerto Rico were declared malaria free midway through the Century after implementing comprehensive LSM campaigns as part of an IVM program. Well into the 21st Century, those who eradicated malaria vectors from over 100 countries and liberated millions from the yolk of mosquito-borne diseases have fallen off the pages of history books. Moreover, IVM continues to play an insignificant role and LSM is considered valid only when mosquito sources are "few, fixed and findable."

After accepting the Nobel Prize, Dr. Ross voiced his concern regarding malaria control by saying: "Malaria will continue to affect the world until the mosquito is taken seriously." Well into the 21st Century, vector-borne diseases continue to afflict millions.

Geographical Information Systems (GIS): Application to the Analysis of Vectors Borne Diseases Distribution in Puerto Rico

José Seguinot-Barbosa

Department of Environmental Health, Medical Sciences Campus, University of Puerto Rico
jose.seguinot@upr.edu

Introduction: Mosquitoes are the best-known transmitter of vectors diseases. They remain hidden to the human eye which cannot be mapped as subjects or as imaginary entities. *Objectives:* This work aims to evaluate the cartographic production of vector diseases transmitted by the *Aedes aegypti* in Puerto Rico. Our central objective is to present the cartographic nature of vector borne diseases (Dengue, Zika and Chikungunya) and the health situation in terms of cases that have occurred in the past, until very recently (2017).

Methods: We intend to produce a cartographic analysis of the maps of the world, United States, and Puerto Rico using criteria provided by the geographic information (GIS) systems. These include the scale, projection, the coordinate system and the resolution. These indicators were applied to maps based on the social imaginary theory.

Conclusions: The main conclusion derived from this work is that one of the characteristics shared by the vectors is that we cannot see them, therefore is almost impossible to map them. Much less we see the viruses and bacteria that they transmit. To solve the problems of representation of vectors and imaginary diseases we suggested the creation of a vector cartographic model based on a scale that is considerably small, which could be called the microscopic scale or the microscale.

The Zika Epidemic: Risk to Offspring and Sexual Transmission

Gabriela Paz-Bailey, MD, PhD, MSc

Centers for Disease Control and Prevention, San Juan, Puerto Rico 00920

Zika virus is now recognized as a cause of congenital neurologic birth defects, notably microcephaly, and has been associated with potentially fatal complications such as severe thrombocytopenia and Guillain-Barre syndrome. Although most Zika infections are transmitted by infected mosquitoes, Zika virus transmission has been documented through sexual contact, blood transfusion, laboratory exposure, and both intrauterine and intrapartum transmission. Zika virus RNA has been detected in semen, urine, saliva, cerebrospinal fluid, vaginal or cervical secretions, and other body fluids. Most transmissions through sexual contact have been from men with symptomatic infection to their female partners. However, sexual transmission has also occurred from asymptomatic men, through male-to-male and female-to-male sex, and possibly through oral sex. Shedding in the female genital tract appears to be of short duration. In contrast, there are reports of prolonged detection of ZIKV RNA in semen, with the longest reported duration of detection up to 370 days after onset. The localization of Zika virus in the human genital tract and its consequences are not fully known. However, studies in monkeys and mice have evidenced Zika virus in different male genital organs and have shown the negative effects of Zika on the testis and epididymis. Prospective studies in humans have shown a transient decrease in sperm count and multiple sperm anomalies among men with Zika virus RNA-positive semen specimens. We have been studying the frequency and duration of detectable Zika virus RNA in human body fluids, by prospectively assessing a cohort of newly infected patients in Puerto Rico. As part of this study, we have also evaluated the individual, sexual, and household factors associated with ZIKV prevalence among household contacts of symptomatic persons who presented to care with viremic ZIKV infection. In this presentation, I will summarize the epidemiology of the Zika virus in the Americas, the spectrum of adverse pregnancy and birth outcomes, and, for how long does Zika virus replicate and hide in the body. I will also discuss what we know about the risk of sexual transmission, and review the current recommendations to prevent Zika virus sexual transmission.

Integrated Vector Management After Two Hurricanes

Ortiz, Marianyoly[1]; Harris, Angela[2]; Nazario, Nicole[1]; DeLeon-Rodriguez, Natasha[1]; Miranda-Bermúdez, Julieanne[1], and Crespo, Lucy[1]

[1]Puerto Rico Science, Technology, and Research Trust, San Juan, PR and [2]Centers for Disease Control and Prevention, Dengue Branch, San Juan, PR (mortiz@prvectorcontrol.org)

In September 2016, the Puerto Rico Vector Control Unit (PRVCU) was established through a cooperative agreement between the Centers for Disease Control and Prevention (CDC), and the Puerto Rico Science, Technology, and Research Trust, to monitor and control the mosquito *Aedes aegypti*, the vector in the Island for dengue, Zika, and chikungunya. PRVCU follows an integrated vector management (IVM) strategy, combining vector surveillance and monitoring, vector control operations, and island-wide community mobilization programs. During the first year, PRVCU focused on implementing vector surveillance program, creating innovative information systems, and boosting community engagement through citizen mobilization and education. After hurricanes Irma and María, PRVCU launched a media campaign with three key messages about appropriate management of personal water reservoirs, water removal from hurricane debris, and personal protection. The community mobilization program started house to house interventions, distribution of educational material and repellents, and educational activities that impacted more than 90% of the municipalities on Island. Most recently, PRVCU started adult mosquito surveillance in the municipalities of San Juan, Bayamón, Caguas and Ponce. Despite the decrease in confirmed arboviral disease cases in Puerto Rico, as reported by the local Department of Health, results indicate a high population of adult female *Ae. aegypti* in most of the areas under surveillance. Mosquito eggs have also been collected and tested for resistance to several commonly used EPA approved pesticides and initial results showed resistance to pyrethroids pesticides. These results support the need of an integrated approach to control the *Ae. aegypti* and the diseases it transmits.

Larval Diversity of Mosquitoes (Diptera: Culicidae) in the Southern of Puerto Rico

Juan C. Orengo, PhD, MPH, MD, Robert Rodríguez, MPH, Mariana D. Padilla, MPH, Alejandro Veintidós MPH, María D. González MPH, Kayra Rosado MPH, Vivian S. Green, PhD, MS, LND

Public Health Program, Ponce Health Sciences University, Ponce.
jorengo@psm.edu.

The knowledge of the diversity of *culicidae* is important to be able to carry out vector control and prevention strategies. As far as we know in Puerto Rico, it has not been evaluated the diversity of *culicidae*. Our main objective was to evaluate the biodiversity of *culicidae* in three geographic areas of the southern of Puerto Rico. An ecoepidemiological study was implemented in three areas (urban, semi-rural and rural). The larvae collection was carried out by means of ovitraps. With standardized taxonomic guides (Belkin) we evaluated the morphology of the samples collected for classification. Samples of larvae that were incomplete or were poorly preserved were discarded. The index calculated were the following: Specific richness, Margalef, Shannon, equitability and Simpson. A Bray-Curtis similarity dendogram was also performed. Conclusions: a) the urban area (0.48) presented greater diversity than the rural (0.42) and semi-rural (0.14); b) in relation to equality, rural area (0.61) was higher than in the urban (0.44) and semi-rural areas (0.20); c) urban area (0.29) showed greater dominance than rural areas (0.26) and semi-rural areas (0.06), due to the presence of *Aedes aegypti*; d) the rural and semi-rural areas show greater similarity; e) urban sprawl should be evaluated due to the identification of non-synanthropic species in the urban area. The characteristics of the areas defined the diversity and abundance of the species. The results of the study will allow the development of more effective strategies in the control of *culicidae* in the communities.

A MAC-ELISA that can Differentiate Dengue and Zika Infections

Freddy A. Medina, Frances Vila, and Jorge L. Muñoz-Jordán

Centers for Disease Control and Prevention, Division of Vector-Borne Diseases, Dengue Branch, San Juan, PR.
fmedina@cdc.gov

The arrival of Zika virus (ZIKV) to dengue DENV endemic areas came along with diagnostic challenges in serology. The current ELISA assays cannot distinguish these viruses. Furthermore, cross-reactive antibodies produced in DENV and ZIKV infections make the PRNT unreliable for diagnostic purposes as most dengue endemic countries experienced ZIKV mainly as a secondary flavivirus infection. The goal of this study was to develop a MAC-ELISA that could simultaneously discriminate between DENV and ZIKV infections during the convalescent phase during which molecular diagnosis is no longer reliable. A ZIKV/DENV MAC-ELISA was developed to detect the presence of ZIKV or DENV IgM simultaneously. We analyzed PCR-confirmed acute and convalescent cases of ZIKV, DENV, and non-flavivirus febrile illness from our established Sentinel Enhanced Dengue Surveillance System (SEDSS) in Ponce, Puerto Rico. The ZIKV/DENV duo MAC-ELISA was able to detect 103/103 (100%) ZIKV+ specimens and discriminated 103/103 (100%) of the specimens correctly. For DENV+ specimens, the ZIKV/DENV duo MAC-ELISA detected 134/134 (100%) and correctly discriminated 133/134 (99.25%). The sole specimen not discriminated was equivocal in the assay. No false positives were detected from 143 negative specimens tested. A novel approach to differentiate DENV and ZIKV infections serologically was developed. Our ZIKV/DENV duo MAC-ELISA displayed sensitivity that was equivalent to both ZIKV and DENV stand-alone assays. The assay specificity was high enough that it can potentially replace the highly laborious PRNT for confirmation of ZIKV or DENV IgM detection.

Zika in Pregnancy: An Update

Carmen D. Zorrilla, MD

Maternal Infant Studies Center (CEMI), PO Box 365067, SJ, PR 00936
carmen.zorrilla@upr.edu

For the past 2 years, we encountered a new and serious epidemic that disproportionately affected fetuses and infants. The Zika virus (ZIKV) infection, often unnoticed, was capable of severe brain birth anomalies, neurologic damage on adults and multiple other disorders and manifestations yet to be described. Unfortunately, this pandemic will not be a single historical event. We have witnessed the re-appearance of many other epidemics in recent years. Globally more than half a million cases were reported. Among the challenges of ZIKV are: the difficulties with testing and diagnosis, the need for preventive and/or therapeutic vaccines, the need for therapies, the need to characterize the short and long-term impact on infants and children, the need to develop and implement vector control measures that are safe and sustained and the need to involve communities. Continuous testing during pregnancy is essential in endemic areas, to be able to identify mothers and exposed fetuses and infants. Despite decreasing numbers, the threat still exists. The official reported number of pregnant women with laboratory evidence of possible ZKV infection in Puerto Rico reached 3,300 cases in 2016 and early 2017, the largest number in the US. A population-based birth defects analysis demonstrated an increase in the prevalence of birth defects potentially related to ZIKV. The prevalence increased 20-fold in territories with local transmission (PR included). Health services need to incorporate prevention and testing for ZIKV not just among pregnant women who might be the most vulnerable at present, but men and children need to be able to be tested particularly in areas of ongoing ZIKV transmission. Care to pregnant women with ZIKV diagnosis need to include a multidisciplinary approach with Obstetricians, Pediatricians, experts in Maternal-Fetal Medicine (MFM) and Imaging (Ultrasound), mental health professionals and family empowerment strategies. The sense of urgency still exists to prevent additional morbidity and to guarantee the health of the next generation.

2nd International Conference on Global Challenges in Neglected Tropical Diseases

June 25-27, 2018, The Condado Plaza Hilton, San Juan, Puerto Rico

ABSTRACTS
POSTER PRESENTATIONS

GCNTD 2018 Abstracts Poster Presentations

P1

Birth Growth Parameters in Newborns with Microcephaly Secondary to Congenital Zika Virus Syndrome

Lourdes García-Fragoso MD, Leticia Gely MD, Juanita Negrón MD, Inés García-García MD

University of Puerto Rico, School of Medicine, Department of Pediatrics, Neonatology section, PO Box 365067, San Juan, PR 00936-5067. Lourdes.garcia1@upr.edu.

The INTERGROWTH-21st is a network dedicated to reducing newborn deaths resulting from poor intrauterine growth. Their standards have been an important tool to assess growth of Zika virus (ZKV) exposed newborns. Our objective is to determine growth parameters in newborns with congenital ZKV syndrome and microcephaly. Data was obtained from the medical records. Data was extracted for gestational age, birth weight, birth length, and head circumference. Percentiles and Z-scores were calculated using the INTERGROWTH-21st standards. IRB approved. Twelve newborns were included from April 2016 to April 2017. Sex distribution was 64% males, 36% females. All infants were born at term (range 38-41 weeks). Median birth weight (BW) was 2600 grams (range 2065- 3825); median BW percentile 8.74 (range 0.51 - 91.22); median BW Z-score -1.090 (range -2.5696 - 0.1262). All infants presented severe microcephaly with head circumference (HC) below the 1st percentile. Median HC percentile was 0.02 (range 0 - 0.78); median HC Z-score was -3.5520 (range -6.09 - -2.4177). Median length percentile was 15.18 (range 0.03 - 94.24); median length Z-score was -0.6472 (range -3.4026 - 1.5851). Although microcephaly has been emphasized as the most devastating anomaly affecting infants with congenital ZKV syndrome, these infants showed overall growth restriction affecting also birth weight and length. The INTERGROWTH-21st standards as well as the WHO and the CDC growth calculators are useful tools for the follow-up of growth in newborns exposed to Zika. These tools are available as applications for mobile phones making them easy to use for the medical providers.

P2

Entomological Assessment on Mosquito Species: Estimation on the Vector Capacity Potential of the Malaria Vector *Anopheles vestitipennis*

Daniel W. Pérez-Ramos, Emilee E. Colón-Lorenzo, Shamika D. Mathis-Torres, Bert Rivera-Marchand, Juan C. Orengo, Adelfa E. Serrano-Brizuela, and Iván Ferrer-Rodríguez.

Inter American University of Puerto Rico, Bayamón Campus, Bayamón, PR.
dperez0025@interbayamon.edu

Efforts to eradicate malaria in endemic countries had been delayed by many factors such as vector and parasite resistance. There has been a substantial growth of malaria cases in the Americas, and after the earthquake that hit the Hispaniola in 2010, malaria cases have grown exponentially. In Puerto Rico, a malaria free territory, imported malaria cases are reported annually. In June 2015, around 14 cases of imported malaria were reported by the media from which 5 were confirmed by the Department of Health. The aim of this study is to evaluate if these imported cases may become a threat to the Island by: (1) assessing the presence of *Anopheles* species in two ecological life zones, (2) assessing the mosquito species abundance and distribution, (3) evaluating the relationship of soils to mosquito species availability and (4) to estimate the vector capacity potential of a potential malaria vector. Four experimental agricultural sub-stations were chosen as representative of two ecological life zones. Light attractant traps were set around a pond in every sub-station during new moon phase for a year-long study. From the total of 476 mosquito collected, 72% belonged to the sub-tropical moist forest. Two species of *Anopheles, An. grabhamii* and *An. vestitipennis,* were collected in the four sites. A relationship between the type of soil and the mosquito could be observed. Based on the vector capacity potential assessment for *An. vestitipennis*, if a re-introduction of malaria were to happen, the southern part of the Island would be the most vulnerable.

P3

Secretome of Monocytes-Derived Macrophages from Patients with Chikungunya-Induced Chronic Arthralgia/Arthritis

Idalí Martínez[1], Edwin López[1], Zelma L. Ríos[1], Luisa Alvarado[2], Vanessa Rivera[2], Loyda Meléndez[1] ,Susan T. Weintraub[3], and Luis M. Vilá[1]

[1]UPR-Medical Sciences Campus, [2]Ponce Health Sciences University and [3]University of Texas Health Science Center at San Antonio. Idali.martinez@upr.edu

Puerto Rico experienced a large Chikungunya virus (CHIKV) epidemic on 2014 and many infected individuals developed chronic arthralgia/arthritis. Since macrophages are involved in the establishment of this chronic disease, our main goal was to identify differentially expressed proteins in the secretome of macrophages isolated from CHIKV-immune individuals with and without chronic arthralgia/arthritis. A case-control study was performed with 61 individuals with evidence of previous CHIKV infection. Macrophages of chronic participants and controls were cultured in heavy or medium SILAC media, respectively. Seven chronic:control pairs were established and equal protein concentrations were mixed prior to analysis by HPLC-ESI-MS/MS. Mascot, Mascot Distiller and Scaffold Q+S were used for protein quantification. Fold change H/M ratio, Z scores and T-test distribution were calculated. Protein validation was performed using ELISA and secretion levels were compared by Mann Whitney test. Of the more than 500 secreted proteins identified, 22 were differentially secreted between the two groups. These proteins were detected in at least four of the seven analyzed pairs and are mainly involved in three pathways: metabolism of proteins, immune responses, and cell death and survival. Proteins selected for validation included macrophage colony stimulating factor (MCSF), macrophage metalloelastase MMP12, metalloproteinase inhibitor TIMP-1, adenosine deaminase and legumain. Unfortunately, no significant differences between groups were observed in the validations results of MCSF, MMP12 and TIMP-1. Proteomic results suggested the involvement of M2 macrophages and MMP12 in the development of chronic arthralgia/arthritis, however additional validation tests are required.

This study was supported by PRCTRC (8U54MD007587) and RCMI (G12MD007600) programs.

P4

Synthesis of Novel Chlorinated and Brominated Haloallylated Fatty Acids with Antileishmanial and Antibacterial Activity

Alequin-Torres, Denisse[1]; Carballeira, Néstor M.[1]; Jauregui-Matos, Victorio[1]; Sanabria-Rios, David J.[2]

[1]Department of Chemistry, University of Puerto Rico, Río Piedras Campus, [2]Department of Natural Sciences, Interamerican University of Puerto Rico, Metropolitan Campus.

Previous studies in our laboratory have shown that 2-alkynoic acids (2-hexadecynoic and 2-octadecynoic acids) exhibit inhibition of the leishmanial TopIB. We have shown that among these the best inhibitor of the *Leishmania donovani* DNA topoisomerase IB enzyme (*Ld*TopIB) was the 2-octadecynoic acid with an EC_{50} of 5.3 μM. The effectiveness of the *Ld*TopIB inhibition depends on the fatty acid (FA) carbon chain length. Our laboratory synthesized and studied the inhibitory effects of 2-nonadecynoic acid towards *Ld*TopIB, which exhibited an EC_{50} of 10.3 μM towards the enzyme. We decided to use 2-nonadecynoic acid and allyl halides following Kotora's procedure to obtain two novel brominated and chlorinated vinylic acids (2-allyl-3-bromo-2-nonadecenoic acid and 2-allyl-3-chloro-2-nonadecenoic acid) that displayed inhibition towards *Ld*TopIB with EC_{50} of 7.4 μM and 25.7 μM respectively. Studies have shown that the 2-alkynoic FA also have antibacterial activity against multidrug resistant bacteria. Specifically, 2-hexadecynoic acid and 2-octadecynoic acid display low MIC/IC_{50} values. The 2-nonadecynoic acid also displayed toxicity towards mycobacteria such as *Mycobacterium* tuberculosis H_{37}RV. In the same work, it was determined that increasing the carbon chain length of the 2-alkylated FA, decreases their antibacterial activity. In this study, we synthesized two more novel brominated and chlorinated haloallylated fatty acids (FA) derived from 2-dodecynoic acid. Using Kotora's procedure we synthesized the chlorinated and brominated FA from 2-undecynoic acid and the corresponding allyl halide. The novel chlorinated and brominated FA were obtained in 73% and 42% yields, respectively. The antibacterial activity of these FA was determined and these results will be presented herein.

P5

Analysis of Mosquito Population During Non-Hurricane and Hurricane Season (2017)

Harry G. Ramírez[1], Robert Rodríguez[2], Vivian S. Green[2], Juan C. Orengo[2], Adelfa E. Serrano[3], Emilee E. Colón-Lorenzo[3]

[1]University of Puerto Rico-Río Piedras Campus, San Juan, PR; [2]Ponce Health Sciences University, Ponce, PR; [3]University of Puerto Rico-Medical Sciences Campus, San Juan, PR. harry.ramirez@upr.edu

Mosquito are responsible for over one million human losses worldwide. *Aedes aegypti* is the vector of dengue, Chikungunya, and Zika, which are endemic in Puerto Rico. Surveillance and control of mosquitoes are important to help control vector-borne diseases. Our aim is to study the presence of mosquitoes and establish correlations with environmental variables during non-hurricane and hurricane seasons in selected sites in San Juan, PR. Mosquitoes were collected during 8 months using lured BG-Sentinel 2 traps. Environmental variables including temperature, humidity, pressure, and precipitation were recorded. Mosquitoes were identified and classified by genus, sex, and species. All mosquitoes were georeferenced at the collection sites. A total of 733 mosquitoes from 21 samplings were identified and distributed as 79.1% *Aedes spp*., 20.1% *Culex spp*., 0.7% *Anopheles spp.* and 0.1% *Psorophora spp.* Analysis of the data from non-hurricane and hurricane season revealed a significant increase during the Hurricane Season in the total population of *Aedes aegypti* mosquitoes ($p<0.05$) during the hurricane season and an increase in females *Aedes aegypti* ($p<0.05$). A significant increase in the temperature ($p<0.05$) was detected. Analysis revealed a positive correlation between temperature and quantity of *Aedes spp.* ($p<0.05$). Results show that *Aedes aegypti* mosquitoes were abundant throughout the samplings, and the mosquito population increases during the hurricane season. Establishing a consistent monitoring system will provide relevant data to help mosquito control and surveillance, to further help prediction of epidemics.

Research supported by the NIMHD-RCMI 8G12MD007600 and U54MD007600 Pilot Project Grants.

P6

Plasmodium Berghei Abcg Null Mutants Exhibits Altered Expression of Antioxidant Genes and Changes in Drug Sensitivity

Angélica K. de Jesús Sosa, Emilee E. Colón-Lorenzo, Jesús F. Muñiz Oliver, Adelfa E. Serrano

University of Puerto Rico - Medical Sciences Campus, San Juan, PR.
angelica.dejesus1@upr.edu

Malaria multidrug resistance is an increasing problem worldwide. Alarmingly, loss of sensitivity to Artemisinin (ART) based treatment has been reported. Members of the highly-conserved membrane transporters, the ATP-Binding Cassette (ABC) has been associated with malaria drug resistance. *Plasmodium* parasites contain 16 members of the ABC transporters and ABCG is the only member of the G subfamily. The ABCG subfamily has been associated with sterol transport, drug resistance, and glutathione transport in other organisms. The aim of this study was to assess the contribution of *Plasmodium berghei abcg* (*pbabcg*) to the antioxidant response and to drug sensitivity using a *pbabcg* null mutant (*pbabcg*-). We hypothesized that *pbabcg*- parasites will display changes in the expression of antioxidant genes which could affect the parasite's sensitivity to antimalarials. Expression of *P. berghei* antioxidant genes: gamma-glutamylcysteine synthetase, glutathione-S-transferase, glutathione reductase, glutaredoxin-like protein, multidrug resistance associated protein, thioredoxin reductase, thioredoxin 1, thioredoxin 2, and plasmoredoxin was measured by quantitative real time PCR. Drug sensitivity to chloroquine, ART, dihydroartemisinin, artesunate, and atovaquone was determined in the *pbabcg*- parasites. The expression of genes in the glutathione and thioredoxin systems was altered in the *pbabcg*- parasites and a displacement of the dose response curve to four of the five antimalarials tested was observed. This study shows an association of the *pbabcg* gene with antioxidant systems and with a change in susceptibility to several antimalarial drugs.

This research was supported by the NIMHHD grants 8G12MD007600 and U54MD007600.

P7

Substituted 1,5-Naphthyridine Derivatives as Novel Antileishmanial Agents

Tejería A[1], Pérez-Pertejo Y[1], Reguera RM[1], Balaña-Fouce R[1], Alonso C[2], González M[2], Rubiales G[2], Palacios F[2]

[1]Dept. de Ciencias Biomédicas, Universidad de León, Campus de Vegazana s/n, 24071, León, Spain
[2]Dept. de Química Orgánica I, Facultad de Farmacia Universidad del País Vasco, Spain.
rbalf@unileon.es

The clinical practice against visceral leishmaniasis needs of new drugs that overcome the drawback of pentavalent antimonials and amphotericin B classically used. Among these drawbacks we can highlight that both of these compounds are nephrotoxic, require parenteral administration and generate drug resistance. Type I DNA topoisomerase (TopIB) has been found essential for the viability of the parasites and it has structural differences with respect to the human enzyme. Thereby, this enzyme represents a promising target in the development of an antileishmanial therapy. In this search, heterocyclic compounds, such as 1,5-naphthyridines, have been prepared by cycloaddition reaction between N-(3-pyridyl)aldimines and acetylenes and their antileishmanial activity on promastigotes and amastigote-infected splenocytes of Leishmania infantum has been evaluated. In addition, the cytotoxic effects of newly synthesized compounds were assessed on host murine splenocytes to calculate the corresponding selective indexes (SI). Some of these 1,5-naphthyridine derivatives showed excellent antileishmanial activity towards *L. infantum* amastigotes, with similar behaviour than the standard drug amphotericin B and higher selective index (SI > 100). In addition, this compound shows remarkable inhibition on leishmanial TopIB. However, despite these interesting results, further studies are needed to disclose other potential targets involved in the antileishmanial effect of these novel compounds.

MINECO, AEI, FEDER: AGL2016-79813-C2-1R, SAF2017-83575-R and CTQ2015-67871-R
Gobierno Vasco (GV, IT 992-16) and Junta de Castilla y León cofinanced by FEDER, UE (LE020P17)

P8

Fluorescent Analogues of Miltefosine as Biomarkers for *Leishmania* Presence in Biological Samples and as a Tool for Detection of Sublethal Miltefosine Accumulation

Gutiérrez-Corbo C[1], Carbajo, R[1], Martínez Valladares M[1], Reguera RM[1], Balaña-Fouce R[1], Hornillos, V[2], Ulises Acuña A[2], and Rivas L[2]

[1]*Dept. de Ciencias Biomédicas, Universidad de León, Campus de Vegazana s/n, 24071, León, Spain*
[2]*Centro de Investigaciones Biológicas (CSIC), 28040 Madrid, Spain.*
rbalf@unileon.es

The accumulation of fluorescent drugs inside their specific target cell is an appealing biomarker to monitor their pathological status. Nevertheless, its practical implementation in clinics is limited by the scarce number of fluorescent drugs. Miltefosine (MT) has already reached a first-line drug status against leishmaniasis. Despite its extensive and rising implementation in clinics, the number of confirmed clinical isolates resistant to MT remains remarkably low. In most cases, this resistance is associated to a dysfunctional uptake and/or accumulation of the drug by the parasite. In this work, we reviewed the process of optimization of fluorescent MT analogues for their implementation into field studies. These improved MT analogues meet as mandatory requirements their recognition by MT transporter, scarce photobleaching, and detection by standard fluorescence analogues. In a second part, we described the ongoing use of the current best analogue, C3-BODIPY-MT for a sensitive detection of living parasites in biological samples, as well as a pre-diagnostic tool to prevent MT treatments in those patients infected with parasites unable to accumulate the drug, sparing the cost of the treatment. In this regard, bone marrow cells from an infected mouse and gangliocytes from an infected dog were exposed to C3-BODIPY-MT. Uptake of the fluorescent drug was analyzed by confoncal microscopy, revealing large accumulation of C3-BODIPY-MT inside the intracellular parasites.

MINECO, AEI, FEDER: AGL2016-79813-C2-1R, SAF2017-83575-R and RETICS-FEDER RICET RD16/0027/0010

P9

Analysis of Non-Linear Growth Functions to Model *Plasmodium Berghei* Parasitemias

José R. Muñiz-González, Emilee E. Colón-Lorenzo, Adelfa E. Serrano, and Ricardo R. González-Méndez

University of Puerto Rico, Medical Science Campus, San Juan, PR.
jose.muniz6@upr.edu

Malaria is an infectious disease caused by *Plasmodium* parasites, it's growth and development is monitored by measurements of parasitemia. The parasitemia (% of infected erythrocytes) is calculated by determining the amount of infected red blood cells (RBCs) in a total of 500 RBCs. Analyses of parasitemia curves are performed using linear regression by plotting the percent parasitemia in the Y-axis and time (in days) in the X-axis. The aim is to evaluate the growth of *Plasmodium* parasites using growth function models and comparing them with the linear regression approach. Previously our lab generated *Plasmodium berghei* mutant parasites for the following genes: gamma-glutamyl cysteine synthetase (*pbggcs-ko*), glutathione reductase (*pbgr-ko*), and multidrug resistance-associated protein (*pbmrp-ko*). The growth of these mutant parasites was analyzed. Parasitemia datasets were previously generated by microscopic examination of Diff-Quick stained blood smears. The percentage of parasitemia was determined during 10 consecutive days. The data was modeled by growth functions using non-linear regression with the GraphPad Prism software. Six non-linear growth functions were evaluated: Weibull growth, Gompertz growth, Logistic growth, Exponential growth, Exponential plateau, and Beta growth. Our results show that Weibull growth provides a flexible curve fitting and is an excellent method to display the growth pattern in the *Plasmodium berghei* parasites and all the mutants studied. This study demonstrated that the Weibull growth is the best model to present the *Plasmodium* parasitemia data in a more accurate and mathematically objective form with simple biological interpretation.

This research was partially supported by the NIMHHD grants 8G12MD007600 and U54MD007600.

P10

Cannibalism in *Aedes aegypti* and *Chironomus spp.* Larvae

Mariana D. Padilla, MPH, Robert Rodríguez, MPH, Vivian S. Green, PhD, MS, LND, Luisa Morales, DrPH, and Juan C. Orengo, PhD, MPH, MD

Ponce Health Sciences University, Ponce, PR.
mpadilla17@stu.psm.edu

Cannibalism is defined as the feeding practice of an organism with its own species. Cannibalism between mosquito larvae and fly larvae has been evidenced. This behavior is relevant, since this causes the reduction of them. The main objectives of this project were, evaluate the occurrence of cannibal behavior between mosquito and fly larvae, and evaluate if nutritional scarcity is a factor that influences the behavior of cannibalism between mosquito and fly larvae. An ecological longitudinal study was realized in the localities of Peñuelas and Ponce, Puerto Rico. Water samples were collected from eight mosquito traps placed in the different localities using ovillantas. The rate of cannibalism was calculated for both mosquito larvae and fly larvae in the two localities. The rate of cannibalism in Ponce (mosquito larvae: 8.9; fly larvae: 15.8) was higher than Peñuelas (mosquito larvae: 1.2; fly larvae: 1.1). Statistical analysis showed differences in variances, but they were not statistically significant. As a result of these findings, the following questions arise: 1) the location would be a determining factor in the cannibal behavior among the larvae? and 2) whether the disparities in population that occur in these localities, can affect the number of larvae of flies and mosquitoes? These questions can help guide other studies to demonstrate cannibalism between vectors taking into consideration other factors with an adequate sample.

P11

Competence in Oviposition between Aedes Mediovittatus and Aedes Aegypti

Kayra Rosado Ortiz, Maria de los A. González Solís, Robert Rodriguez, Vivian S. Green, Luisa Morales, and Juan C. Orengo

Ponce Health Sciences University, Public Health Program, 338 Zona Ind. Reparada 2, Ponce, PR 00716-2347. krosado15@stu.psm.edu

Vector competence is the ability of arthropods to acquire, maintain and transmit microbial agents. The study of vector behavior between *Aedes mediovittatus* and *Aedes aegypti* is relevant since it will allow us to recognize if there is any difference between these species. Today in Puerto Rico, there is a lack of information about the behavior of *Aedes mediovittatus*. Our objective was to evaluate the competence of *Aedes aegypti* and *Aedes mediovittatus* by an area. An ecological study was implemented in the municipalities of Ponce, Peñuelas, Coamo, Villalba and Juana Diaz. This process was performed in both rural and urban areas. During the first six months of 2017, 1,668 mosquitoes were collected including 4 *Aedes mediovittatus* collected in Coamo near an area with livestock. Between January-February 2018, 415 mosquitoes were collected in Coamo, Ponce, Peñuelas, Juana Díaz and Villalba and 3 *Aedes mediovittatus* were found. Our conclusion was that the *Aedes mediovittatus* was found in a rural area near livestock before the Hurricane Maria. We developed several questions: 1) Did Hurricane Maria decreased density of *Aedes mediovittatus* from his breeding site? 2) the displacement of cattle in the rural area (Coamo) has produced a decrease in the number of *Aedes mediovittatus*?

P12

The Effects of Different Substrates on Mosquito Oviposition Behavior: A Field-Based Pilot Study

Alejandro J. Veintidós Feliú, Robert Rodríguez González, Vivian S. Green, Luisa Morales, Juan C. Orengo Valverde

Address *Public Health Program, Ponce Health Sciences University, Ponce, PR.*
aveintidos17@stu.psm.edu

Variations in mosquito oviposition behavior can occur depending of certain visual and olfactory cues associated with aquatic habitats. Organic material can achieve better ovitrap performance, either as mosquito attractants or deterrents. Our objectives: 1) Evaluate oviposition competency by type of substrate and 2) estimate prevalence of species and sex of mosquitoes. We used a field based experimental study design with a total of 9 different and usable substrates in ovitraps (*L. alba, O. basilicum, A. barbadensis, A. indica, T. erecta, R. officinalis, E. heterophylla, C. elegans, Aloe vera*) being compared with one reference group (water). Eleven eggs and 45 larvae (six pupae included) were collected. Green grass and *L. alba* showed significant differences in quality and quantity of mosquitoes. Differences between number of eggs and larvae by type of substrate were not statistically significant. Green grass ovitrap presented the highest quantity of larvae (n = 13), but this was reducing until only one live 4th instar larva was left. However, the *L. alba* ovitrap facilitated full growth and development among live pupae (n = 6) and one live 4th instar larva, producing *Aedes aegypti* (n = 7). Findings can have immediate public health implications for vector control and management.

P13

Total Synthesis and Leishmanicidal Evaluation of Novel w-Phenyl Δ6 Fatty Acids

Christian Morales-Guzmán, Ester Álvarez-Benedicto, Rosa M. Reguera, Yolanda Pérez-Pertejo, Rubén Carbajo-Andrés, and Rafael Balaña-Fouce, and Néstor M. Carballeira

University of Puerto Rico, Department of Chemistry, Río Piedras Campus, San Juan P R.
christianmoralesguzman@gmail.com

Fatty acids (FA) are important biomolecules which have shown potential against Leishmaniasis, a neglected tropical disease (NTD). Its most severe form, visceral leishmaniasis (VL), has a high mortality rate. Recently, our laboratory studied the antileishmanial properties of the naturally occurring 6-heptadecynoic acid (**1**), 6Z-heptadecenoic acid (**2**), and n-heptadecanoic acid (**3**). The acids **1** and **2** inhibits *Leishmania* Topoisomerase IB(*L*TopIB) enzyme with EC_{50} values between 72 ± 4 μM and 80 ± 9 μM, respectively. The *L*TopIB enzyme is an important molecular target used for the design of antileishmanial therapeutic agents. Our results demonstrated that the 6-alkynoic FA are better inhibitors of *L*TopIB than other olefinic and saturated analogs of comparable chain length. Recent studies with other FA structural motifs revealed that introduction of a phenyl group into FA increases its Topoisomerase I (TopI) inhibitory potential. Based on this, the synthesis of ω-phenyl analogs of the Δ6-alkynoic acids became of our interest. In this work, we present the first total syntheses of a series of C_{10} and C_{16} ω-phenyl Δ6 FA and describe their leishmanicidal properties. Among the studied ω-phenylated acids, we determine that 16-phenyl-6-hexadecynoic acid (**4**) was the most toxic towards *L. infantum* promastigotes with an IC_{50} of 61 ± 7 μM. On the other hand, 16-phenylhexadecanoic acid (**5**) presented the best toxicity towards *L. infantum* amastigotes with an IC_{50} of 3 ± 1 μM. The syntheses and the bioactivity results of these unusual FA will be presented.

C. Morales-Guzmán thanks the NIH Research Initiative for Scientific Enhancement (RISE) program of UPR-Río Piedras (Grant No. 5R25GM061151-17) for a graduate fellowship, while E. Álvarez-Benedicto thanks the Minority Access to Research Careers (MARC) program of UPR-RP (Grant No. T34GM007821-38) for an undergraduate fellowship.

P14

Animal Models in Chagas Disease

Alicia Schinini

Instituto de Investigaciones en Ciencias de la Salud, Departamento de Medicina Tropical, Universidad Nacional de Asunción, Paraguay.
aschinini@gmail.com

The Instituto de Investigaciones en Ciencias de la Salud was created by resolution of the Rector of the National University of Asunción on July 8, 1980. The Department of Tropical Medicine initiated research focused on expanding the little knowledge of Chagas Disease existent at that time. To do this, it was proposed to use the *Cebus apella* monkey as a model for the acute and chronic stages of the disease. An animal model is defined as a non-human species used in research that can extrapolate aspects of a disease of our species or other animals. The animals were infected with the Brazilian Y strain of *Trypanosoma cruzi* and developed the infection showing fever, blood changes and presence of parasites in the blood for 3 months, and an immunological follow-up could be performed. Electrocardiographic alterations were detected in the monkeys and they developed heart disease. In the autopsy, concentric hypertrophy of the heart left ventricle was found in the infected animals, moderate in the acute stage and more important in the chronic stage. In three of the four animals in the chronic stage, aneurysm of the heart apex also developed, and one of them presented cardiac hypertrophy. Currently, a line of experimental research is being developed using BALB/c mice in search of new therapeutic possibilities derived from Paraguayan plants, using CL Brener clone for the infection.

P15

Performance of the Trioplex Real Time RT-PCR during the Zika epidemic in Puerto Rico

Gilberto A. Santiago, Jesus Vázquez, Jorge L. Muñoz-Jordan

Centers for Disease Control and Prevention, Division of Vector Borne Diseases, Dengue Branch, San Juan, PR.
GSantiago@cdc.gov

The emergence of Zika virus presented a challenge to diagnostics in areas pre-exposed to dengue and chikungunya viruses. In response to this public health emergency, we developed the Trioplex Real Time RT-PCR Assay designed for the simultaneous detection of dengue, chikungunya and Zika virus in a variety of clinical specimen types. We determined the analytical and clinical performance characteristics of the Trioplex in detecting each target virus in serum, urine and whole blood-EDTA specimens. The assay was adapted to RNA extraction, PCR equipment and procedures commonly found in public health laboratories. The overall limit of detection of the Trioplex on each these modalities in every specimen type was determined to approximate 10^3 genome copies per milliliter of specimen for every target virus. The modality with the highest sensitivity included RNA extraction from 1 mL of specimen and independent studies confirmed that the sensitivity of Trioplex is similar to other CDC and non-CDC tests. The clinical sensitivity of Trioplex was determined during the first 6 days of illness with 373 concurrently collected serum, urine and whole blood samples from patients in Puerto Rico with positive Zika IgM, where the Trioplex detected 85% in serum, 83% in urine and 82% in whole blood. Testing simultaneously collected serum and urine or whole blood provides an additional 5% sensitivity over serum alone. The high sensitivity of the Trioplex demonstrates the utility of the assay resolving Zika cases in endemic areas. More than 39 thousand Zika cases in Puerto Rico have been confirmed with the Trioplex.

P16

Mannosylated Polyglycerol Nanoparticles as Delivery Systems in Macrophages Infected with *Leishmania infantum*

Dominguez-Asenjo, B[1], Gutiérrez-Corbo, MC[1], Vonssen L[3], Balaña-Fouce R[1], Calderón M[3], Muñoz-Fernández, MA[2], Reguera RM[1]

[1]*Dept. CC Biomédicas, Universidad de León, Campus de Vegazana s/n, 24071, León, Spain rmregt@unileon.es*
[2]*Hospital General Universitario Gregorio Marañon, IiSGM and CIBER-BBN, 28007, Madrid, Spain*
[3]*Institut für Chemie und Biochemie, Freie Universität Berlin, Takustrasse 3, 14195, Berlin, Germany*

Nowadays, there is an urgent need to discover new antileishmanial drugs, since current drugs against visceral leishmaniasis are expensive; have many undesirable side effects and most of them must be administered parenterally. The amastigotes are the parasite form that live and grow inside the parasitophorous vacuole of host resident macrophages in liver, spleen and bone marrow. Drugs must penetrate inside the infected cells and then access the phagolysosome. In this regard, antileishmanial drugs should accumulate in this compartment at such amounts that can kill the parasite but do not produce toxicity to cell host. Therefore, drug release at the target site is one of the challenges of antileishmanial treatment. One solution is to combine these drugs with nanoparticles to overcome these limitations. Mannose receptors are expressed mostly in the surface liver and spleen macrophages. Thus, using mannose as the targeting moiety, nanoparticle uptake would be more selective. Our results show that mannosylated polyglycerol nanoparticles are actively internalized through the acidic endocytic pathway and colocalized surrounding the amastigotes in the phagolysosomes. Only inside the phagolysosomes, there are the necessary conditions to trigger the release of the active drugs. We also studied the pattern of distribution and uptake of mannosylated polyglycerol nanoparticle. Our results point to mannosylated polyglycerol nanoparticles as promising controlled release vehicles for antileishmanial drugs.

This work has been partially supported by MINECO, AEI, FEDER: AGL2016-79813-C2-1R, SAF2017-83575-R

P17

Assessment of *Aedes aegypti* in Puerto Rico using BGS-2 and CDC-UV Traps

Shamika D. Mathis-Torres, Emilee E. Colón-Lorenzo, Daniel W. Pérez-Ramos, Bert Rivera-Marchand, Juan C. Orengo, Adelfa E. Serrano-Brizuela, and Iván Ferrer-Rodríguez

Inter American University of Puerto Rico, Bayamón Campus, Bayamón, PR. smathis1655@interbayamon.edu

Aedes aegypyi has adapted to new geographic locations and increased interactions with humans, which have resulted in important implications for the public health in Puerto Rico. According to Puerto Rico Department of Health, in recent years cases of Dengue virus have increased, alongside with emergence of diseases like Chikungunya and Zika. This study aims to: (1) perform a field evaluation of the effectiveness of the Biogents Sentinel-2 (BGS-2) and Centers for Disease Control and Prevention Miniature UV Light (CDC-UV) traps for capturing *Aedes aegypti*, and (2) assess gene flow of *Aedes aegypti* in three ecological Holdridge life zones (HLZ) of the Island. Three representative cities were selected for the study, San Juan as the sub-tropical moist forest, Río Grande as the sub-tropical wet forest, and Ponce as the sub-tropical dry forest. Mosquitoes were collected in peri-domestic areas inside and outside houses using the 2 × 2 Latin square experimental design. This experimental design provides rotations between two BGS-2 and two CDC-UV, reducing any position-specific effect. Preliminary results show that 58 mosquitoes were collected using the BGS-2 traps, while seven mosquitoes were collected with the CDC traps. The BGS-2 trap seems to be a better tool, both indoors and outdoors, for monitoring *Ae. aegypti* mosquito's population. Additional experiments are underway to assess the genetic variability of *Ae. aegypti* by means of analyses of nine SNPs, although no significant differences are expected due to a high rate of homogenization between *Ae. aegypti* population in the three HLZ..

P18

Potential Anthelmintic Activity of a Certain Series of New Molecules (Benzalphthalides And Phtalazinones) against Different Phases of the Gastrointestinal Nematode *Teladorsagia Circumncincta*

Elora Valderas-García, Rafael Balaña-Fouce, Esther Del Olmo, María Martínez-Valladares

Departamento de Ciencias Biomédicas, Facultad de Veterinaria, Universidad de León. Campus de Vegazana, 24071 León, España. rbalf@unileon.es

Gastrointestinal nematode infections are an important medical problem throughout the world, especially in developing countries. Consequently, the objective in this study is to test the anthelmintic activity of a certain series of synthetic molecules against different phases of the gastrointestinal nematode *Teladorsagia circumncincta.* A total of 41 molecules were tested to prove their anthelmintic activity in *Teladorsagia circumcincta* eggs and larvae. Molecules belong to two famlies, benzalphthalides and phtalazinones, with previously antiparasitic activity. All compounds have been tested by means of the Egg Hatch Assay (EHA) using an initial concentration of 50 µM of each compound. After an incubating period of 48 hours, the ovicidal and larvicidal activity were calculated by the percentage of hatched eggs inhibited and dead larvaes observed, respectively. In those molecules that showed ovicidal activities higher than 85%, the concentration required to inhibit the 50% of the activity (IC_{50}) and the cytotoxicity were calculated to determine the selective index (SI). Initially testing all molecules at 50 µM, only 4 compounds showed ovicidal activity, 2 of them had an activity higher than 90% (molecule A and B), and the other two between 50-90%. The ovicidal and larvicidal activity in molecule A were 99% and 31%, respectively, and in molecule B were 94% and 67%, respectively. We can conclude that the only compounds with good potential belong to the benzalphthalides family and not to phtalazinones. Furthermore, their activity is mainly effective against eggs and not against larvae, since they did not reach activities higher than 70%.

Study funded by AGL2016-79813-C2-1-R; AGL2016-79813-C2-1-R and Junta de Castilla y León LE020P17 co-financed with Fondos FEDER (UE). 79813-C2-1-R.

P19

Anthelmintic Activity of Synthetic Amino Alcohols on Eggs and Larvae of the Gastrointestinal Nematode *Teladorsagia Circumncincta*

Elora Valderas-García, Rafael Balaña-Fouce, Esther Del Olmo, María Martínez-Valladares.

Departamento de Ciencias Biomédicas, Facultad de Veterinaria, Universidad de León. Campus de Vegazana, 24071 León, España. rbalf@unileon.es

Helminthiases caused by nematodes are one of the most common parasitic diseases in the world and mainly affect developing countries. The objective in this study is to test the potential anthelmintic activity of synthetic molecules against different phases of the gastrointestinal nematode *Teladorsagia circumncincta,* which was used as model in this study. A total of 21 amino alcohols were tested in *Teladorsagia circumcincta* eggs using the in vitro Egg Hatch Assay (EHA) at a single concentration of 50 µM. After an incubating period of 48 hours, the ovicidal and larvicidal activity were calculated by the percentage of hatched eggs inhibited and dead larvaes observed, respectively. In those molecules that showed ovicidal activities higher than 85%, the concentration required to inhibit the 50% of the activity (IC_{50}) and the cytotoxicity were calculated to determine the selective index (SI). To discard another possible mechanism of action (laryngeal paralysis), Larval Feeding Inhibition Assay (LFIA) was performed with those molecules with high larvicidal activity (>85%). From all the molecules tested, 8 showed high larvicidal activities in a range between 85 and 100%, and 3 of them also showed an egg hatching inhibition higher than 80%. The IC_{50} of the 8 molecules tested ranged between 2 and 10 µM; the most effective molecule had a SI of 20,93 and 10,11 when the cytotoxicity was tested in mammalian Vero cells and in mouse splenocytes (BALB/c strain). LFIA showed that one molecule inhibited the larvae food ingestion, showing a similar mechanism of action as imidazothiazoles and macrocyclic lactones.

Study funded by AGL2016-79813-C2-1-R; AGL2016-79813-C2-1-R and Junta de Castilla y León LE020P17 co-financed with Fondos FEDER (UE).

P20

Identification of Snps Associated with Benzimidazole Resistance in *Ascaris Lumbricoides* and *Trichuris Trichiura* Recovered from Humans in Honduras

Gabriela Matamoros[1], Carol Rodríguez[2], María Mercedes Rueda[2], Maritza Canales[2], Gustavo Fontecha[1], Ana Sánchez[1,3]

1. *Microbiology Research Institute, Universidad Nacional Autónoma de Honduras, Tegucigalpa, Honduras*
2. *School of Microbiology, Universidad Nacional Autónoma de Honduras, Tegucigalpa, Honduras*
3. *Department of Health Sciences, Brock University, Ontario, Canada.*

gabriela.matamoros@unah.edu.hn

Soil-transmitted helminths (STH) represent a global health concern. In most endemic areas, free of onchocercosis, such as Honduras, mass drug administration (MDA) with single-dose benzimidazoles have been implemented as main control strategy. In Honduras, however, childhood STH prevalence continues to be high, with rural areas exceeding 50%. In addition to low efficacy, likely explanations for this high prevalence include low monotheraphy efficacy, sub-optimal MDA coverage and/or drug intake. Less likely but plausible -drawing from the experience in veterinary medicine-, is the possible emergence of resistance towards benzimidazoles. A pilot study was performed in a highly endemic region (70% *T. trichiura*) in northern Honduras, to obtain baseline data on the occurrence of point-mutations associated with benzimidazole resistance in two STH species. Codons 200, 198 and 167 of the beta-tubulin gene were genotyped, from adult worm specimens expelled by infected children up to 4-days after treatment with combination anti-helminthic therapy. Of more than 500 adult worms collected, 123 were genotyped and 85 bi-directional sequence reads were obtained (40 *A. lumbricoides* and 45 *T. trichiura*). SNPs associated with benzimidazole resistance were not identified among the specimens analyzed. Although the absence of SNPs in this small sample does not exclude the possibility of their occurrence, these preliminary results, suggest that challenges in STH control in Honduras may not be related to drug resistance but to environmental conditions and/or host factors permitting re-infections. While a more integrated STH control program is required, continued anti-helminthic drugs surveillance is recommended in Honduras.

P21

Paleomicrobiological Studies Show the Presence of Phytopathogenic Fungi in Coprolites Revealing the Diets of Ancient Caribbean Cultures

Jelissa Reynoso Garcia, Rosana Wiscovitch Russo, Jessica Rivera Perez, Yvonne M. Narganes-Storde, Raul Cano and Gary A. Toranzos

University of Puerto Rico, Department of Biology, Rio Piedras Campus, San Juan, PR.
Jelissa.reynoso@upr.edu

Paleomicrobiology is the study of the microbiota in ancient specimens (such as coprolites), which are contributing information of the microbiome of ancient cultures in the Caribbean. In this study, we analyzed coprolites of two ancient cultures (Saladoid and Huecoid) from Vieques, Puerto Rico to determine the fungibiome and the possible presence of phytopathogenic fungi to infer their dietary habits. After ancient DNA (aDNA) extraction, Shotgun Metagenomics sequencing with Miseq was performed, allowing us to sequence most of the aDNA isolated from the samples. The analyses with the Basic Local Alignment Search Tool (BLAST) revealed a greater proportion of Basidiomycota in the Huecoid versus the Saladoid; However, a similar proportion of Ascomycota was observed in both cultures. The alignments showed sequence homologies with *Fusarium spp., Puccinia spp.,* and *Ustilago spp*. Regarding the sequences with homology to *Ustilago spp*., this genus from the Basidiomycota phylum is a fungal pathogen of maize and these results confirm its early presence in the Caribbean. These results were consistent with previous study based on amplicons. The study provides an insight into the diets of these ancient cultures, health and lifestyle. Phytopathogenic fungi sequences might enable us to also determine the presence of nuisance microorganisms in the foods used by ancient populations. This in turn may also give us insights on extant nuisance plant pests and their ancient phylogeography. The study reveals the importance of paleomicrobiology to better understand ancient cultures and perhaps to explain current phytopathogens.

P22

Synthesis of a New Series of 1,2,3-Triazolyl Fatty Acids as Potential Novel Leishmania Topoisomerase IB Inhibitors

Yazmary Meléndez-Contés, Néstor M. Carballeira, and Jan-Louis Cosme-Silva

Department of Chemistry, University of Puerto Rico, 17 Ave Universidad STE 1701, San Juan, PR 00925-2537

Leishmaniasis is a known neglected tropical disease originated by the protozoal parasite *Leishmania donovani*, which primarily affects developing nations and has the potential to be fatal. Many fatty acids have demonstrated to be cytotoxic compounds towards *L. donovani*. Moreover, our group has previously demonstrated that the addition of unsaturations and/or 2-methoxy groups to a fatty acid chain enhances their potency against cancer cell lines, as well as against protozoal and bacterial organisms. Based on this, we aimed at exploring other unsaturations that could potentially enhance inhibitory activity, such as nitrogen heterocycles. Of interest are the 1,2,3-triazoles because they have a structural resemblance to amide bonds, as well as being stable towards enzymatic degradation. Furthermore, from a synthetic standpoint, incorporation into a fatty acid chain is facilitated by the Cu(I)-catalyzed Azide-Alkyne Cycloaddition (CuAAC) reaction. Triazolyl fatty acids have been previously synthesized and analyzed against various pathogens and exhibited cytotoxicity toward mycobacteria such as *M. avium* and *M. tuberculosis*. Herein, we report the synthesis and characterization of a library of 1,2,3-triazolyl fatty acids that were synthesized over a 4-step synthesis with overall yields of 11-24%. Characterization of all the compounds was done using ^{1}H-NMR and ^{13}C-NMR. These 1,2,3-triazolyl fatty acids are being tested as inhibitors of the leishmania topoisomerase IB enzyme (LdTopIB).

J-L Cosme-Silva acknowledges the UPR-RISE Program for financial support (Grant Number: 5R25GM061151-16)

P23

Localization of Pedal Peptide 4-Like Immunoreactivity in the Central Nervous System of *Biomphalaria Glabrata*, an Intermediate Host for Schistosomiasis

Alexandra Acevedo[1], Mariela Rosa Casillas[1], Mohamed R. Habib[2], Roger P. Croll[3], and Mark W. Miller[1]

[1]Institute of Neurobiology and Department of Anatomy & Neurobiology University of Puerto Rico Medical Sciences Campus; [2]Theodor Bilharz Research Institute, Cairo Egypt; [3]Dalhousie University, Halifax, Nova Scotia Canada
alexandra.acevedo9.@upr.edu

Approximately 200 million people live at risk of contracting the parasitic disease schistosomiasis. The digenetic trematode worm species *Schistosoma mansoni,* which causes the most common form of intestinal schistosomiasis, requires freshwater snails from the genus *Biomphalaria* to serve as its primary intermediate host. Within the snail, *S. mansoni* larvae multiply and transform into cercariae that can infect humans. As infection by trematode parasites can alter neuropeptide expression in snail hosts, a neural transcriptomics approach was undertaken to explore the neuropeptidomes of *Biomphalaria glabrata*, the major intermediate host in the Western Hemisphere, and *Biomphalaria alexandrina*, the principal intermediate host in Egypt. A *B. alexandrina* transcript (4,038 nucleotides) encoded a precursor prohormone (762 amino acids) from which 13 distinct pedal peptide 4-related neuropeptides could be liberated at dibasic cleavage sites. For this investigation, an antiserum (rabbit polyclonal) generated against C-FDSIGESGLSGIHQNYL-NH_2 was used to localize pedal peptide 4-like immunoreactivity (PP4li) in the central nervous system (CNS) of *B. alexandrina* and *B. glabrata.* In both species, a single symmetrical pair of large (30-40 µm) lateral cell bodies was present in the buccal ganglion. Small (5-15 µm) PP4li cells were scattered across the surface of the pedal and cerebral ganglia. These results suggest that members of the pedal peptide 4 family could regulate feeding and reproduction, two classes of behavior that are altered during the course of infection in this host-parasite system.

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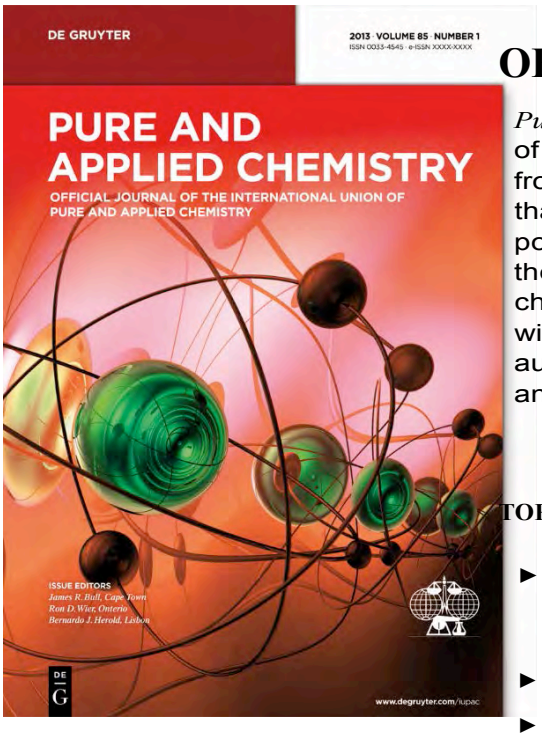

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DOI: 10.1515/pac-2014-1117

Pure and Applied Chemistry, 2015; 87(9-10): 1051-1069

Keywords: *IUPAC Physical and Biophysical Chemistry Division; nanostructured materials*

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DOI: 10.1351/PAC-REC-12-11-20

Pure and Applied Chemistry, 2013; 85(8): 1715-1724

Keywords: *coordination chemistry; coordination networks; coordination polymers; inorganic chemistry; IUPAC Inorganic Chemistry Division; materials chemistry; metal complexes; metal– organic frameworks (MOFs); nanostructured materials; polymers*

Thompson, David W. / Ito, Akitaka / Meyer, Thomas J.

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DOI: 10.1351/PAC-CON-13-03-04

Pure and Applied Chemistry, 2013; 85(7): 1257-1305

Keywords: *excited-state chemistry; metal-to-ligand charge transfer; photochemistry; tris(bipyridine)ruthenium(II) cation*

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Pure and Applied Chemistry, 2015; 87(1): 15-41

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Pure and Applied Chemistry, 2016; 88(3): 189-206

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