

Ministry of Health Fundação Oswaldo Cruz Instituto Oswaldo Cruz

INSTITUTO OSWALDO CRUZ Scientific Report 2016

ORGANIZERS

Wilson Savino Hugo Caire de Castro Faria Neto Elisa Cupolillo Eliane Veiga da Costa Valber da Silva Frutuoso

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Valber da Silva Frutuoso

DEPUTY-DIRECTOR FOR EDUCATION, INFORMATION AND COMMUNICATION

Elisa Cupolillo

DEPUTY-DIRECTOR FOR RESEARCH, TECHNOLOGICAL DEVELOPMENT AND INNOVATION

Hugo Caire de Castro Faria Neto

DEPUTY-DIRECTOR FOR REFERENCE SERVICES AND BIOLOGICAL COLLECTIONS

Eliane Veiga da Costa

COLLABORATORS FOR THE SCIENTIFIC REPORT 2016

Claudia Kamel Daniele Lobato Ingrid Santos Mônica Jandira Raquel Aguiar Saada Fernandez Teresa Santos

PHOTOS

Gutemberg Brito

HISTORIC PICTURES

Acervo da Casa de Oswaldo Cruz (COC/Fiocruz)

GRAPHIC DESIGN

SB Comunicação

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Message from the Board of Directors

Dear colleagues

We present below the scientific report of the Instituto Oswaldo Cruz (IOC) on the activities carried out in 2016. Among several research activities carried out in 2016 (and the most important points can be seen below in each of its 72 research laboratories), We highlight the fact that the Institute has contributed decisively to the generation of scientific knowledge related to the public health emergency of national relevance related to congenital Zika virus infection.

Another relevant aspect is the scientific connectivity seen between different Research Laboratories of the Institute, and which undoubtedly potentiates the actions of each Laboratory. In fact, through the publications of 2016, we have seen a high level of cooperation among the IOC Research Laboratories.

Finally, it is important to thank everyone who contributed to the production of this document, not only in terms of its scientific content, but also in the final formatting and editing.

We wish everyone an enjoyable reading

Wilson Savino

Director

Hugo Caire de Castro Faria Neto

Deputy Director for Research, Technological Development and Innovation

Elisa Cupolillo

Deputy Director for Education, Information and Communication

Eliane Veiga da Costa

Deputy Director for Reference Services and Biological Collections

Valber da Silva Frutuoso

Deputy Director for Institutional Development and Management

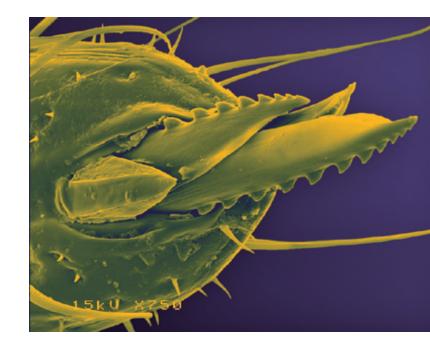
Research

Research is the IOC's primary area of interest, and it supports the activities of education, innovation, reference services and biological collections of the Oswaldo Cruz Institute. Research activities are carried out in the 72 laboratories that constitute the basic units of the institute, and the topics covered reflect a diversity of interests and expertise, as well as the complexity of the Brazilian public health epidemiological scenario, where endemic and epidemic infectious and parasitic diseases coexist with non-infectious chronic degenerative diseases typical of developed countries. In this way, despite being traditionally dedicated to the study of infectiousparasitic diseases, today in the Institute we find research in areas ranging from viruses with epidemic and pandemic potential, Chagas disease, leishmaniasis, malaria, leptospirosis, including vectors and reservoirs, To cancer, diabetes, hypertension, genetic diseases and neurodegenerative diseases, to exemplify some of the various themes. This diversified research activity is supported by a significant technological park, distributed among research laboratories, and also organized in a total of XX multiuser platforms that meet both internal and external demands of the institution. The management of innovation projects at the Institute is supported by the Research and Innovation Support Platform of the Oswaldo Cruz Institute, where researchers have a specialized team to assist in the exploration of financing opportunities, preparation and submission of projects, financial management and monitoring of approved projects, and targeting projects with potential for technological development and innovation.

In the year 2016 we made important contributions in the field of the Zika epidemic and its implication in the nervous system, not only in newborns, but also in adults. The importance of the research carried out at the institute can also be defined by the large production of scientific articles, which in 2016 reached a total of 519 articles in journals of international circulation; by theses and dissertations and by the number of lectures and conferences given by our researchers nationally and internationally.

As a whole, we are sure that the IOC continues to fulfill its mission of generating scientific knowledge of relevance to health in Brazil.

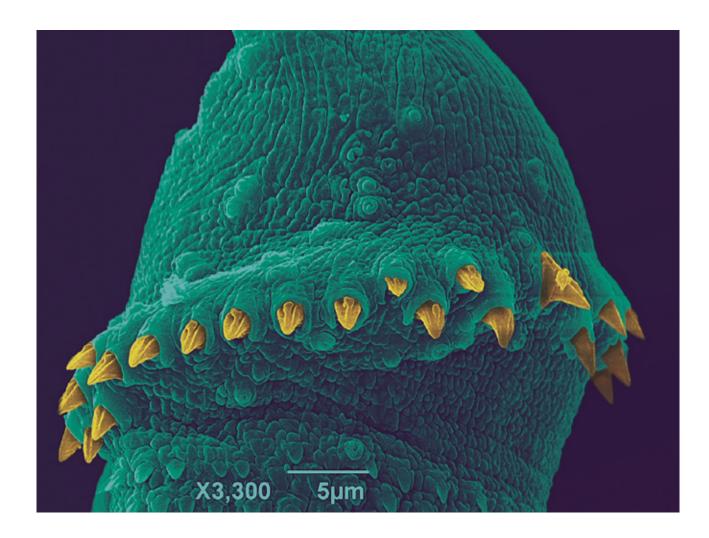
Many of the papers published by the IOC come from the Health Reference activities that exist in several of our Laboratories. Also on Zika, the reference service at the Flavivirus Laboratory was fundamental for the format of a molecular kit for simultaneous diagnosis of



Zika, Chikungunya and Dengue viruses. Also of great importance was the National Reference Laboratory of the Ministry of Health and Regional of the World Health Organization for Measles and Rubella in the Measles Elimination Plan of Brazil and the Americas, which resulted in the issuance of the measles elimination certificate for Brazil and the Americas in 2016.

Another important type of service offered at various IOC Laboratories is to host biological collections. In this sense, in 2016, several collections benefited from BNDES financing from the PRESERVO project, which allowed an advance in the quality of storage of the

respective collections. For example, for the Yellow Fever Collection, a set of sliding cabinets were installed that will house the biological collection, guaranteeing the correct safeguarding of the material, and the start of operation of the VSlide histological preparation digitizer system, which will enable the production of digital back-ups and dissemination of the collection. Because of this same project, the collection of Mollusks and the Helmintological collection also had substantial improvement in the packaging of their collections



About the Institute

Research represents a primordial activity of the Oswaldo Cruz Institute, being structured harmoniously with activities of innovation, teaching, reference services and biological collections (http://www.fiocruz.br/ioc).

These research activities are developed in the 72 IOC laboratories (see Annex 1), and the topics covered comprise a wide range of themes and expertise, also reflecting the complexity of the epidemiological situation of the Brazilian public health, where endemic and epidemic infectious and parasitic diseases coexist with chronic noninfectious degenerative diseases typical of developed countries. For example, we find today in the Institute, research of international quality level in areas ranging from viral diseases with epidemic and pandemic potential, Chagas disease, leishmaniasis, malaria, leprosy, leptospirosis (including the corresponding vectors and reservoirs) to cancer, diabetes, hypertension, genetic diseases and neurodegenerative diseases

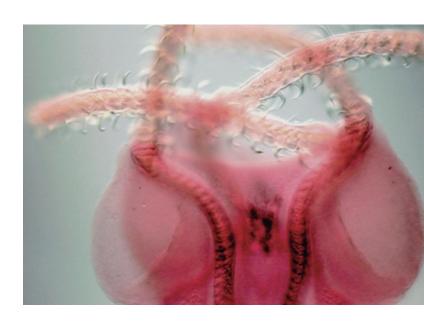
This diverse research activity is supported by a set of technological platforms, which meet both internal and external demands. Research activities and innovation actions in the Institute also count with the support of a project management office, where researchers have a specialized team to contribute significantly in prospecting of funding opportunities, preparation and submission of projects, financial management and monitoring implementation of approved projects, and also targeting projects with potential for technological development and innovation.

The importance of research conducted at the institute can be inferred by the great scientific production, which in 2015 exceeded 530 articles in refereed international journals, as well as Ph.D. theses and

M.Sc. dissertations, books (see Annex 2) and numerous lectured given by our researchers in Brazil and abroad. Thus, the Oswaldo Cruz Institute is characterized as a major biomedical research institution in the country, playing a leading role in generating scientific knowledge oriented to health problems of the population.

Based on the Open Access Policy of Fiocruz, established in 2014, the Institute has been working to include its scientific production in the free access database ARCA (http://www.arca.fiocruz.br). In 2015 over 1100 scientific articles, 140 doctoral dissertations and 240 masters theses were deposited in this database.

The dissemination of scientific knowledge is also conveyed through the scientific journal Memórias do Instituto Oswaldo Cruz (www.memorias.ioc.fiocruz.br), published since 1909, presently occupying a prominent position in the fields of Tropical Medicine,



Parasite Biology and Microbiology, and offering free online access and providing the complete collection of volumes for free download.

In addition, the knowledge generated in Institute is transmitted directly to the society through articles published in major newspapers, television programs and other media. In particular, the discoveries made at IOC by the end of 2015 on the Zika virus infection and its relationship with microcephaly, had great impact on the national and international media.

Ш

In the research environment, the doors are open for **Education.** The Oswaldo Cruz Institute (IOC) plays an important role in the formation of human resources in Health Sciences. Trainees, technical training, and future masters and doctorates have the opportunity to learn in the Research Laboratories.

The set of educational activities includes Stricto Sensu and Lato Sensu programs, technical training, scientific

initiation and post-doctoral assignments, besides holiday courses available to undergraduate students. Still under the scope of Education, the IOC has a strong national and international cooperation through institutional agreements. In 2015, 15 students who were public employees at the Federal University of Ceará (UFC) received doctorate degrees through Interdoctoral Program (DINTER) signed between the UFC and the Postgraduate Program in Tropical Medicine. Eight students were enrolled in the DINTER signed between the Federal University of Roraima and the Postgraduate Program in Parasitic Biology. Furthermore 10 master students graduated at the International Postgraduate Program in Health Sciences, promoted by Fiocruz and the National Institute of Health of Mozambique, with intense participation of IOC. The IOC received two students from Mozambique to develop activities related to their projects in our Research Laboratories.



Students during the vacations courses.

Ш

The integration of Research and Education resulted in a number os **awards** on 2015:

CAPES Thesis Award — Best thesis in Biological Science II area (Postgraduate Program in Cellular and Molecular Biology): Mechanisms for platelet activation in dengue: contributions to the pathogenesis. Author: Eugênio Hottz.

CAPES Thesis Award – Honorable Mention in Medicine II area (Postgraduate Program in Tropical Medicine): Evaluation of epidemiological, mycological, clinical, and therapeutic factors associated with sporotrichosis. Author: Francis Dayvison Freitas.

CAPES-INTERFARMA Innovation and Research Award — Best thesis in Medicine II area (Postgraduate Program in Tropical Medicine): NS1 antigen of dengue virus: commercially available tests performance and alternative applications for early diagnosis of dengue infections. Author: Monique da Rocha Lima.

Ш

Inserted in various research laboratories, 21 **IOC's Reference Services** develop activities for the Ministry of Health in epidemiological surveillance, prevention and control of a number of diseases, assuming a strategic role for the Brazilian Unified Health System (SUS), contributing to the reference diagnostic and vector identification (see Annex 3). In addition, some of these services work at the international level with the Pan American Health Organization (PAHO) and the World Health Organization (WHO). For example, the Reference Service for Leptospirosis (also a Leptospirosis Collaborating Centre for WHO), organized in 2015 an international event leading experts in the area that



delivered a very important document for the scientific community. The PAHO-WHO Regional Reference Service for diagnosis of Rotavirus joined in 2015 the validation network for the Taqman Array Card / WHO system, which simultaneously detects 22 enteropathogens. Also in 2015, the National Reference Laboratory for Leishmania typing, which works in line with the IOC Leishmania Collection, was accredited as regional PAHO reference.

Noteworthy, IOC reference services are included in the complex of producing scientific knowledge, through projects involving researchers, technologists, technicians and students of the Institute. A blatant example in 2015, was the research on Zika virus and its relationship with microcephaly, held in the corresponding reference service.

Within research laboratories there are two out patient structures, one for leprosy and other for viral hepatitis, whose assistance activities are also linked to research projects, thus generating scientific knowledge and training of specialized personnel.



Ш

IOC Research Laboratories are also responsible for the custody of 21 **Biological Collections**, and the corresponding samples are part of the history of Brazilian science (see Annex 4). Needless to say that such collections are also used for activities of research and technological development, not only by researchers from IOC, but also by national and international institutions.

With the recent funding by BNDES (the Brazilian National Bank for Economic and Social Development), the yellow fever collection initiated a process of modernization, including digitalizing microscopic slides containing histological tissue sections.

Ш

It is this complex network of activities that IOC develops interconnected form, its scientific production, whose most important points are presented below, separately for each Research Laboratory.

Ш

Since 1909, IOC publishes the scientific journal **Memórias do Instituto Oswaldo Cruz** (MIOC), which is going through an intense process of internationalization and currently occupies a prominent position in the fields of Tropical Medicine, Parasite Biology, and Microbiology.

The gratuity for publishing and accessing articles and the digitalization of the full journal collection is part of the MIOC's commitment to widely disseminate scientific knowledge, including more than four thousand articles. Since 2012, the journal uses the ScholarOne platform, which facilitates the process of submission and evaluation of articles, benefitting

authors, reviewers, and editorial staff. In addition, the MIOC remains indexed in several international databases, including PubMed Central, Journal Citation Report – ISI Web of Knowledge, SCImago, Scopus, Bioline International, among others.

By keeping a strong and centennial attitude, the MIOC has been exerting its role as disseminator of knowledge in the scientific community with excellence, reaching top positions in international rankings, such as the 20th place in the Parasitology field and 8th place in the Tropical Medicine field, predominantly at the intersection of these areas. As a result, the journal holds a steady performance at impact factor evaluation, with a recent elevation and maintains its solid 2,001 on average of the last five years.

In 2015, the MIOC stopped publishing a printed version, maintaining free online access and its complete collection for free downloads. In 2015, 466 papers submitted to MIOC were processed and 136 were accepted and published. Production over 2015 accounted for eight regular numbers, including a special issue devoted to studies on Chagas disease (memorias.ioc.fiocruz.br).

Ш

The **interaction with society** through educational activities is a commitment of IOC, either in the idealization of activities or participation in events. The course Community health: a construction of all is an example of this interaction. Founded in 2010, the initiative has trained over 500 participants, residents of about 30 communities located in the metropolitan area of Rio de Janeiro, to act as local promoters of health. Another example is the set of video classes entitled: Aedes aegypti - Introduction to scientific vector aspects. Designed to help the routine of students, teachers, media professionals, and people interested in knowing a little more about dengue and its impact, the project brought scientific knowledge in a simple and objective way that can actually help the theme approach ensuring the quality of information that reaches the public. So far, the 10 modules that constitute this initiative have already amounted over 150 thousand views. The performance in events involving the universe of Boy Scouts, also part of the actions developed by the IOC, as well as the

participation of the IOC in editions of the National Week of Science and Technology (established by the Ministry of Science, Technology and Innovation) especially at Fiocruz, and activities organized by other institutions, such as the National Institute of Science and Technology of Drugs and Medicines.

Ш

To disseminate the results of its scientific activities, researchers and students of the IOC publish scientific articles, dissertations, and theses developed in their graduate programs in national and international journals. Based on Fiocruz's **Open Access** Policy, established in 2014, the IOC has been working to make its scientific production available at Arca, a free access database (**arca.fiocruz.br**).

- 1,133 scientific articles deposited in 2015
- 146 doctoral theses
- 246 master's dissertations

arca

Repositório Institucional da Fiocruz

The research activities are the target of external **communications** activities. In 2015, 604 articles about the IOC's activities were published in the media.

Highlights include the launching of the Urban Climate Change Research Network Center in Latin America, with more than 50 positive insertions published in the media. The IOC's actions in addressing the Zika virus issue were also an intense target of media interest, including the unprecedented detection of Zika virus in amniotic fluid samples from two pregnant women from the state of Paraíba, whose fetuses were confirmed with microcephaly by ultrasound exams. The initiative attracted national and international media coverage.

Great communication efforts to disseminate information about Aedes aegypti mosquito control were conferred, including the consulting to TV Globo broadcaster and the partnership with the newspaper Extra, resulting in an event held to clear questions from readers about Aedes aegypti and Zika virus. The initiative 10 Minutes Against Dengue, created by the IOC in 2010 and reedited by the State Government of Rio de Janeiro with title update for 10 Minutes Against Aedes, was also used by the State Government of Minas Gerais.

Reports from the research laboratories

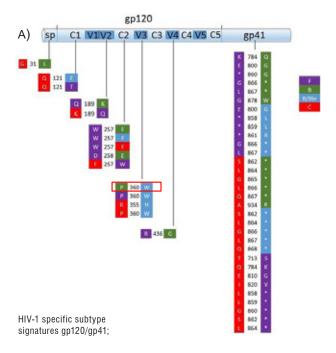
Laboratory of Molecular Immunology and AIDS (LABAIDS)

Leadership: Monick Lindenmeyer Guimaräes

E-MAIL: monicklg@ioc.fiocruz.br

LABAIDS has been accredited in 1991 and, since then, has the mission of conducting research, teaching activities, technological development, innovation, clinical trials and reference activities on different aspects of HIV infection, aiming to the promotion of health. Our group works in close collaboration with clinical research groups of the National Institute of Infectious Diseases Evandro Chagas (INI/Fiocruz) and the General Hospital of Nova Iguaçu (HGNI), of epidemiology at the Institute of Scientific and Technological Information and Communication in Health (ICICT)/Fiocruz, of the National Institute Of health of the United States of America (NIH) and the Pasteur Institute of Paris, among other groups in the country and abroad adding a set of clinical, epidemiological and laboratory data, as well as a specific biorrepository to each study/research line. Since its accreditation, LABAIDS collaborates with the National Department of STDs, Aids and Viral Hepatitis in their actions and in health research and, from 2011, is national reference laboratory of the World Health Organization (WHO) for surveillance of transmitted HIV-1 resistance to antiretroviral drugs (HIVResNet). Through this network and scientific projects, the lab has been bringing scientific and technological support to laboratories from different countries in South America, Central America and Africa, Therefore, we have contributed heavily in the construction of molecular epidemiology of HIV scenario, adding relevant information about the evolutionary and demographic history of viral subtypes and resistance to antiretroviral drugs. Regarding the host, we've been studying pathogenic processes involved in HIV infection in association or not with other comorbidities

and evaluated the influence of this genetic profile. The results produced in therapeutic or clinical trials to prevent acquisition of HIV infection, in collaboration with the NIH networks, have generated changes in public health policies with respect to the clinical management of individuals living with HIV/Aids. In recent years, accompanying the changes in the epidemiological setting, the lab went on to incorporate studies on other viruses of interest in public health, including: ZIKV, DENV-1, Influenza, HCV and HEV. Our research activities are divided into macroprojects which highlights are below. These results resulted from internal collaboration or in association with different national and international research groups.

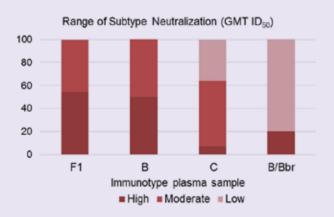


2016

HIGHLIGHTS

Laboratory of Molecular Immunology and AIDS (LABAIDS)

(i) the replacement of proline by tryptophan at the top of the loop of the gp120 V3 in HIV-1B is associated with low neutralizing response to HIV, leading to important impact on HIV/Aids vaccine development. (ii) In relation to molecular epidemiology of HIV-1, we see that: (a) analysis of the northern region of Brazil have shown high complexity and molecular epidemiological pattern varied among the different States, reflecting a complex epidemic with multiple viral independent introductions; (b) the high prevalence of BCAR lineages in North and northeast regions States probably reflects strong epidemiological link with the Caribbean's epidemics; (c) check the occurrence of rare data on Brazil related to CRF45_cpx and rebuild its evolutionary history; (d) we have detected, in Mozambique, the introduction and circulation of new HIV-1 genetic subtypes, depending mainly of intense migration between the countries of the Sub-Saharan region; (e) we find that differentiated the different prevalence CRFs that circulate in Africa is probably multifactorial. (iii) We note that at least two haplotypes carrying different alleles associated with the risk of intolerance to non-nucleoside reverse transcriptase inhibitors and viral protease. (iv) in the context of clinical studies involving the coinfection by HIV-1 and other micro-organisms, we emphasize: (a) the study of HIV/Leishmania Association, in which we identify important differences in the immune profile of cases of visceral leishmaniasis, indicating a reduced



Neutralizing potential of each subtype.

ability of immune modulation in patients who present with episodes of reactivation; (b) from the assessment of HIV-infected individuals re-submitted to vaccination for H1N1 vaccine Influenza, triple the importance of periodic update of immunogen and of individuals regular HIV vaccination against H1N1, relevant data to optimize the strategies adopted by the National Program of Immunizations (PNI). The study of prevention of HIV transmission in serodiscordant couples followed in long-term confirmed that the early initiation of antiretroviral therapy combined reduces the rates of sexual transmission of HIV-1 and clinical events. The studies of mother-child network has shown that sexually transmitted infections in pregnant women with HIV infection are associated with adverse clinical outcomes in children exposed but not infected with HIV.

Laboratory of Environmental Assessment and Health Promotion (LAPSA)

Leadership: Cláudia Portes Santos Silva cpsantos@ioc.fiocruz.br

Multidisciplinary studies on biodiversity associated with public and environmental health are associated with the axes: (i) Taxonomy, Bionomics, control and diagnostic strategies of parasites and vectors — with studies focused on helminths, fungi, arthropods, and mollusks that can act as pathogens or vectors of medical and veterinary importance; (2) Ecotoxicology and environmental health surveillance — with developing indicators of water quality in public water supply and superficial water. The research respond to the demands of actions to meet the Ministry of health in order to support health

surveillance epidemiological and environmental, for SUS, Ministry of environment, State and local health agencies and environment and federal regulatory agencies. The axles are linked and fall on the prospects for meeting the guidelines of SUS contemplated in the strategic map of Fiocruz for 2022 regarding the Strategic Process — Health, Environment and Sustainability. The lab also invests in the training of human resources, keeping regular guidance of high school students, undergraduate, master, doctorate and post-doctorate, among other forms of professional qualification.



Field work, growing algae.

HIGHLIGHTS

Laboratory of Environmental Assessment and Health Promotion (LAPSA)

Publications in taxonomy, Bionomics, control and diagnostic strategies of parasites and vectors focused on morphological and molecular taxonomy of species of Nematodes Anisakidae medical and veterinary interest, although the diversity of freshwater fish in the new world,

new morphological data of filarioid Litomosoides chagasfilhoi, testing in vivo on the effects of herbicides on development of Echinostoma paraensei and effects of the introduction of tilapias on morphology and life cycle of Daphnia species.



Experiments with molluscs, culture of fungi, helminth and fish.

Assessment Laboratory in Teaching and Philosophy of Biosciences (LAEFIB)

Leadership:: Maurício Roberto Pinto da Luz mauluz@ioc.fiocruz.br

LAEFIB is based on the CNPq research of group *Teaching in Biological Evolution and Health*, led by Mauricio Luz (ML) and Ricardo Waizbort (RW), and solid links with the graduate program in life sciences and health education. LAEFIB operates on three lines of research: (i) evaluation of teaching in biosciences and health, conducted by ML, developing projects which identify and propose original approaches to teaching problems of current health themes; (ii) philosophy, history and education in Biosciences, conducted by RW, which develop projects that seek to study the theory of evolution throughout history, its philosophical implications and its applications in teaching biology; (iii) teaching in biological evolution and health, research

the latest lab, conducted by ML and RW, in which educational projects based on so called evolutionary or Darwinian medicine, to understand harms to health in the light of the concepts of natural selection and evolutionary adaptation. Our general objective is to investigate the relevant health topics education, developing, evaluating and distributing educational materials/strategies. Our proposal is to highlight the relationship between evolution, ecology and human health. In this context, activities are developed in association with research on relevant education research themes, such as cooperative learning, history of science and continuing education, especially through educational technology and distance education.

12016 HIGHLIGHTS

Assessment Laboratory in Teaching and Philosophy of Biosciences (LAEFIB)

LAEFIB has sought new fields of research and science, with special interest by introducing, in the field of Brazilian education, the theme of the relationship between biological evolution and human health. We highlight the regular collaboration researchers from the lab with the magazine Ciência Hoje, in which six texts were published in 2016, many of which relate to biological evolution and human health. Are examples of these relationships, the relentless Parasites text: virus transported by Europeans decimated Amerindian populations in a few years (which deals with infectious diseases) and

Conscious and realistically choice what ecological pyramids have to do with the best cut of meat at our table? (regarding nutrition). These works come from establishing the scientific dissemination as a central line for the lab. Collaborations in the area of Education with other institutions took place through two editions of the course The hepatitis that is not on the map: how mapping helps to solve problems related to viral hepatitis, held at the Federal Institute of Acre, contributing to the spread of educational activities developed by our team.

Entomological Biodiversity Laboratory (LABE)

Leadership: Jane Margaret Costa Von Sydow jcosta@ioc.fiocruz.br

Working in different areas converge to the mission and the values of the IOC, the LABE, in 2016, activities related to (i) scientific research, with a multidisciplinary approach covering several species of Hemiptera (Auchenorrhyncha and Heteroptera); (ii) education and scientific dissemination; (iii) training of human resources; (iv) coordination of post-graduate courses; (v) Organization of national scientific events; (vi) curator of the Entomological Collection of the Instituto Oswaldo Cruz (CEIOC). The organization and laboratory procedures aligned with the institutional criteria of ethics, safety and quality in research, according to the standards of VPPLR and VPGDI. In addition, the use of animals in procedures have been approved by the Ethics Committee for Animal Use (CEUA) (licenceLW-18/11) and the various collections of biological material were performed according to the criteria of the MMA, CNPg and SisBio. Research activities in the LABE are based on collaborative projects and propitiated the interaction with several laboratories of the IOC (six), with other units of

Fiocruz (two) and several national (12) and international (9) institutions. In 2016, the LABE published 14 scientific papers in national and international journals with impact factor ranging from 0.35 to 8.98. The LABE comes bringing relevant contributions to the knowledge of the biodiversity, the importance of which is related to environmental health and the lifting of the Entomological fauna. In this context, we highlight research related to Cicadellidae, one of the 10 largest families of insects, with emphasis on description of new species. With relation to Heteroptera, the main focus is on the vectors of Chagas' disease and bedbugs. A comprehensive approach, which goes from the classic morphological systematics to molecular biology, clarifying relevant issues come these evolutionary groups. In addition, with respect to Chagas disease vectors, unpublished results were obtained on the complex *Triatoma brasiliensis*, which include the main vectors species of the semi-arid areas of Northeast Brazil.

HIGHLIGHTS

Entomological Biodiversity Laboratory (LABE)

Several works of the laboratory are in 2016. Among them, we can mention:

The study recording and featuring 13 different phenotypes of Triatoma. brasiliensis in Pernambuco, with nine of the phenotypes were intermediaries between species of the complex. The results obtained by analysis of the intermediate chromatic patterns, molecular analysis and the experimental crossings, corroborate the existence of a natural hybridization that gave rise to T. b. nacromelasoma (Infection, Genetics and Evolution 37, 77-87). The study showing that access to aquatic habitats occurred in association with morphological and behavioral changes that led to the increase of the displacement speed on Gerromorpha (Insecta: Heteroptera). Subsequently, the variability in locomotor behavior in different lineages is correlated with the specialization in different niches (Current Biology 26, 1-7). The study describing four new species of Paravelia (Hemiptera: Veliidae — demi-aquatic bedbugs, unique genre of tropical America (Canadian Entomologist 148, 642-667). The study on the taxonomy and biogeography of the family Cicadellidae, one of the largest, with about of 25,000 known species. In the article, two new species of the tribe Portanini (Portanus restingalis and Paraportanus marica) are described from material from the Restinga de Maricá (State of Rio de Janeiro) (Zootaxa 4196 (3), 399-406).



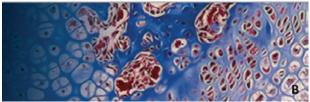
Cellular Biology Laboratory (LBC)

Leadership: Maria de Nazaré Correia Soeiro soeiro@ioc.fiocruz.br

The goals aligned to the research and technological development in health include (i) pre-clinical tests of new pharmacological agents and therapeutic schemes innovations, antitumor and anti-inflammatory agents anti-interference. Investigate the activity (isolated and combined) of new parasitic agents (synthetic, biomolecules or repositioning of drugs) through studies on monoinfections caused by intracellular parasites (*Trypanosome cruzi* and *Leishmania spp.*) as well as coinfections (i.e., with helminths); (ii) investigate the antitumor activity of new agents (biomolecules and synthetic agents), correlating biological activity with chemical structure; (iii) explore, for testing, the profile of toxicity and toxicological potential of promising pharmacological agents; (iv) evaluate (electronic microscopy and fluorescence, biochemistry, flow cytometry, fluorimetric and oxigraphy) mechanisms of action and validate targets cell phones of selected compounds; (v) investigate molecular events involved in the process of programmed cell death forward to the exposure of parasites, tumor cells the compounds, as well as explore these events over the course of the parasitic infection; (vi) study of safety and efficacy aspects of alternative therapies (e.g., electrotherapy, autologous blood) that can be combined with conventional therapies for parasitic diseases and tumors. The approach related to the biological aspects, inflammatory and cell death pathways involved in host-parasite interaction includes: research autophagous/apoptotic pathway in host/parasite during its interaction, featuring molecules involved, besides the oxidative metabolism and energy analysis

of protozoa through induction of resistance. The development of clinical/behavioural murine models for use in pre-clinical trials in the field of Parasitology, and chronic pathologies neoplastic and neurological clinical and behavioral profiles featuring objective aiming at the application of studies: parasitic infection (acute and chronic), ischemic acute renal injury models, models of neoplasms, and neurological changes in preclinical trials of effectiveness of new chemotherapeutic drugs antiparasitic agents, antitumor and psycho modulators.





A: scanning electron microscopy of *T. cruzi*, the causative agent of Chagas disease (blood trypomastigotes, Y strain); B: histological image obtained by optical microscopy of the femoral epiphysis of mice underwent autologous blood management.

HIGHLIGHTS Cellular Biology Laboratory (LBC)

LBC presents intense participation in projects in multidisciplinary networks, with funding from agencies or national (CNPq, Faperj) and international European Community, Consortium for Parasitic Drug Development, Inserm, Cofecub/Capes, among others, seeking to contribute to (i) pre-clinical trials (in vitro and in vivo) of potential new medicines, including those already licensed to other pathologies ("repositioning") and share mechanisms of action and targets mobile phones with Trypanosomatidae; (ii) in silico and phenotypic screening of new molecules from compound libraries; (iii) search for new targets and rational synthesis of inhibitors of targets or metabolic pathways sectionals; (iv) identification of pharmacological properties of products/natural extracts, as well as (v) analysis of complementary alternative therapies (i.e., rehearsals electrotherapy). This act makes use of innovative and well standardized approaches monotherapies and/or Combinatorial (synthetic agents and/or biomolecules and/or alternative therapies, such as electrotherapy and cell therapy), aiming at a synergistic action and/or more potent and selective additive and thus more promising in the identification of new drug candidates for antitumor and anti-inflammatory, anti-parasitic therapy, assessing the impact of coinfections and comorbidities in success or failure. The LBC actuation in large national and international scientific networks is due to partnerships with various groups of medicinal chemistry, pharmacology, laboratory animal science, molecular modeling studies, among other areas of expertise with bilateral projects with groups of Georgia State University/United States of America (USA), Jackson State University/USA, North Caroline University/USA, Vanderbilt University/USA; VU University/ Holland, Universidad Complutense de Madrid/ Spain, Universidad do Oriente/Cuba, Centro

Nacional de Electromagnetismo Aplicado/Cuba,

School of Health, Sport and Biosciences, University of East London/England, Swiss Tropical and Public Health Institute/Switzerland, Laboratory of Microbiology, Parasitology and Hygiene, Faculty of Pharmaceutical, Biomedical and Veterinary Sciences, University of Antwerp/ Belgium, among others, as well as networks and consortia including the Consortium for Parasitic Drug Development (http://www.unc. edu/~vwingate/pipelines.html) Phosphodiesterase Inhibitors, is Neglected Parasitic Diseases (http://www.pde4npd.eu/ publications.html), RESNET (http://www. uni-muenster.de/Chemie.pb/forschen/ ResNetNPND/), among others. In 2016, the LBC highlights, in the area of preclinical studies of new antiparasitic agents, including those assessed on Trypanosoma cruzi, the etiological agent of Chagas disease, relevant pathology neglected that affects more than 6 million individuals in areas of extreme poverty of Latin America, including Brazil, as well as other non-endemic regions, including Europe, Asia, and Europe, due to population migration of infected carriers for these regions: (i) proteomics analysis of the mechanism of action of naftoimidazoles derivatives of beta-lapachone in blood of *T. cruzi*. In this study, published in **PLOS Neglected Tropical Diseases, we identified** 34 proteins which expression levels were modulated by treatment with the compounds. These findings point to a wide variety of metabolic pathways involved in the mechanism of action, opening up new prospects for the development of tripanocide agents. (ii) biological action of other natural and synthetic compounds on different forms of this Protozoan, including effect of different fractions of crude extracts of the plant Zantozilium spp (collaboration with Dr. Julio Scalona, of Universidad do Oriente, Cuba), copper (II) complexes bound to the Schiff base 2-[(5-nitrofuran-2-il) metilenamino] phenol (HL1) and 2-(4-nitrobenzilidenoamino) phenol (HL2)

(collaboration with Dr. Leticia Teixeira, University of Minas Gerais) and of diamidines and its analogues (collaboration with Dr. David Boykin, University of Georgia/USA and Drs. **Donald Patric and Richard Tidwell, North** Carolina University/USA, whose manuscripts are in the process of submission). Part of the data obtained from the activity of diamidines and its analogues, such as the arilimidamides (AIAs), presented in the form of posters and lectures at national conferences (SBPZ, 2016, Caxambu, Minas Gerais, Brazil) and international (Brisbane, Australia). As for the data obtained with copper complexes, were published in the Journal of the Brazilian Chemical Society. In this article, the physical measurements of the molecules by means of different techniques, in addition to the description of the synthetic route and the tests of cytotoxicity and biological cytotoxicity tripanocide in vitro. With regard to the experimental chemotherapy, it is worth mentioning the studies that were part of the defence of theses and dissertations in 2016 that revealed: (iii) interference of different experimental models to assess their tripanocidal action of new compounds and the reference medicinal product, and the evaluation of the effectiveness (in schemes of monotherapy and in combination) of AIAs (provided by Drs. Tidwell and Boykin) and which are aromatic molecules that interact with crack less DNA and imidazolyl inhibitors of the biosynthesis of sterols (CYP51), such as NIV and ELV (collaboration with Dr. Galina Lepesheva, Vanderbilt University/USA). In vitro data published in Antimicrob Agents Chemother, on revealed that the derived AIA m-terfenil has been promising, showing activity (EC50/24 h) in the range of 40 nM and index of selectivity (IS) of 480, being still able to stimulate the genesis of lipid bodies, although there is no correlation between this finding and to assess their tripanocidal action. Studies in 2016 and published at the beginning of 2017 on **Antimicrob Agents Chemothercom with** imidazole VFV revealed strong action on

intracellular forms (EC50/48 h 380 nM and IS > 263), low toxicity in models of acute toxicity (Noael 200 mg/kg), being able to suppress completely the parasitemia and provide 100% survival at doses of 25 mg/kg (oral twice a day). Our results reveal, yet important differences related to the course of infection and impact of experimental therapy depending on the: (a) gender of the animal, (b) beginning of the administration of the test compound and the treatment time, apart from (c) nature of the vehicle used to dilute the same. In General, females are less vulnerable than males to T. cruzi infection and more sensitive to therapy, the greater solubility of a compound results in its better bioavailability and potential therapeutic and treatment success, 24 h after infection (preventive scheme), results in higher rates of reduction of parasitism, but is less predictive for displaying weak correlation with the actual conditions of human infection. Our data also revealed important reductions in parasite burden and increased levels of healing among using combination therapy. Another aspect evaluated has been the action of drugs in mixed infections and parasitic coinfections and helmintic in experimental models, enabling the development of project (CNP/FAPERJ/STPH) in partnership with the Swiss Tropical and Public Health Institute, as well as performing in Leysin (Switzerland, January 2017), the lecture at the 34th Annual Swiss Meeting (http://wp.unil.ch/ trypmeeting/), Trypanosomatid sponsored by Schweizerische Kommission für Molekularbiologie. Still in this area, it is worth highlighting the coordinated project in Brazil by a Professor of the program about multidisciplinary study related to the identification of potential new drugs for therapy of Chagas disease, leishmaniasis, sleeping sickness and schistosomiasis. This project, approved and supported by the European Union (General coordination of Dr. Rob Leurs), entitled Parasitespecific cyclic nucleotide phosphodiesterase inhibitors to target neglected parasitic diseases,

2016

aims to identify and synthesize new specific phosphodiesterases inhibitors as target for parasitic diseases neglected and integrates the international platform called PDE4NPD (http:// pde4npd.eu/). Additionally, we conduct the characterization of immunoproteomic quantitative of T. cruzi, master's thesis of a student in the lab, using antibodies of patients in different stages of chronic disease, which led to the identification of two major antigens that can be used as biomarkers of heart lesion progression, with the objective of improving the quality of life of patients. About research related to the development and implementation of clinical/behavioural models in mice for preclinical trials in the fields of Parasitology, Pathology and Psychiatry, we emphasize that our studies have shown that the Group of male individuals after weaning reduces the incidence of aggression in adulthood. In addition, with regard to the aspect of environmental enrichment, equipment/materials for shelters

(igloo) and nesting (tissue paper), we highlight the use of interconnected cages system developed by LBC, as described in the normative resolution No. 33 of the National Council for the **Control of Animal Experimentation (Concea).** Using the spontaneous model of aggression (MEA), also developed by LBC, we suggest the efficiency of the use of antipsychotics in aggressiveness of male mice under stress situation of regrouping in adulthood, as published in Behavioural Brain Research, in manuscript Use of haloperidol and risperidone in higly aggressive Swiss webster mice by applying the model of spponteneus aggression (MSA). Finally, we highlight the clinical/ behavioural course description of murine models of Chagas disease as reference to experimental acute infection by T. cruzi in the manuscript Use of noninvasive parameters to evaluate Swiss webster mice during T. cruzi experimental acute infection, published in the Journal of Parasitology.

Computational Biology and Systems Laboratory (LBCS)

Leadership: Alberto M. R. Dávila davila@fiocruz.br

LBCS doing research related to molecular evolution, phylogeny and phylogenomic parasites and vector insects, as well as studies on health related metagenomics. *Mycobacterium* spp, Protozoa (*Trypanosoma*, *Leishmania*, *Plasmodium*, *Cryptosporidium* etc.), *Streptococcus*, *Escherichia coli* and *Serratia* are some of the pathogens studied by the laboratory, as well as the vectors *Rhodnius prolixus* and *Aedes aegypti*. As regards the metagenomic approach, the lab has focused on microbioma description of beach Anjos of Arraial do Cabo (Rio de Janeiro), in the sewers, as well as in mining of genes

encoding possible new natural compounds, like polyketide synthase (PKS) and non-ribosomal peptide Synthase (NRPS), assessing the presence and abundance of anoxigenic phototrophic bacteria (AAP) in the marine environment. The LBCS also develops methodologies and software for bioinformatics analysis and comparative genomics, as the ortholog enhanced databases and the Stingray system. Are also conducted studies aimed at identifying and in silico characterization of pseudogenes, as well as studies on evolution of enzymes and metabolic networks.

HIGHLIGHTS

Computational Biology and Systems Laboratory (LBCS)

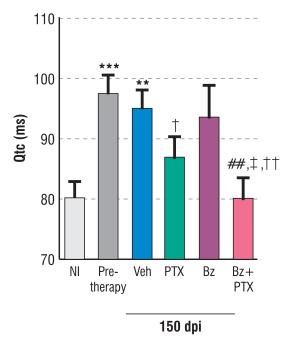
Among the highlights of LBCS, are publications on the research of serine betalactamases and bacteria AAP in hospital sewage metagenomas and Arraial do Cabo (both in the State of Rio de Janeiro), respectively, with participation in the publication of the article about the genome of Rhodnius prolixus. The Organization of the event A day with genomics in high school (GenomicDay) as part of the IOC on the school, obtained great prominence and success (http://www.fiocruz.br/ioc/cgi/cgilua.exe/sys/start.htm?infoid=2637&sid=32).

Biology Laboratory of the Interactions (LBI)

Leadership: Joseli Lannes Vieira lannes@ioc.fiocruz.br

LBI, created in the IOC in September 28 1998 (then named Research Lab in Autoimmunity and Immunoregulating), was re-accredited in 2004, 2009 and 2015 (2015-2021 period). It is organized in two sections: Immunobiology and Scientific Literacy. The Immunobiology Section is focused on the development of basic research in Experimental Biology in the areas of immunopathology and immuno-regulation of parasitic infections (Chagas disease, toxoplasmosis). and chronic degenerative diseases and/or genetic (such as cystic fibrosis), as well as to the development of vaccines against parasitic infections. The main focus of our study are immuno-patogenic mechanisms, using in vivo experimental models (i) cardiomyopathy and the changes (behavioral and cognitive) nerve in chronic Chagas disease and (ii) of opportunistic infections for people with cystic fibrosis. We have also developed in vitro models of cellular interaction (macrophages, astrocytes, cardiomiocites) with parasites (Trypanosoma cruzi and Toxoplasma gondii) and opportunistic microorganisms (Burkholderia SP.), seeking the understanding of cellular and molecular mechanisms of these interactions and the adaptive immune response. In the Sector of Scientific Literacy, the research leads to the development of social technologies in science education and health, with studies on the public understanding of key concepts and educational intervention processes linked to scientific literacy. We have the social actors of the municipal education schools and State and main target audience, but we also work with training of undergraduate and graduate students in biosciences and health, in addition to

populations at risk of infection and chronic issues approach related to the promotion of health and quality of life. Develop research, still, about the use of educational materials through face-to-face and/or virtual, with investigative tours that guide teaching strategies and practices for the popularization of knowledge in science and health. We operate also in scientific dissemination. We have as one of our main goals the training of human resources at all academic levels. Currently, for reasons of lack of space and suitability of biosecurity, Immunobiology is located at the Wing Cardoso Fontes and the Sector of Scientific Literacy in Wing Lauro Travassos.



Beneficial effects of the combined Bz-plus-PTX therapies on electrical alterations in CCC.

HIGHLIGHTS

Biology Laboratory of the Interactions (LBI)

Advance in the challenge of the proposal that the unbalance of the immune response is associated with the pathogenesis of chronic chagasic cardiomyopathy (CCC). Also showed, by other authors, that the CCC is associated with persistence of *T. cruzi* in cardiac tissue. We have proposed a combination therapy with immunorregulador Pentoxifylline and the medicine trypanocidal benznidazole. This therapy, administered to mice with CCC, reverted changes, such as long QT syndrome, a major biomarker of prognosis and evolution of CCC. So, we showed, for the first time, that the therapy based on the control of the parasite and the unbalance of the immune response has beneficial effect on CCC. This data is in the article published in Antimicrobial Agents and Chemotherapy. Also using experimental model for depression and anxiety, behavioral changes found in patients with chronic Chagas disease, brought new therapeutic perspectives for these Comorbidities. We collaborate with teachers of the Federal University of Rio de Janeiro (Claudia Paiva and Marcelo Bozza), showing that the therapy with the antioxidant resveratrol in animals with CCC reverts changes, improves cardiac function and reduces the parasite

burden, opening new therapeutic perspectives to the CCC, as shown in article in PLoS Pathogens. In order to consolidate the line of opportunistic infections in contexts of low immunity, such as cystic fibrosis, seek and receive external funding of Faperj and CNPq. In research Scientific Literacy and health promotion, we continue on ABC program coordination on science education - Mão na massa/RJ, connected to the Brazilian Academy of Sciences, which encourages a rapprochement between scientists, professionals in Education and Health. The strategy, based on research, encourage observation and proposal of consensus on transdisciplinary experiences that address curricular issues in their relationship with their daily life, from the perspective of health promotion. The work has been recognized by their commitment to encouraging the questioning and the logical-rational thinking connected to risk perception and re-elaboration of conceptions about health issues, supported by municipal departments of education and Faperj, for interventions with innovative strategies and educational materials. Finally, we highlight the Honorable mention *Prize Capes of 2016* in Thesis area life sciences II, with the thesis defended by Isabela Resende Pereira.

Biology Laboratory of Trypanosomatids (LABTRIP)

Leadership: Ana Maria Jansen jansen@ioc.fiocruz.br

Perform research, technological development, innovation and human resources related training, knowledge of the factors that regulate the transmission of Trypanosoma cycles of mammals of the genus *Trypanosoma* (*T. cruzi* and *T. evansi*) and *Leishmania* major Brazilian biomes. In this context, the Mission of this lab includes macro and micro-ecological aspects

that interfere in the interaction of these parasites with their reservoirs and vectors. The lab provides assistance to federal and State health agencies in studying wild reservoirs of leishmaniasis and Chagas disease and the risk factors of outbreak of leishmaniasis and Chagas disease.

2016
HIGHLIGHTS

Biology Laboratory of Trypanosomatids (LABTRIP)

Between the various contributions, the publication of multidisciplinary study on the integration of parasitological and molecular approaches to trace the origin and profile of helminth infection of ancestral groups of the Canary Islands (J Parasitol, 102:222-8). Also the publication of study in which we demonstrated the mixed infection by four DTUs of *T. cruzi*, in addition to *T. dionisii*, in cardiac tissue of a child who died of acute Chagas disease (Parasite & Vectors, 9:477).

Laboratory of Biology and Parasitology of Wild Mammals and Reservoirs (LABPMR)

Leadership: Arnaldo Maldonado Júnior maldonad@ioc.fiocruz.br

The lab has conducted interdisciplinary research, including the areas of Zoology, Ecology, Parasitology and Epidemiology, questions relating to the reemergence of Chagas disease orally and the emergence of hantavirus in the country, the introduction and distribution of angiostrongyliasis in the country, equinostomiasis as a model of study, as well as to the effects of fragmentation and alteration of natural landscapes in diversity and ecology and health of host species and its parasites in human occupation disorderly urban areas or impacted by the expansion of anthropogenic activities. Generated information with a view to the solution of issues related to the role of species involved in the cycles of transmission of

zoonosis, the taxonomic revisions with description of new species of mammals with the potential to act as reservoirs of new species of helminths, to the discovery of new variants of pathogens and the studies of ecology of reservoirs and the host-parasite interaction. The lab develops, too, searches for the parasite-host relationship through experimental models with *Biomphalaria glabrata* and related to the extensive use of pesticides and their effects on the environment, using as a model, the *Echinostoma paraensei*. In the field of Epidemiology, infectious endemics investigated in various localities of the country, with a predominance in regions of northeastern Brazil and the Amazon region.

HIGHLIGHTS

Laboratory of Biology and Parasitology of Wild Mammals and Reservoirs (LABPMR)

One of the highlights of the research conducted by LABPMR was an important publication in PLoS One, Natural Schistosoma mansoni infection in the wild reservoir Nectomys squamipes leads to excessive lipid droplet accumulation in hepatocytes in the absence of liver functional impairment, performed by means of interinstitutional collaboration with the Cellular Biology Laboratory of the Biology Institute of Federal University of Juiz de Fora. The natural infection by S. mansoni in wild reservoir N. squamipes causes fatty liver disease in the absence of liver functional lesion and the

accumulation of lipids, markedly PUFAs (polyunsaturated fatty acids), which coexist in the process of granulomatous inflammation, suggesting that lipid reserves may be acting as a protective mechanism to the rodent in to deal with the infection. This work answers, by means of the Cellular Biology and Biochemistry, the question initially raised by Drs. Rey and Lenzi on the why of the livers of these rodents infected with S. mansoni won't be harmed with the infection, i.e. that N. squamipes is a good reservoirs for schistosomiasis in their liver functions.

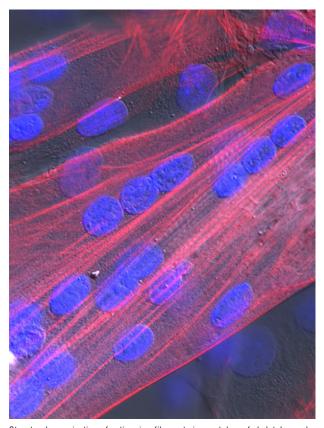


Structural Biology Laboratory (LBE)

Leadership: Helene Santos Barbosa helene@ioc.fiocruz.br

The lab, in the line of research on experimental toxoplasmosis, outlines in five sections: (i) the acute phase and establishment of historicamente, analyzing the cellular and molecular response of skeletal muscle cells (mice and cattle) to infection; (ii) congenital toxoplasmosis in developmental biology and autodeclarações, investigating the interference of the infection in the maturation of nerve and muscle cells with emphasis on expression of transcription factors, besides the molecular factors that determine the infection of endothelial cells of umbilical cord in humans and mice; (iii) biology of the parasite in enterocytes and other cells of cats, studying cellular and molecular aspects during the anticoncorrencial cycle and historicamente; (iv) genotype and molecular epidemiology of *Toxoplasma gondii* in wild mammals by assessing the prevalence of the parasite and identifying the genotypes in the environment and in humans (pregnant women) and cattle, investigating the biological and genetic diversity of lineages of T. gondii; (v) innate immune response in the intestinal epithelium of cats and mice during the T. gondii infection, evaluating the cellular and molecular constituents of intestinal immunity to infection and the role of inflammatory cells in the dissemination of the parasite in the intestine. In the line of research on leishmaniasis, the approaches are outlined in three ways: (i) participation of TLR in the inflammatory process caused by Leishmania, evaluating the participation of receptors TLR-2 and 4 in recognition and immune response targeting residents and inflammatory cells during infection by Leishmania amazonensis and Leishmania braziliensis; (ii) application of agonists and antagonists of TLRs in immunotherapy of integumentary leishmaniasis and visceral, identifying the profile of immune response produced by fibroblasts of DermIS and fibrocytes

after treatment on infection by *Leishmania* amazonensis; (iii) mechanisms for formation of fibrosis in experimental visceral leishmaniasis and canine, studying cells and inflammatory residents on the skin, liver and spleen and the kinetics of modulation of extracellular matrix proteins in fibrosis formation in these organs.



Structural organization of actin microfilaments in myotubes of skeletal muscle cells C2C12 lineage. Differentiated cell culture observed by differential interferential microscopy overlapped with fluorescence. Arrangement of actin filaments (in red) in myotubes presenting bundles of microfilaments parallel to the sarcolemma. The striations of these cells were revealed by the F-actin marking. Nuclei visualized by DAPI staining (blue). Bar: 20 μm .

HIGHLIGHTS Structural Biology Laboratory (LBE)

Skeletal muscle cells, as a model for study of cystogenesis of *T. gondii*, showed the structural modulation of tubulin, desmin and plectin, constituents of the cytoskeleton proteins, during this process. These findings can be potentially exploited as target molecules in the intervention of the establishment of the chronic phase of infection. In the area of technological development, advances have been achieved in large-scale production of cysts of *T. gondii* in cell culture, which is the principle of 3Rs of sustainability. In the context of scientific collaborations, the LBE is strengthening research in the area of congenital toxoplasmosis, interacting with medical teams: (i) the National Institute Fernandes Figueira (IFF-Fiocruz), seeking the isolation and biological characterization and genotyping of circulating strains in the State of Rio de Janeiro, and (ii) the Hospital Marcílio Dias, in the area of congenital toxoplasmosis in an experimental

approach with endothelial cells from the umbilical cord. In partnership with the Federal University of Rio de Janeiro, we identify the major components of the signaling pathways involved in the production of neutrophylic extracellular traps (NETs) in response to L. amazonensis, identifying the role of ERK, PI3K, PKC and Ca2+ in the process. This set of results contributes to a better understanding of the molecular mechanisms present in Leishmania interaction with Human neutrophils. Potentially in the area of innovation, opens up prospects for the development of new therapeutic strategies for the treatment of leishmaniasis. In addition, in the area of human resources training, there was the entry of five master students and a doctoral candidate in LBE, alumni of undergraduate and master's degrees. That quota should increase and/or introduce new approaches in the areas of experimental leishmaniasis and toxoplasmosis.

Molecular Biology Laboratory Applied to Mycobacteria (LABMAN)

Leadership: Philip Noel Suffys psuffys@ioc.fiocruz.br

LABMAM has three lines of research: (i) genetics of microorganisms, which works basically with genetic variability of Mycobacteria of the Mycobacterium tuberculosis complex, Mycobacterium leprae, and non-tuberculous (MNTB); (ii) study of gene expression; (iii) human genetics. In the area of bacterial genetics, the LABMAM has, as its main challenge, studying genetic variability for better characterization of population structure of Mycobacterial species, studying Phylogeography, studies of molecular epidemiology and molecular identification and antibiotic resistance, including strains of Mtb MDR and XDR. The tools used for this purpose are conventional sequencing, SNPs analysis and repetitive sequence and genome analysis complete. In leprosy, molecular epidemiology studies, detection of resistance and MDR in relapse and new cases and we are studying the participation of wild animals in the transmission of the disease. Main studies started with MNTB are related to lung disease. with emphasis on Mycobacterium kansasii and

Mycobacterium abscessus. In the area of human genetics, the group worked, basically, in the development of projects related to Pharmacogenetics applied to different models of disease (leprosy and tuberculosis, TB/HIV) and in the elaboration of new project for study of pharmacogenetics in asthma. In leprosy, the main focus was the study of the genetic variability of the G6PD gene and their connection with the occurrence of hemolytic anemia induced by Dapsone in leprosy patients treated with Dapsone containing schemas. This work led to the formation of a master student. In the model of tuberculosis, the group is involved in a project evaluating the variability of genes coding for protein drug carriers (basically the fluoroquinolones), and finally, in relation to the TB/HIV co-infection, the Group participated in the elaboration of project for pharmacogenetic study applied to this co-infection. In this context, given the concomitant treatment for both diseases using a group of drugs, patients will be genotyped for each gene involved in the metabolism of anti-TB drugs and antiretroviral drugs.

Molecular Biology Laboratory Applied to Mycobacteria (LABMAN)

Some important contributions of LABMAM was the delineation of the molecular epidemiology of isolates of m. tuberculosis resistant to multiple drugs, of crucial importance in the control of tuberculosis at national and regional level, since individuals with resistant TB represent an important link in the chain of transmission of the disease. Through the sequencing on the platform of the IOC and international collaborations, we are in the process of analyzing hundreds of genomes of Mtb isolates sensitive and resistant to drugs. Another highlight was the characterization of Brazilian strains of Mtb Beijing and our contribution in an international study of genomes of Mtb, identifying strains generalists (generalists: wide geographical distribution) and experts (specialists: with restricted distribution), published in the journal Nature Genetics. It stands out, too, the beginning of the multinational project analysis of genetic variability of M. kansasii, through the study of the genome and collaboration with Institute of

Tropical Medicine in Antwerp, Belgium, started during a post-doc in this Institute. In the area of leprosy, we conducted the first study of molecular epidemiology in Brazil (Fortaleza) and look at the transmission level alarming of M. leprae strains resistant (and MDR) the drugs in northern Brazil. Finally, the development of a methodology for genotyping and resistance detection of *M. leprae* simultaneously. The main highlight in the area of human genetics was to attract external resource for the development of this project of pharmacogenetics in TB-HIV, generating wave for human resource training of master's and doctoral degrees, producing results with translational potential (application in clinical practice) and incorporating the researcher Coordinator, LABMAM server, staff researcher collaborator of the National Institute of Health of the United States of America (NIH) In addition to the international fundraising for the lab and to the institution.

Molecular Biology Laboratory of the Flavivirus (LABMOF)

Leadership: Myrna Bonaldo mbonaldo@ioc.fiocruz.br

We operate in the field of scientific research in studies of pathogenesis, viral replication and gene expression of flaviviruses and technological development of vaccines against viral infections and parasitic diseases. We investigate the dynamics and the mechanisms involved in resistance to insecticides of Brazilian populations of *Aedes aegypti*, as well as Entomological surveillance and control alternatives. Labmof has a strong performance, in collaboration with the Department of journalism of the IOC, in scientific dissemination and communication activities, awareness-raising and community engagement with a focus on preventive actions.

2016

HIGHLIGHTS

Molecular Biology Laboratory of the Flavivirus (LABMOF)

The Labmof actively participated in the research on the Zika virus during the disease in Brazil. The detection and isolation of infective particles in urine samples and saliva of patients with Zika were relevant contribution. This discovery was immediately released, one day before Carnival, with the purpose of guiding the society about the potential risk of contamination for these fluids. The news has had repercussions worldwide and fostered discussion about vector not pathways of disease transmission. The results were published in the journal PLoS Neglected Tropical Diseases, in June. There were important technical advances in the establishment of the yellow fever vaccine virus as a vaccine for other infectious diseases that have resulted in patent deposit in Brazil (heterologic expression cassette, DNA construct and vaccine composition to immunize against Flavivirus/and *or other pathogens* — BR10201601084304;

10/8/2016). The 10-minute Campaign Against Dengue Fever, released in 2010, changed its name and status. Developed in partnership between academic and professional communication of the IOC, now called 10 Minutes Against the Aedes, to contemplate the other viruses transmitted by this mosquito. In addition, acquired character of concept, to be aired throughout the year, as a way to stimulate change in individual and collective attitudes. Adopted by the State health Secretariat (SES) of Rio de Janeiro for the seventh consecutive year and inspiring initiatives in other States, the concept of "10 minutes" won, the SES, the character that makes it even more concrete preventive actions — Dezinho, a boy from Rio de Janeiro who teaches you how to invest in the control of domestic breeding sites —, and manifestation of the role of the institution in the interaction with the Brazilian society.

Insect Molecular Biology Laboratory (LABIMI)

Leadership: Rafaela Vieira Bruno rafaelav@ioc.fiocruz.br

The main lines of research from the lab and general objectives of the proposal are: (i) analysis of genes that control the previously characterized circadian rhythms in *Drosophila* and its functions in the control of different behaviors in mosquitoes, sandflies and barbers; (ii) analysis of the function of the clock genes

in circadian processes such as embryogenesis of *Aedes aegypti*; (iii) study of cryptic species complexes and the possible role that genes that control behavior may have on the mechanisms of reproductive isolation in vector insects; (iv) relationship between behavior and reproductive isolation.

2016
HIGHLIGHTS

Insect Molecular Biology Laboratory (LABIMI)

We started the study of the behavior of mosquitos Ae. aegypti infected with the Zika virus. After the ap pearance of this virus of Brazil and the early cases, became imperative to join effort in studying the effects of this virus in its main vector. In this way, LABIMI started, in collaboration with several laboratories, doing tests of infected females and locomotor activity, examined rates of oviposition and vertical transmission.

Molecular Biology Laboratory of Parasites and Vectors (LABPMV)

Leadership: Yara M. Traub Cseko utraub@ioc.fiocruz.br

Lutzomyia longipalpis is the main vector of visceral leishmaniasis in Brazil and has the potential to transmit bacteria and viruses. However, little is known about the molecular aspects of this insect or on mechanisms of interaction with Leishmania or other pathogens. Sandflies are tiny insects and difficult maintenance, which led us to use the LL5 cell line of L. longipalpis in several studies. By means of gene silencing pathways immune regulators, we demonstrate that these cells are able to activate Toll

and IMD pathways and that show immune response to bacteria, fungi and *Leishmania*. Previously, we found that cells LL5 develop nonspecific antiviral response when exposed to double-stranded RNA (dfRNA), in a similar manner to the interferon response in mammals. In proteomics study comparing LL5 cells transfected with dfRNA, we identified several molecules with antiviral function or related to the interferon response in other models; these molecules are being now validated the antiviral function.

2016 HIGHLIGHTS

Molecular Biology Laboratory of Parasites and Vectors (LABPMV)

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Molecular Biology and Endemic Diseases Laboratory (LABIMDOE)

Leadership: Constança Felicia De Paoli de Carvalho Britto chritto@ioc.fiocruz.br

Activities related to the improvement of molecular diagnosis of Chagas disease are being conducted, including the development of molecular diagnostic kit for quantitative PCR in real time, the identification of markers for genotyping of *Trypanosoma cruzi* and later optimizing PCR Protocols for this purpose. In the field of leishmaniasis, are being offered new markers and use of more effective methodologies that allow to differentiate between species of Leishmania to the accurate diagnosis of the disease, in addition to the proposed alternative strategy to the treatment of leishmaniasis. Additionally, we are committed to the biochemical studies of proteases and nucleotidases of parasites, which correspond to one of the key factors in host-parasite interaction. We hope to generate knowledge on biological aspects of the interaction of Leishmania and T. cruzi and their hosts, contributing with information on potential targets for therapeutic, vaccine and Diagnostics.

The biochemical research in the field of Proteomics is also being conducted in human urogenital trichomoniasis, with purpose to evaluate the effect of iron ion in the mechanisms of cell proliferation and programmed cell death, by means of ultrastructural analysis and protein expression. In relation to the technological platforms in the lab, we harboured PDTIS expand the services offered by real-time PCR platform RPT-09A, offering the use of microarray Ampliprepobas in Viia7 system, as well as increasing the flow and accuracy of PCR reactions through the use of 384 wells and EpMotion pipetting robot. With the RPT03E platform surface plasmon resonance, our research will be strengthened by the use of advanced methods in Molecular Biophysics to develop bioproducts and bioassays with application potential in control of human infectious diseases and chemotherapy and immunodiagnostic tests.

Molecular Biology and Endemic Diseases Laboratory (LABIMDOE)

The lab has completed the proof of concept for the development of diagnostic kit for real-time PCR (qPCR) triplex, employing the Ampliprepobas system for assessment of parasite burden in blood samples of patients with suspicion of Chagas disease.

The methodology of qPCR-Ampliprepobas has been enhanced for simultaneous use of three targets for detection and quantification: two for *T. cruzi* (nuclear DNA satellite and kDNA), besides the internal amplification control heterologous (IAC plasmid containing the gene

for Aquaporin in *Arabidopsis thaliana*). This system will be made in prototype format of diagnostic kit for Bio-Manguinhos and was standardized using national inputs produced by the Inputs of the Molecular Biology Institute of Paraná (IBMP). The prototype will contain all the reagents and controls arranged in a 96-well plate in the form gelled, to enable the storage and transport at a temperature of 2-8° c. We hope that in 2017, we can conduct stability tests and request the product registration at Anvisa.

Trypanosomatids Biochemistry Laboratory (LABQT)

Leadership: Eduardo Caio ects@ioc.fiocruz.br

The laboratory has, as its mission, carry out research, technological development, innovation and human resources training in areas related to knowledge of specific metabolic pathways of the Trypanosomatids, the definition of targets and the determination of the activity of new drugs with antitrypanosomatid activity. In this way, has been studying the *in vitro* and *in vivo* activity of new synthetic substances, semi sinthetic and natural, with potential activity against Trypanosomatids and exhibiting less toxicity than the drugs currently used in the treatment of these parasitic infections. In addition, emphasizing the definition comes the possible mechanisms of action for these compounds, through the study of different metabolic

pathways and cellular events that occur in the parasites. The laboratory maintains integrated research lines aimed at linking the biological aspects with biochemists of parasites *Leishmania* spp directed to the development of new chemotherapeutic drugs associated with the study of the mechanism of action of these drug candidates and also the study of enzymes as potential candidates for molecular targets. These studies are integrated with two macroprojects entitled (i) evaluation of the activity and *in vitro* and *in vivo* toxicity of synthetic and natural compounds against *Trypanosoma cruzi* and *Leishmania* spp. and (ii) metabolic Targets in Trypanosomatids.

Trypanosomatids Biochemistry Laboratory (LABQT)

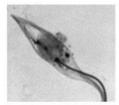
We invest in promising drug repositioning strategy, which consists in finding new applications for drugs already licensed. This strategy presents the advantage of shortening the way the bench to the patient, since all clinical safety testing have been performed. In this regard, we published data demonstrating the leishmanicide activity of imipramine, Ezetimibe and Cyclobenzaprine, drugs with wide use in the clinic to other pathologies. Also advance in the study of transport and the role of cholesterol in the effectiveness of pharmaceuticals ergosterol biosynthesis inhibitors to identify the molecules involved in transport of free sterols in Leishmania spp, its role in resistance and susceptibility to drugs and the influence of cholesterolaemy in efficacy of treatment with azoles. Other studies are being conducted on the metabolism of L-arginine from Leishmania and your participation in in vitro and in vivo infectivity, to define the importance of arginase of the parasite in the infectivity of murine macrophages with different genetic backgrounds (inbred, outbred) using some parameters such as the expression and activity of arginase and the strains of Leishmania infantum from the old

world and the new world. Our group has shown that flavonoids of subclasses of catechins, flavanonas and flavones showed activity on the longipalpi and *Leishmania amazonensis* intracellular amastigote and Leishmania braziliensis, as demonstrated in vivo effect in model of cutaneous leishmaniasis. Despite the flavonoids are recognized as antioxidants, these can have Pro-oxidant activity. Laboratory studies have shown that flavonoids increase concentration of reactive oxygen species, including H2O2, leading to change in the cell cycle, the potential loss of mitochondrial cell membrane, leading to decrease in the intracellular ATP concentration, culminating in the death of the parasite. These results were the subject of interviews on national and international sites, such as CheckOrfan.com, with the title *Promising remedy for the parasitic* disease found in lemons, IOC portal, the portal Fiocruz, health blog, the Ministry of health, and in Manguinhos Magazine. The LBqT also participated in the National science and Technology Week of 2016 with the Celery work against leishmaniasis.

Insects Biochemistry and Physiology Laboratory (LABFISI)

Leadership: Patricia de Azambuja Penna azambuja@ioc.fiocruz.br

Study of immune system of insects and vectors its interaction with parasites (isolation and identification of molecules with antimicrobial activity in Triatominae). Study of the interactions between the insect vector, the intestinal microbiota and parasites (identification of bacteria of intestinal microbiota of insect vectors of field and laboratory). Treatment of vector insects with natural substances, to affect insect development and/or interrupting transmission of the parasite by the insect. Characterize digestive enzymes of insects, vectors by means of biochemical, molecular and physiological studies (study of digestive enzymes of insect vectors for detection of new targets to control and developing alternative techniques of population control of these insects)



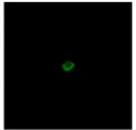


















Insects Biochemistry and Physiology Laboratory (LABFISI)

The team of the lab has been working on models of parasite-vector insect interaction, in studies on endocrinology and physiology of insects, as well as analyzing bioactivity of natural products, some with insecticide and other immunosuppressants. The study of the interaction between insect vector, parasite and microbiota demonstrates that Rhodnius prolixus presents humoral immune response modulation by infection with bacteria and Trypanosomatids. In addition, it was observed the importance of different species of bacteria of intestinal microbiota of triatomine in the development of the parasite by trypanolytic activity by activation of insect immune responses. Thus, intestinal bacteria of the insects, which have the ability to interrupt the cycle of the parasite, could be studied for insect control via use of paratransgenic insects. As for the blood supply of Triatominae, there is change in the bacterial microbiota which modulates the immune response. The volvulus, activities of betaglucosidase, Alpha-glucosidase, betagalactosidase, Alpha-fucosidase, N-acetylglicosaminidase and Alpha-manosidase, which, with the exception of Alpha-fucosidase, are secreted in response to the blood supply.

Trypanosoma cruzi modulates the activity of Alpha-glucosidase, beta-glucosidase and Alpha-fucosidase of *R. prolixus*. In relation to the proteases of *R. prolixus*, duplication and expansion were recent gene in families A1 (catepsines D), C2 (calpaines) and M17 (aminopeptidases). Chitinase genes also had its function studied. We were able to demonstrate the occurrence of sugary food in R. prolixus, breaking the paradigm that Triatominae feed exclusively on blood. The observation that barbers feed on sugar opens development perspective of sugary bait for these insects. In flebotomineo *Lutzomyia longipalpis*, studied the activities of trehalase, beta-glucosidase and Alpha-glucosidase and some vegetables have compounds effect on the longevity of the insects and infection by Leishmania. In addition, the development of gene silencing by RNAi techniques using non-invasive methods can be the basis for the development of new insecticides or bioinsecticides as dsRNA-producing bacteria. In this line of research, already we have silenced genes of Aedes aegypti, Lu. longipalpis and R. prolixus, resulting in different phenotypes of developmental delay or mortality.

Experimental and Computational Biochemistry Laboratory of Drugs (LaBECFar)

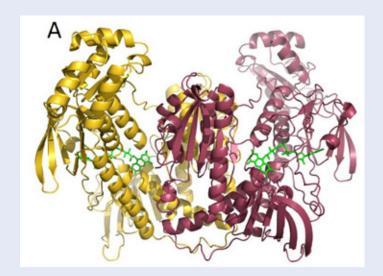
Leadership: Floriano Paes Silva Junior floriano@ioc.fiocruz.br

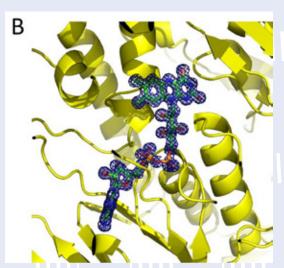
LaBECFar has, as its main feature, the aim of dialogue between experimental and computational methodologies in biochemistry to advance knowledge about the mechanism of action and structure-function relationship of drugs and their biological targets. Thus, interdisciplinarity is an intrinsic part of all projects carried out by the group. From the technological point of view, the LaBECFar is dedicated to the development of high-flow testing for biochemical and phenotypic screening of chemical libraries for the discovery of

new molecular frameworks with potential application, such as pharmaceuticals or chemical probes. Another feature of the lab is that this is not limited to a specific biological model, being able to use its expertise to a wide variety of biological systems and harms to human health. Thus, the projects developed in the LaBECFar have application in neglected tropical diseases (helminthiasis and protozoonosis), but also in neurodiseases and chronic degenerative (cancer, diabetes and diseases resulting from defects in protein folding).

Experimental and Computational Biochemistry Laboratory of Drugs (LaBECFar)

The LABECFar gave major contributions to the discovery and development of new drugs, especially against Chagas disease and schistosomiasis. Regarding the last, three articles have been published, combining for the first time, automated phenotypic testing by HCS and molecular modeling techniques for the identification of new bioactive compounds.





Crystallographic structure (1.2 Ang) of the enzyme TGR of Schistosoma mansoni. A; Dimer model; (B): FAD.

Viral Infections Biotechnology and Physiology Laboratory (LABIFIV)

Leadership: Ada Maria de Barcelos Alves ada@ioc.fiocruz.br

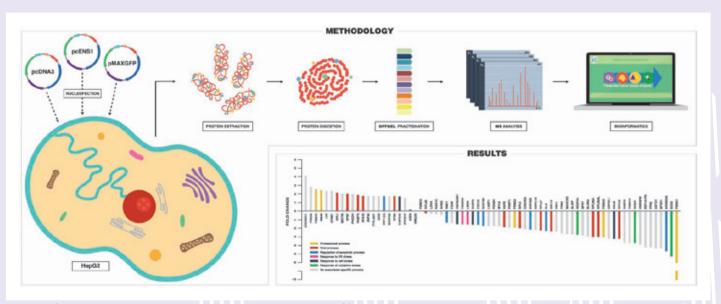
The laboratory is dedicated to the study of the pathogenesis of viral infections and the development of vaccines. The main focus of study, until 2015, was the dengue virus. We work on the development of DNA vaccines containing different genes of the dengue virus (DENV), assessing the protective effect of these vaccines and the immune responses generated in preclinical trials. For this, it was necessary the establishment of experimental murine models of infection with DENV by different routes and samples,

adapted or not to mice. These multidisciplinary studies, evaluate different aspects of the pathogenesis of dengue fever, including innate and adaptive immune response, histopathological and ultrastructural analyses, detection, and viral replication in different tissues and cells. In parallel, we have a line of research with material collected from patients with dengue and fatal human cases aimed at evaluating the effect of infection with DENV in different organs and compare with what we observed in experimental models.

Viral Infections Biotechnology and Physiology Laboratory (LABIFIV)

(i) Began his studies with the Zika virus for establishment of experimental models and vaccine development; (ii) we have continued to study with DENV, showing the effect of systemic infection in mice inoculated via an intracerebral and activation of cellular immune response mediated by a DNA vaccine containing the NS1 gene of dengue 2 (PloS One, 2016 and Virology, 2016); (iii) We concluded the proteome studies

with mass spectroscopy and confirmation by PCR in real time about the effect of the protein NS1 dengue fever on expression of cellular proteins in a line of human liver. We show that the expression of NS1 changes plenty of dozens of cellular proteins, highlighted by eight specific proteins. This study won several awards and was recently published (J Proteomics, 2017).



Schematic representation of the proteome study evaluating the effect of NS1 on cellular proteins.

Laboratory of Cellular Communication (LCC)

Leadership: Luiz Anastacio Alves alveslaa@ioc.fiocruz.br

The lab develops various lines of research ranging from countertop to educational applications. The first subset involves the screening of new agonists and antagonists of purinergic receptors, signaling mechanisms P2X7 receptor and hemichannel of conexin or panexin that are aligned to the goals of Fiocruz for developing drugs. These lines are developed in collaboration with the Laboratory of Immunopharmacology of IOC and Institute of Medical Biochemistry at the Federal University of Rio de Janeiro. The second subset of projects is related to the treatment of some brain tumors by photodynamic action. This work has the collaboration of the laboratory of bio-products and Innovation of the IOC and is inserted into the line of degenerative diseases of Fiocruz and the Neurosciences Program to be implemented at Fiocruz. In the area of infectious diseases, Fiocruz, we are studying applications of purinergic receptors in tuberculosis and began collaboration with the laboratory of Clinical Immunology of the IOC. We have promising results in this project. We also have project in cellular therapy

with hepatocytes to treat acute liver failure in collaboration with the laboratory of Viral hepatitis of the IOC. Part of the results of this project received important Prize of Brazilian Society of Hepatology (Luiz Carlos da Costa Gayotto Award). In addition, we conduct research in science education and work in the production of teaching materials for basic education and higher education. It is noteworthy that we have three projects approved in course: (i) assessment of the *Innovative High School Program* in public schools in the State of Rio de Janeiro, (ii) production and evaluation of educational resources and use of social networks for continuing training of community health agents (ACS) that Act on the Program of the Family Health Strategy (FHS) and (iii), also approved by Faperj, on the line of development and evaluation of educational software such as the software for teaching of Immunology (Virtual Immunology) and Pharmacology (*Pharmavirtua*). All educational resources produced by the laboratory are available in its page on the internet (lcc.kftox.com).

Laboratory of Cellular Communication (LCC)

Over the past few years, the LCC has been inserted, so striking, in the area of Translational and Biophysics in the production and evaluation of educational materials, a fact that has generated in the last year, several highlights. The first highlight was the patent granted (registry number: BR1020140308970) to extract the P2X7 receptor antagonist activity, which has important role in some inflammatory diseases. This work is developed in collaboration with the laboratory of Immunopharmacology of the IOC. The second highlight was the Luiz Carlos da Costa Gayotto Award, granted by the Brazilian Society of Hepatology to a project on Cellular therapy with hepatocytes to treat acute liver failure. This project has been developed in our laboratory in collaboration with the laboratory of technological development in Virology and laboratory of innovations in therapies, education and bio-products. The third highlight is in the area of experimental Oncology with the use of photodynamic therapy for the treatment of

malignant neoplasms. Despite the progress on the understanding of the biology of tumors, the number of new drugs clinically approved is still relatively low and conventional therapies, in General, do not present any selectivity. In addition, several side effects. Thus, it is necessary to search for new therapeutic approaches. In this sense, the lab began to develop, in collaboration with other groups outside the Fiocruz, nanoparticles sensitive light stations to low-intensity x-rays, which can circumvent the problem of photodynamic therapy for its future use in the SUS, the ability of light penetration in the tissues. In addition to the work of basic research and technological innovation, we have produced and evaluated educational resources that can be found at the following addresses: https://www.youtube.com/user/ canallcc_and http://www.lcc.kftox.com/. Such resources can be used for continuous formation of ACS that act in the ESF programme for training of health professionals from various fields.

Technological Development Laboratory in Virology (LADTV)

Leadership: Marcelo Alves Pinto

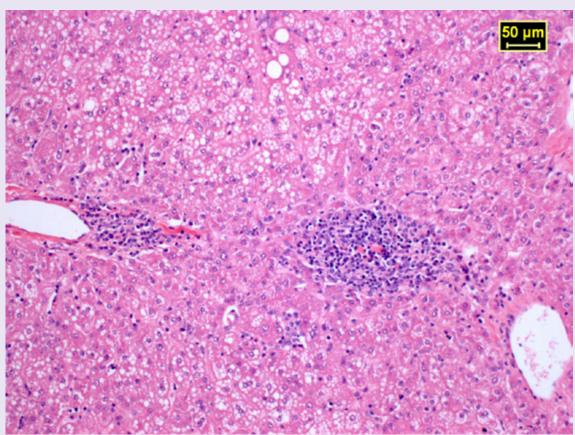
marcelop@ioc.fiocruz.br

Currently, the main research lines of the LADTV are: (i) experimental models for studying the pathogenesis and preclinical testing (vaccine and antiviral prototypes); (ii) development and application of immunological and molecular biology methods for diagnosis of viral hepatitis and other viruses. In alignment with these lines of research, the LADTV carries out laboratory diagnosis, from clinical and environmental samples for clarification of outbreaks and sporadic cases of acute viral hepatitis, chronic and percussion caps.

Technological Development Laboratory in Virology (LADTV)

(i) completion of the research project the Immunopathogenesis of hepatitis and chronic: effect of immunosuppression by tacrolimus in pathogenesis of hepatitis virus infection and 3 genotype using experimental model Macaca fascicularis (financial resources: Faperj and-26/110,088/2013 and E - 26/10,848/2013) and article submission Cynomolgus monkeys are successfully and persistently infected with hepatitis and genotype 3 (HEV-3) after long-term immunosuppressive therapy to the journal PLoS One; (ii) development of research, Laboratory

and ultrasound clinical follow-up of Zika virus infection in Macaca mulatta (scientist of our State and-26/203,033/2016-BBP) in progress; (iii) Master thesis presented to the graduate school in biology the Parasitic IOC, establishment of the methodology for the detection and quantification of virus B-19 applied to the differential diagnosis of acute fulminant hepatitis, and Parvovirus B19 infection manuscript in a fatal case of acute liver failure, which was referred to The Pediatric Infectious Disease Journal.



Chronic Hepatitis E in monkey Cinomolgo. Histopathology demonstrating interface hepatitis.

Diptera Laboratory (LABDIP)

Leadership: Anthony Érico Guimarães anthony@ioc.fiocruz.br

LABDIP aims to carry out research, technological development, innovation and human resources training in taxonomy, biology, ecology and biodiversity of insects, especially of Culicidae, Sandfly, Ceratopogonidae and Muscoides, in urban areas, environmental preservation and under risk of human action by installing hydroelectric complexes, settlements and extractive exploitation. The research aimed at the development of innovations that minimize harms to human health, for control of fly vectors. The lab also works in the development of alternative measures to combat the Aedes aegypti mosquito, using natural biocides, investigates the occurrence of West Nile fever in the country and is responsible for the collection of Ceratopogonidae, whose collection has thousands of specimens of neotropical fauna of health and agricultural interest, constituting one of the largest collections of the family in Latin America.









Collection of mosquitoes in streams that flow into river São Marcos, considering the surroundings of AHE Batalha reservoir .

Diptera Laboratory (LABDIP)

Among the activities developed by the LABDIP, carrying out monitoring and studies on the ecology of mosquitoes (Diptera: Culicidae), potential vectors of human diseases in areas under severe environmental impact by the construction of hydroelectric projects in Brazil. The information generated from these studies, published regularly in original articles and presented in dissertations and theses of postgraduate studies, have enabled us to minimize the occurrence of damages to the health of the communities in the vicinity of these

ventures, particularly malaria and yellow fever. In 2016, the monitoring and studies on the presence of *Haemagogus janthinomys* in wild areas around the reservoir of the hydroelectric plant of Battle, the border of the States of Minas Gerais and Goiás, contributed to the implementation of preventive measures, educative and prophylactic (vaccination), in order to prevent the occurrence of wild yellow fever in the towns of Paracatu (Minas Gerais) and Cristalina(Goiás) inserted in areas with strong track record for the disease in Brazil.

Laboratory of Parasitic Diseases (LABDP)

Leadership: José Rodrigues Coura coura@ioc.fiocruz.br

The study of the dynamics of the transmission of the main endemic diseases of Brazil, including the parasite-host-environment relations to control actions of these diseases, are part of the scope of the search of the lab. The main macroprojects in progress are: (i) epidemiological and Clinical Studies of Chagas disease in different regions of the country to assess its prevalence and morbidity, including its search Etiologic Agent, their vectors and reservoirs; (ii) Characterization of isolates of *Trypanosoma cruzi*, vectors and reservoirs, by genotyping; (iii) studies on the interaction *T. cruzi*-vectors through the investigation of the production capacity of infective forms (metaciclogenese), as well as its elimination by vector insects; (iv) assessment of regional differences of Chagas disease; (v) epidemiological studies, clinical trials, molecular and immunological for malaria control in areas of the Amazon region and in the Atlantic forest of Rio de Janeiro and responses to antimalarials: (vi) Polymorphisms in human genes of cytokines and susceptibility to endemic diseases in

Brazil: malaria, Chagas disease and leishmaniasis americana; (vii) study of the distribution of integumentary and visceral leishmaniasis in Brazil, their vectors and vector attraction mechanisms for man and any non-human reservoirs; (viii) evaluation of urbanization of visceral leishmaniasis in Brazil, its mechanisms and control measures to eliminate or reduce the urban endemic; (ix) Extension of sectional and longitudinal studies of schistosomiasis mansoni, its current prevalence and evolution of specific treatment morbidity and sanitation; (x) study of the immediate response of schistosomiasis and other helminthiases to specific treatment in different areas of Brazil, the risks of reinfection and the prospects of its control through repeated treatments; (Xi) Extension of the new line of research on onchocerciasis in indigenous populations of the Brazilian Amazon, study of simulidae and surveillance of onchocerciasis and mansonellosis in different areas of Brazil; (Xii) Development of studies on health geography at international borders.

2016

HIGHLIGHTS

Laboratory of Parasitic Diseases (LABDP)

Another highlight in the research on Chagas diseases, participation in the Brazilian Group of experts in this disease that culminated with the systematization of strategies for diagnosis, treatment, prevention and control in Brazil. Also presented a proposal for a baseline assessment in areas of interruption of vectorborne transmission of Chagas disease; new evidence of the importance of the use of more accurate molecular tools in areas of co-infection of Chagas disease and leishmaniasis for differentiation of these infections were identified by the research group. leishmaniasis studies have enabled notification of occurrence of Lutzomyia longipalpis in an area of the Atlantic forest which possibly represents the first wild population of this phlebotominae in an area with risk of transmission of Leishmania infantum. Also reviewed-if the natural history of communication by pheromones, as well as its diversity and aggregation on Lu. longipalpis. In these studies, are discussed the different evolutionary forces, possibly involved in the presence of these pheromones, and its importance in the recognition of the species and of the sexual pairing. Described for the first time, the presence of Lutzomyia cavernicola with DNA

of L. infantum, Sciopemyia sordellii with DNA of Leishmania spp. and Evandromyia sallesi with DNA of Leishmania braziliensis complex. In research on malaria, showed results of clinical studies with evidence of the importance of the use of the Association artesunate-Mefloquine as first-line drugs for treatment of Plasmodium falciparum, emphasizing the need for the addition of gametocitocide medicines to reduce the potential transmission of patients treated with this Association. The research on diseases caused by helminths and schistosomiasis presented evidence, with the use of various molecular tools, small differences of the nucleotides of the species Ascaris lumbricoides and Ascaris suum, considered species with zoonotic potential, being discussed these differences for evaluation of separation of species. Another study has shown that infection with Schistosoma mansoni and Schistosoma haematobium in Brazilian military of UN peacekeeping mission in Mozambique, and healing after treatment. Research in health geography, proved the necessity of use of climate information for monitoring the risk of Arboviruses and pointed the main opportunities and challenges in this area.











Research in the field and in the lab.

Ecoepidemiology Laboratory for Chagas Disease (Ledoc)

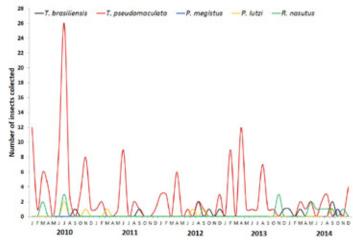
Leadership: Marli Maria Lima

mmlima@ioc.fiocruz.br

Chagas is neglected and affects mostly low-income rural populations. The presence of indigenous triatomine in endemic areas requires constant surveillance and prevention, with entomological supervision of home environments and in the surroundings. Based on this Foundation, Ledoc has investigated the vulnerability to Chagas disease in rural semi-arid locales, Ceará, correlating economic and cultural aspects, attitudes and practices of the inhabitants about the construction techniques and investigating the knowledge of the population about the vectors and mechanisms of disease transmission. In socio-demographic survey, we collect information about types of walls – masonry, rammed earth or mixed — that provide shelter to vectors. We investigated the ability of the residents have to identify the insect vector, the levels of knowledge about Chagas disease and characteristics of dwellings as facilitators or no triatominic infestation. In areas where houses are still of rammed earth and Triatominae natives, we found that financial and cultural issues are the main factors contributing to the perpetuation of this housing type, making the control of endemic disease. The knowledge of the dynamics of reinfestation of households and surrounding structures by Triatominae natives is incipient, requiring more information as to the origin of the outbreaks of reinfestation, with or without treatment with insecticides, the reservoirs and protozoa and human population exposed. In the Northeast, the intense occurrence of household infestation by Triatominae and Trypanosoma cruzi/interaction/human reservoirs

configures suitable model for identifying ecoepidemiologic factors of Chagas disease. Thorough knowledge of these factors and the

Thorough knowledge of these factors and the expertise of the researchers of Ledoc are contributing to control vectors in the region and serve as a model for application in other endemic regions Triatominae natives. Our research indicates that reservoirs play an important role in the dispersion of vectors and of *T. cruzi* among distinct environments; the investigation of environment/axis human health, with a focus on molecular ecology and epidemiological factors and social, evaluates the process of reinfestation of Triatominae shortly after the purge of the houses. With regard to environmental aspects, the emphasis at Ledoc educational and housing improvement, seeking definitive control of vectors in the residences.



Spatial distribution of the triatomines collected in the urban region of Sobral, Ceará state.

Ecoepidemiology Laboratory for Chagas Disease (Ledoc)

The main highlights of Ledoc were scientific papers publications in international journals, clearly showing the Group's collaborations with other researchers. Although small (two researchers), our lab has published five works and one was accepted in reputable journals in Parasitology, Ecology and Molecular Biology. One of the papers was published in collaboration with researchers of the IOC (Rafael Maciel de Freiras, Fernando Monteiro and Mariana David) and the Federal University of Rio de Janeiro. The article addressed the marking of Triatominae with chemicals, which can contribute to capture and recapture of Triatominae in the field and for genetic and molecular studies. The work was published in PNTD. Another publication, the P&V, was with the Group of Dr. Fernando Ariel Genta, on account of Triatominae in power plants (vegetables). With the Group of Dr. Jane Costa, involving researchers from the IOC, the center of technological development in health (CDTS), the Federal University of Paraíba, the Centers for Disease Control and Prevention (CDC/United States of America) and of Valencia, Spain, addressed the phenotypic variability confirmed by ribosomal DNA, suggested a possible hybrid zone complex natural Triatoma brasiliensis.

We had a work accepted in magazine PONE, investigating the dispersion of Triatominae in the urban region of Sobral, one of the most important cities of Ceará. We analyze data from community-based entomological surveillance carried out from 2010 to 2014. The natural infection by *T. cruzi* with Triatominae was evaluated by examination of feces of insects by optical microscopy. Triatominae capture sites were georeferenced by means of Google Earth and analyzed with ArcGIS. Collected 191 Triatominae, consisting of 82.2% of *Triatoma* pseudomaculata, 7.9% of Rhodnius nasutus, 5.8% of *T. brasiliensis*, 3.7% of *Panstrongylus* lutzi and 0.5% of Panstrongylus megistus, with natural infection rate of 17.8% overall. The majority of infestations, with a clear tendency to form colonies, was reported in urban neighborhoods, inside houses, including a focus on the main church of the city, located in the center. This work had the collaboration of researchers from the IOC (Ledoc, LESM and Biotrip) and the Federal University of Ceará (Faculty of medicine; Center for Zoonosis of Sobral) and is part of the doctoral thesis of a Professor of that University, driven by Marli M Lima, Dinter program.

Health and Environment Education Laboratory (LEAS)

Leadership: Lucia Rotenberg rotenber@ioc.fiocruz.br

The lab aims at the production of technical and scientific knowledge and training of human resources for research in the fields of public health and education in biosciences and health. Studies combine approaches of the humanities and social sciences. epidemiology and biology, from the perspective of public health, which emphasizes the biopsychosocial aspects underlying preventive and curative actions, as well as the improvement of health policies appropriate to the socio-cultural and economic context. The studies reflect a feature of Brazilian epidemiological transition in which the chronic degenerative diseases coexist, on a large scale, with communicable diseases, different from the model of most developed countries and neighbouring countries. With regard to chronic diseases, the laboratory develops research about the new cardiovascular and metabolic risk factors linked to working conditions at the present time. With regard to communicable diseases, the projects aim the control/elimination of schistosomiasis, deloused and ixodideans (ticks),

based on strategies of education and health promotion related to the *Plan Brazil Without Misery*, of the Federal Government. There is also research on the implications of socio-cultural and economic factors in the control and prevention of Aids and sexual and reproductive practices of people with HIV/Aids. The laboratory covers, still, interventions and studies for formative processes of professionals in the areas of education and health. The research projects are aligned to the plan for combating diseases of Fiocruz and encompass social dimensions framing of the quality of life of the population, such as health, work and education, from two axes: (i) Health and gender: social, occupational and epidemiological aspects and (ii) Health promotion and education: formation, biological and epidemiological aspects. Together, the activities carried out by the laboratory show the ability of the team to contribute to the control of diseases and to the improvement of actions and policies within the health system and the health and education institutions in Brazil.

Health and Environment Education Laboratory (LEAS)

As the lab research highlights include the recognition obtained in the thesis work of our students, among them: Honorable Mention — Prize Capes of 2016 for the Thesis work of Maria Leticia Santos Cruz, on adherence to the treatment of children and adolescents with HIV, directed by Simone Souza Monteiro and Francisco Inácio Pinkusfeld Monteiro Bastos, graduate program in public health from the National School of Public Health Sérgio Arouca; Thesis: Children and adolescents living with HIV in monitoring services: analysis of vulnerability factors on adherence to antiretroviral treatment. Honorable mention — Prize Capes 2016 for the thesis work of Aline Silva Costa, on the

relationship between work schedules and diabetes, driven by Roxanne Härter Griep and Lucia Rotenberg, postgraduate program in Epidemiology in Public Health from the National School of Public Health Sérgio Arouca; Thesis: Work schedules and prevalence of diabetes type: Elsa-Brazil. It stands out, too, the selection of the doctoral candidate Priscilla Soares, as a Note, 10 by Faperj graduate degree in Public Health from the National School of Public Health Sergio Arouca; Thesis: Sexual and reproductive rights of women living with HIV/Aids: a look at Aids services in Rio de Janeiro, under the guidance of Simone Souza Monteiro.

Enterobacteria Laboratory (LABENT)

Leadership: Dalia dos Prazeres Rodrigues dalia@ioc.fiocruz.br

The LABENT has, as main scope the assessment of enteropathogenic bacteria occurring in the food chain obtained from receipt of strains for conclusive diagnosis, in activities such as National reference laboratory (SVS/MS) and in support of other institutions, such as laboratories and public and private universities, institutions and industries engaged in food production. This evaluation includes the laboratory diagnosis conclusive of enteropathogenic bacteria occurring in the food chain belonging to the families Enterobacteriaceae, Vibrionaceae and Aeromonadaceae, Staphylococcaceae, recognition of its role as Etiologic Agent in different nosologies, the characterization of the circulating species, serve in different ecosystems, and the monitoring of antimicrobial susceptibility to drugs used in human and veterinary areas. From this, different methods are employed to conduct the study of the mechanisms of virulence and antimicrobial resistance and, through Subtyping techniques, effective tracing of circulating clones and recognition regarding the introduction of strains with emerging features and/or different aquatic ecosystems in exotic and terrestrial.



Enterobacteria Laboratory (LABENT)

The LABENT plays a fundamental role with regard to knowledge about the prevalent enteropathogenic and circulating in our environment, developing different projects inserted in five research lines. In 2016, conducted surveillance of the microbiota resident and the floating period prior to the completion of the Olympic Games and Paralympic Games (April to December) in cooperation with the management of Sewage Treatment, environmental monitoring of the Municipality of Rio de Janeiro, the Central Public Health Laboratory (LACEN Noel Nutels), the **Municipal Laboratory of the Municipal Health** Secretariat and the Products control laboratory of the Municipality of Rio de Janeiro. Completed the phase of collection and identification, will be evaluated by means of different methods of

subtyping, the introduction of pathogens or microorganisms carrying exotic features that may pose a risk condition, in short, medium and long term, to the resident population. Regarding the scientific production, include: (i) sequencing the genome of Salmonella enteritidis PT4, which will be published in Genome Announcements -ASM; (ii) Subtyping of Salmonella spp. isolated from wild birds seized in illegal trade with the same clonal profile detected among isolates of human origin in southern Brazil; (iii) recognition among strains of Community origin of resistance to antimicrobial drugs of last generation (cephalosporins and fluoroquinolones), aspects that indicate the relevance of such activities from the point of view of public health and animal health.

Laboratory of Enteroviruses (LEV)

Leadership: Edson Elias da Silva enterolb@ioc.fiocruz.br

Viral infections represent an important share of acute infections that affect the central nervous system (CNS), among which we can highlight: polio, meningitis and meningoencefalites. Many viral pathogens, including enteroviruses, have the ability to invade and cause disease in the CNS. The lab's mission is to research, diagnose, characterize genomic level and develop molecular techniques for the study of viral agents involved in CNS syndromes, acute flaccid paralysis with emphasis on viral meningitis and, besides the formation of human resources. The lab serves as a regional reference for

who and national reference for the Ministry of health. Work with sensitive technology in the realization of the viral diagnostic tests, including nucleotide sequencing and real-time PCR, as well as virological techniques, such as classic viral isolation in cell cultures. These techniques have allowed us to get answers fast and accurate in the detection and analysis of samples of poliovirus and other enteroviruses that cause relevant clinical pictures, as well as in the realization of the laboratory surveillance on possible import and spreading of viral samples in our territory.

Laboratory of Enteroviruses (LEV)

(i) on the theme of global eradication of polio, two highly relevant scientific issues have been reported through high impact publications. The first consisted of molecular and phenotypic characterization of a poliovirus vaccine of serotype 2 isolated environment, containing highly divergent sequences when compared to the Sabin Vaccine prototype. The virus, having recombinant genome with other enteroviruses, had also neurovirulence characteristics comparable to those demonstrated by wild

poliovirus. The second was the detection of the mutation, generating a rare site of recombination (PV2/PV3), VP1 gene of a poliovirus vaccine of type 2. This finding provides important information about the evolutionary process of poliovirus; (ii) it is necessary to emphasize the guidance of two students of National Institute of health of Mozambique and a student of the University de la República, Uruguay, on topics related to environmental monitoring.



Scientific activities at the Laboratory.

Forensics and Medical Entomology Laboratory (LEMEF)

Leadership: Margareth Maria de Carvalho Queiroz mmcqueiroz@ioc.fiocruz.br

Perform research, technological development, innovation and human resource training with two main lines of research: Bio-ecology, morphology and integrated taxonomy of Diptera Muscomorpha and *Triatominae*. The bionomics of the flies of forensic importance health and is designed to meet its biological cycle. Morphological analyses are carried out (optical and electronic scanning microscopy), molecular (mitochondrial and nuclear DNA) and chemotaxonomic (cuticular hydrocarbons profiles by means of GC-MS). These techniques have high resolving power and the characters that have potential diagnostic value to forensic entomology, aiding in the identification process of the different species of muscoides, broadening the knowledge of the variety of species and feeding the database with information

about the scavenger entomofauna in our country. The LEMEF develops techniques for quick and simple removal of larvae in Myiasis, giving subsidies for improvement in care of the population. In parallel, like flies and Triatominae are transmitters of pathogens and therefore its population density must be controlled, the second line of research is the alternative control of insects of medical importance and the microbiota of *Diptera Muscomorpha*, applying the control by substances extracted from plants and bacteria. Is searched for the presence of bacteria and their mechanisms of antimicrobial resistance of clinical importance in flies collected in containers in intra-and extramural environments, collaborating with data on risk analysis (transmission of pathogens).

2016

HIGHLIGHTS

Forensics and Medical Entomology Laboratory (LEMEF)

The LEMEF performed research, technological development, innovation and human resources training to develop multidisciplinary studies related to bio-ecology, morphology, integrated taxonomy of Diptera muscoides and Triatominae. The integration of our team in the project Alternative control of mosquitoes of the genus Aedes with emphasis on Aedes aegypti by using natural substances from plants, Zika 1 Network, public notice N° 18/2015, in collaboration with the Federal Rural University of Rio de Janeiro and the Severino Sombra University. In addition, the doctoral thesis entitled Safety and effectiveness of extracts obtained from Pouteria mammosa (I.) Cronquist system for the control

of fly muscoides, Carlos Manuel Sánchez Dutok, under the direction of Margareth M. C. Queiroz, received the award Alexander Peixoto at the postgraduate course on Biodiversity and Health. The thesis of Alexander S. Xavier, entitled Post-embryonic development, scanning electron microscopy, and DNA sequences of fly family Sarcophagidae muscoides of medical-veterinary and forensic importance, unpublished results presented in the field of scanning electron microscopy of Diptera Muscomorpha. We analyzed the total genome of the bacterium isolated from laterosporus, used in biological control of insects and Bacillus toyonensis.



Dipterae (Diptera: Calliphoridae) of sanitary and forensic importance.

Congenital Malformations Epidemiology Laboratory (LEMC)

Leadership: Maria da Graça Dutra mgdutra@ioc.fiocruz.br

The LEMC have, by mission, epidemiological and etiological investigation of congenital malformations and degenerative diseases of etiology genetics, especially inherited neurodegenerative diseases, hereditary cancer and pediatric solid tumors. With regard to congenital malformations, the LEMC is proposed to task the Latin American collaborative study epidemiology of congenital malformations (ECLAMC), optimize it according to the new available technologies, as well as expand the study methodologies, including the molecular part congenital malformations and chronic degenerative diseases. The LEMC research in congenital malformations focuses its efforts on the themes: (i) epidemiology of congenital malformations as a study case-control and cohort that fluctuations in frequencies of several birth defects; (ii) medical and population genetics of Craniofacial anomalies with focus on oral cleft and the relevant subphenotypes, as well as in skeletal class III malocclusion, sorted by a mandibular excess (prognathism) or maxillary deficiency of family origin. The LEMC research in

chronic degenerative diseases of genetic etiology contemplates the following research lines: (i) investigation of the epidemiology and etiology of hereditary cancer in Brazil, with a focus on breast cancer, colorectal cancer and hereditary retinoblastoma; (ii) investigation of neurogenetic to focus the hereditary spinocerebellar ataxias, Huntington's disease and the Rett syndrome; (iii) study of vitamin D receptor polymorphisms in Crohn's disease and evaluation of the presence of the gene polymorphism of the cascade immunoinflamatory in patients with inflammatory bowel disease and chronic periodontitis, since both are degenerative chronic diseases of complex nature that result of aberrant immune response in a host susceptible; (iv) genes associated with the formation of dental enamel in families with Molar-Incisor Hypomineralisation, genetic and environmental aspects. In common with the different lines of research, the LEMC's mission is the production of knowledge, the training of human resources and the contribution to the improvement of health care in Brazil.

Congenital Malformations Epidemiology Laboratory (LEMC)

Published nine articles in indexed journals and completed the guidance two PhD theses and dissertation. Among the topics covered in the publications, theses and dissertation are: (i) identification and characterization of new genetic markers associated with the development of facial clefts (cleft lip, cleft palate); (ii) identification and characterization of additional genetic variants associated with the development of neoplasms in the Li-Fraumeni syndrome, predisposing syndrome to develop multiple tumors, autosomal dominant hereditary character. The changes currently in operation in the LEMC is the growth of molecular biology and medical genetics of population, the creation and implementation of the national registration system and the Latin American major congenital malformations, a process that accelerated with the advent of Zika outbreak in the country and the need for rapid response to this major public health problem. With that, the LEMC actively participates as a contributor to major national

and international projects on this subject, as listed in the Collection System. One of the jobs of the LEMC that deserves highlight is the participation in the project *The epidemiological* surveillance of congenital anomalies and twins in Latin America (LAMCAT), approved by MS-Decit paragraph 14/2016 in the great theme of Preventing and combating Zika Virus. In this big project there are four subprojects (Figure) whose main objective converges for increased epidemiological surveillance of congenital defects in Latin America to fill the knowledge gaps on the teratogenicity of Zika virus and to provide better instruments able to guide public health actions in cases of birth defects epidemics in the region. Finally, with respect to research hereditary retinoblastoma, two PhD theses which have as objective the research of genetic/genomic changes in the development and evolution of hereditary retinoblastoma are in progress.

Laboratory of Molecular Epidemiology and Systems (LESM)

Leadership: Fernando Araujo Monteiro fam@ioc.fiocruz.br

The proposals of scientific work to be undertaken between 2015 and 2021 for the laboratory team are its main line related investigative, representing the Mission of "developing research and staff training in epidemiology and molecular systematics, phylogeny and diagnostics of pathogenic organisms and vectors of infectious diseases, in order to contribute to the programs of the epidemiological surveillance of communicable diseases in Brazil. There is the prospect of using modern methods of molecular epidemiology and evolutionary genetics of pathogens and vectors for the response to questions arising from field studies, community or hospital-based ".

That way, the field epidemiology is also inserted in the activities developed in the laboratory, half being able to raise questions related to the behavior of communicable diseases that the research team intends to address in the 2015 period to 2021.

Are currently active in the lab three research lines derived from that main drive shaft: (i) epidemiology and molecular systematics of bacteria associated to infections of the central nervous system, (ii) epidemiology and molecular systematics of insects and infectious disease vectors (iii) epidemiology and molecular systematics of enteropathogenic.

Laboratory of Molecular Epidemiology and Systems (LESM)

The LESM contributes to the implementation of the Regional Office Fiocruz Piauí through the coordination of Actions and implementation of the education doctorate in health, environment and society in the State. Still in Piauí, if I update course in Clinical Epidemiology applied to

Neonatology (Maternity Dona Evangelina Rosa, Regional reference center Microcefalias). The lab has received students graduate programs established in Piauí, with third class of masters in interinstitutional cooperation with the graduate program in tropical medicine of the IOC.



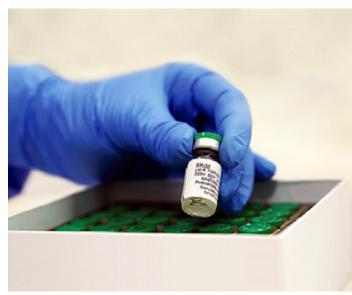
Rhodnius prolixus.

Laboratory of Experimental Schistosomiasis (LEE)

Leadership: Marilia Sirianni dos Santos Almeida sirianni@ioc.fiocruz.br

After getting the results of phase I clinical trials that proved the tolerability and specific immune responses after vaccination with rSm14/GLA in adults volunteer in an area endemic for schistosomiasis, began the next phase of the development of the vaccine. The phase IA, initiated in December 2016, is an open, randomized study in adults living in areas endemic for schistosomiasis and aims to study the safety and immunogenicity of the vaccine in adults with a history of infection with Schistosoma mansoni and Schistosoma haematobium and pretreated with praziquantel. The evaluation will be carried out in two treatment arms, with the candidate rSm14 (50 μ g), associated with different amounts of GLA adjuvant (2.5 μ g or 5 $g \mu$). The Phase IIA clinical trial in adults can be considered preliminary step in security before considering tests on children in areas endemic for S. mansoni or S. haematobium, the target population for the vaccine. Chosen as the site for the conduct of the clinical trial, the Valley of the river Senegal in Senegal, Africa, for being an area of high prevalence and transmission of both S. mansoni and S. haematobium. The study is being carried out in collaboration with the non-governmental organization Centre de Recherche Biomédicale Espoir pour la Santé (EPLS), based in Saint Louis, Senegal, and occurs between December 2016 and July 2017, being funded by the Orygen, through Finep

financing. The Phase IIA clinical trial is being carried out with the same batch of vaccine used in phase I clinical trials. The preparatory stage of the study, phase II (preparation of documents, regulatory submissions, mapping of towns, certifications of lots of vaccine and adjuvant) was held and the recruitment started in September 2016. The first regulatory submission seeking approval of the clinical study protocol by the National Ethics Committee of Senegal, in Dakar, on May 19, 2016 and approval was received in August 2016.



Sm14: Brazilian vaccine against schistosomiasis in phase of clinical trials.

Laboratory of Experimental Schistosomiasis (LEE)

Throughout the year, the steps necessary for the beginning of the Phase IIA clinical trial of the vaccine against schistosomiasis Sm14, for which started in December, vaccination of adult volunteers residents of endemic area for the disease. Actions that preceded the start of the clinical trial include: completion of the design of the Protocol; preparation of synopsis of the study; full Protocol written in French, including the term of informed consent; definition of goals and results/calendar; maintenance and update of the investigator's brochure (BI); approval of regional authorities (medical, religious and educational); submission to the National Ethics Committee (CNERS Senegal); monitoring of the **Protocol until approvals for CNERS and Ministry** of health; request to authorise the imports of products to the vaccine; creation of the Data Safety Monitoring Board (DSMB Senegalese); preparation of specific POPs Sm14 test and manual update. Field activities include: pre selection of villages, including the assessment of the prevalence of schistosomiasis mansoni and S. haematobium, to check the endemic situation

(this phase of prospecting waged among themselves around the villages around the EPLS Investigation Antenna); visits to the community and information and awareness-raising meetings; selection of villages; creating Sm14 committees in the village and recruitment of representatives of the village; treatment with praziquantel; selection of patients (medical examinations); randomization of patients; opening of Case Report Forms (CRF); opening of individual medical files; ecotomography scans for selection; medical examinations; internal monitoring to CRF and completion of medical files; the insurance contract for the clinical trial; database. Additional activities include: analysis of the vaccine batch and issuing the certificate of Sm14 analysis; first meeting of the Advisory Council (Advisory Board) organized in Dakar. After completion of all requirements, vaccinations for volunteers for Phase II was initiated on 5 December 2016 in the region of Saint Louis, with the presence and supervision of the project coordinator, Dr. Miriam Tendler.

Laboratory of Integrated Studies in Protozoology (LEIP)

Leadership: Claudia Masini d'Avila Levy davila.levy@ioc.fiocruz.br

The LEIP acts at the interface between the areas of Biochemistry, molecular biology and cell biology, aiming at contributing essentially with two main aspects: study of virulence factors of pathogenic protozoa, with breakdown for chemotherapy, and studies of biodiversity and taxonomy, with breakdown for evolution and phylogeny. The virulence factors of the research focus LEIP are peptidases in trypanosomatids. We seek to unravel its participation in the interaction with hosts vertebrates and invertebrates, as well as explore them as target for chemotherapy from compounds with clinical use approved, as the and peptidase inhibitors of HIV and calpain inhibitors. The LEIP is also involved in biodiversity prospecting of cinetoplastídeos, tricomonadídeos and enteric protozoa, aiming to contribute to the taxonomy and molecular phylogeny of protists, ultimately contributing to the understanding of the evolution of species. In line with this goal, the LEIP houses the Protozoa collection at Fiocruz (www.colprot.fiocruz.br), which enables the ex situ conservation of biodiversity and its availability for the scientific community. The theme evolution, both cell phone as of species, can be approached by several strategies. The LEIP is also involved in the study of evolution of organelles, through the investigation of the relationship between trypanosomatids and their symbionts in a evolutionary stage between an organelle and a bacterium, constituting excellent models for studies of evolution. This relationship is investigated by means of comparative Proteomics analyses that are also employed for the study of other models.



Laboratory of Integrated Studies in Protozoology (LEIP)

The LEIP promoted the debate about the relevance of preservation of species and specimens in biological collections at the international event 2nd TryTAX-Trypanosomatid Taxonomy, Evolution, Phylogeny and Biology through scientific publication. The event, organized and coordinated by LEIP in partnership with the University of Ostrava, was held at the University of Ostrava (Czech Republic). In addition, part of the Protozoa collection housed by the lab was characterized by means of two sequencing the three targets which will result in proposal for taxonomic revision of trypanosomatids, in addition to valuation of the collection. Taxonomic and biodiversity studies are the basis for biochemical studies and drug discovery. In this sense, the lab also is dedicated to the analysis of compounds with clinical use approved for the therapeutic treatment of patients affected by tropical diseases, like HIV protease inhibitors, which are part of the powerful anti-retroviral therapy (HAART). These compounds can have direct action on opportunistic pathogens like fungi and protozoa. In this regard, we declare the action of these

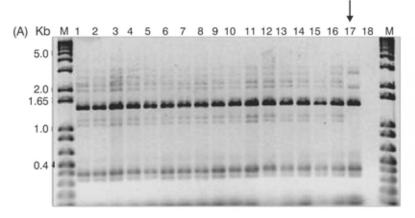
compounds on tripomastigota and amastigota forms of *Trypanosoma cruzi*. In the same line of reasoning, the other class of proteases inhibitors, the calpains, can be exploited to get a shortcut to therapeutic approaches of tropical diseases. The unregulated activity of these enzymes leads to a series of human pathologies such as Alzheimer's, diabetes and post-traumatic neuronal degeneration. Because of this, a series of inhibitors are in clinical screening and some with clinical use approved. Accordingly, we propose the use of these compounds as chemotherapy choice. The LEIP, in line with its mission, has worked in scientific activities. We participate in events of Frank visitation to the general public, promoted by the Brazilian Society of clinical pathology (SBPC) and the Ministry of Science, Technology and Innovation, as the SBPC young and the national week of science and technology, respectively. The workshops were organized: Playful microbiology and micro-organisms and vectors: from the House to the laboratory, in addition to lectures and exhibitions in schools and provision of short courses of SBPC meetings to the general public.

Bacterial Physiology Laboratory (LFB)

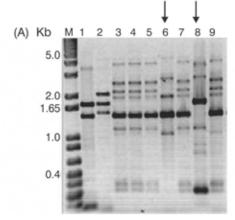
Leadership: Leon Rabinovitch leon@ioc.fiocruz.br

The laboratory is dedicated to the study of bacteria of the genus *Bacillus* and related genres. Its activities are being developed in some main lines of research, such as: (i) study and isolation of *Bacillus* strains with entomopathogenic potential for production of biological insecticides to control insect vectors of diseases of importance in public health and agricultural pests; (ii) production of standard powder of *Bacillus thuringiensis israelencis* for determination

of bioinseticidas and power supply of the same to the undertakings concerned; (iii) study of *Bacillus* strains with metabolic characteristics of degradation of organic materials or recalcitrant chemicals, with its potential for bioremediation assessment and development of such products in partnership with companies; (iv) studies of phylogeny, molecular typing and potential assessment of virulence of strains of *Bacillus cereus lato sensu*.



Rep-PCR profiles polymorphic strains of *B. thuringiensis* amplified by Bc-rep-1 primers and Bc-rep-2 in 1.2% agarose gel. The arrows indicate the electrophoretic profiles.



Bacterial Physiology Laboratory (LFB)

(i) the gradual consolidation of the collection of cultures of the Genus Bacillus and Related Genres (CCGB/IOC) as believable that the bacterial collection Community national science interested in strains of Bacillus and related genres, as a consequence of technical gueries and/or technical information provided, as well as the increased transfer of strains that produce industrial products. In addition, the CCGB/IOC has promoted training of doctorate student at the University of Brasilia in the identification of Bacillus and related genres; (ii) the increase of the formal citations of scientific papers generated in the LFB or partners of which laboratories participating researchers as authors or contributors; (iii) publication of the first edition of the book *Coletânea de procedimentos* técnicos e metodologias empregadas para o estudo de Bacillus e gêneros esporulados aeróbios correlatos, authored by LFB staff, published by Montenegro. (iv) gain significant momentum in the implementation of new

methods and techniques in the National reference laboratory For Anthrax/LFB for diagnosis of Bacillus anthracis, the anthrax agent, and in deliberate preparations with this agent; (v) significant Expansion of relations with the Center for Diseases Control and Prevention (CDC/United States of America) with a view to the diagnosis of B. anthracis; (vi) Establishment of relationships with the Public Health England for training in diagnosis of B. anthracis, with donations of reagents and strains, as well as the exchange of protocols and know-how in the area; (viii) intellectual protection. Request for registration of a patent of invention to the INPI (2016) as a result of joint research involving the IOC laboratories (laboratory of innovations in therapies, education and Bioproducts and LFB), laboratories of the State University of Norte Fluminense, laboratory of Universidade Federal Fluminense, with financial support of Petrobras and the National Agency of Petroleum, Natural Gas and Biofuels (ANP) (BR 1020160296285).

Arthropod Vectors Physiology and Control Laboratory (Laficave)

Leadership: José Bento Pereira Lima jbento@ioc.fiocruz.br

The mission of the laboratory is to conduct studies in the fields of biology, genetics, physiology and insect vectors of disease control, promoting scientific, technological advancement and training human resources. We develop science in the field of Entomology, directly applied to health needs in calling for the Ministry of health for disease control. Our research comprises: (i) evaluation and development of new methodologies for monitoring and control of culicidae vectors; (ii) biological studies and molecular mechanisms of resistance to insecticides, with evaluation of natural populations, genomics and transcriptomic of the resistance. Aim to identify selected changes, as well as enhance molecular tools for monitoring their frequencies in natural populations, in addition to the investment in genomic analysis of mosquitoes resistant to insecticides used in the country; (iii) studies on biology, evolution and vector capacity of culicidae tools of population genetics. In collaboration with Yale University (United States of America), we seek to understand the origin and the gene flow of populations of these vectors, dynamics of emergence and spread of resistance to insecticides and target gene for vector competence. In partnership with the Federal University of Rio de Janeiro (UFRJ),

we seek to understand the sexual maturation processes and training hematophagic of Aedes aegypti, with use of omic technologies, in order to characterize molecules, the process involved and generate an innovative set of information for new control strategies. Another study involves the construction of recombinant interbreeding bloodlines in Ae. aegypti, with genomic sequencing to generate reference panel and the correlation of genomic analysis with the phenotyping of aspects of insect life table; (iv) Actions of communication, mobilization and awareness related to the control of harms to health. participating in events, exhibiting biological material and information about mosquitoes vectors; (v) maintenance of the colonies of Aedes, Anopheles and Culex used to our studies and donation to other research groups and private institutions. The Laficave's Brazilian representative of the international consortium for the promotion of studies on resistance to insecticides and control alternatives, the Worldwide Insecticide Resistance Network (WIN). We have participated in meetings promoted by the Ministry of health, PAHO and who on strategies to assess and prevent resistance to insecticides.

Arthropod Vectors Physiology and Control Laboratory (Laficave)

The Laficave continued developing applied research directly in the field, without neglecting technological innovation in partnerships with national and international institutions. In this context, we have developed some research that will generate or tools will help you directly in control of vectors as: (i) evaluation of the methodology "test house" for determining the residual effect of insecticides used in the control of malaria; (ii) approval of a patent trap for anopheles collection and other insect vectors; (iii) Continuation of project on the island of Paquetá (Rio de Janeiro), which allowed to develop methodology to monitor and direct control of Aedes mosquitoes and that has been turning into efficient tool and being deployed experimentally in four municipalities of Amazonas successfully; (iv) Continuation of partnership with Yale University, with funding from the National Institute of health of the United States of America (NIH), developing research seeking to understand the origin and the gene flow of populations of Ae. aegypti and new molecular markers for resistance to insecticides and vector competence; (v) Continuation of partnership with Group of UFRJ, in which we generate the population of Ae. aegypti Carioca. Transcriptomic analyses are in progress to

understanding of genes involved in the empowerment of females to the first blood and sexual maturation repast; (vi) Continuation of innovative proposal, starting in 2015, with the generation of the population of Ae. aegypti Brazil to create a genetic mosaicism and segregation of the variants in isogenic strains. This approach will facilitate the identification of genomic and molecular markers association with phenotypic characters related to the capacity of the vector; (vii) carrying out, at the invitation of PAHO, to update course on surveillance methodologies Aedes resistance to insecticides used in public health in the region of the Americas, with participation of representatives from 11 countries, aiming at the formation of a resistance surveillance network in the Americas; (viii) coordination of a project involving young researchers of Rio de Janeiro (Fiocruz, UFRJ and Universidade Gama Filho) about the diversity of Ae. aegypti from the State in terms of population genomics, metagenomics, metatranscriptomic and vector competence, besides actions of information to society about the mosquito control; (ix) Organization of the first International **Workshop on Insecticide Resistance in Vectors** of Emerging Arboviruses, which took place in Rio de Janeiro in December 2016.













Highlights of the laboratory in 2016.

Flavivirus Laboratory (LABFLA)

Leadership: Ana Maria Bispo de Filipis abispo@ioc.fiocruz.br

The LABFLA was created in 1986 to meet the two diseases of great impact for the Brazilian population: dengue and yellow fever. Highlight that isolated, for the first time, all serotypes of dengue fever in the State of Rio de Janeiro and the dengue virus serotype 2 and 3. The Zika virus (ZIKV) and the Chikungunya virus (CHIKV) were incorporated as research lines after the introduction in the State of Rio de Janeiro, in 2015. LABFLA research lines involve aspects since the biology of these arbovirus surveillance studies, implementation of new methodologies, evaluation of diagnostic methods, epidemiology, molecular epidemiology and pathogenesis. Investigation of the interaction between the virus-vector are also carried out in partnership. Surveillance of dengue virus (DENV), evaluating the emergence and re-emergence in the State of Rio de Janeiro, has been carried out to evaluate the impact on the population. The ongoing investigation of DENV genotypes circulating in Rio de

Janeiro and Brazil has also been of relevance, since the movement of more virulent genotypes can be one of the factors resulting in severe cases. The study of fatal cases suspected of flaviviruses, also LABFLA current research line aims to contribute to the knowledge related to the pathogenesis of the disease. The implementation and evaluation of laboratory diagnostic methods have been important and used in partnership projects with the assistance. The introduction of the ZIKV and of CHIKV in 2015, brought the opportunity of studying the immune response to both viruses; with respect to ZIKV, the impact on a population widely exposed to dengue fever and, in relation to CHIKV, its potential of chronicity. The results of these studies are in dissertations, PhD theses and postdoctoral projects, all aimed at the academic requirements aimed at fulfilling its application in Brazilian public health with a view to fulfillment of institutional mission.

Flavivirus Laboratory (LABFLA)

The observation of an increase in the number of notifications of microcephaly in the country led to the investigation of the possible relationship with CHIKV. As featured in the research activity, we can cite the ZIKV confirmation in amniotic fluid for the first time in the international literature. This finding led to the development of national and international standards. Original scientific publications on the subject have contributed to the understanding of the impact of the infection, especially for pregnant women.



Laboratory of Human Genetics (LGH)

Leadership: Pedro Hernan Acero Cabello cabello@ioc.fiocruz.br

The LGH performs basic and applied scientific research in the study of hereditary factors involved in susceptibility and resistance to infecto parasitic disease, on molecular epidemiology of diseases of complex inheritance and development of strategies for the diagnosis of genetic diseases. The lab has worked for 30 years in continuous training of human resources of high level (undergraduate, master's, doctoral and postdoctoral) and in the production of scientific knowledge, focusing on human genetics in health development and the transfer of that knowledge to the productive sector, to clinical care protocols and for society as a whole. We conduct research to study

how mutations in DNA affect the manifestation, diagnosis, progression and treatment of genetic diseases, such as Parkinson's disease, amyotrophic lateral sclerosis, cystic fibrosis, monogenic diabetes and muscular dystrophy. In addition, we work in the study of human poligenic complex features resulting from genome interactions with the environment, such as obesity, bipolar disorder and high blood pressure. We have a multidisciplinary team composed of biologists, clinicians, biomedical and nutritionists and integrated a wide collaborative network that brings together universities and health centres in Rio de Janeiro and other States.

Laboratory of Human Genetics (LGH)

It was a year of important achievements in the various lines of research conducted in this laboratory. There was significant expansion of molecular analyses applied to human genetic diseases, with tracking of mutations and polymorphisms in dozens of genes with essential functions for different molecular pathways in the body. In the field of neuroscience, the study of bipolar disorder continues to expand and has the analysis of nearly a dozen genes into more than 300 individuals participants of this study. In the study of the molecular causes of Parkinson's disease, we continue producing and publishing results from the sample of more than 600 patients, with impacts on elucidation of the pathophysiology of the disease and in clinical practice. In relation to amyotrophic lateral sclerosis, are being carried out massive sequencing of several genes related to this disease and spinal muscular atrophy late start, aiming the differential diagnosis for this disease. In this project, are also quantified the expression of miRNAs in plasma of patients with different mutations found earlier in this project.

These strengths can help in the early diagnosis of new patients. In the study of complex diseases, enhance significantly the number of genes analyzed and the number of patients and healthy volunteers that make up the sample. Results of more than 30 genes have been collected and are being analyzed in relation to their influences on the manifestation of obesity and hypertension, diseases that affect a large part of the population. On the study of cystic fibrosis and diabetes monogenic, diseases whose genetic diagnosis has fundamental importance for the treatment, the DNA of more than a hundred patients was sequenced and were identified, in addition to the known mutations as the causes of the disease, new mutations that will have important impact on diagnostic protocols and in clinical practice. Finally, structural and organizational significant physical changes were implemented in space and on LGH routine, for enhancement of their experimental and managerial processes, following the current standards for quality control in research laboratories.

Microorganisms Molecular Genetics Laboratory (LGMM)

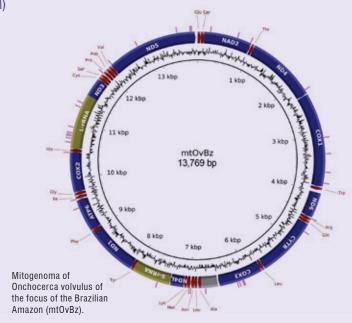
Leadership: Ana Carolina Paulo Vicente anapaulo@ioc.fiocruz.br

LGMM's activities involve research of infectious agents and parasitological and their vectors, with genetic approach, using genomic approaches, metagenomic and phylogenomic. Studied under the genomic point of view, the emergence/re-emergence of strains of bacteria resistant to antibiotics and profile of virulence. To do this, we perform *in silico* and *in vitro* analyses. Also we address the issue of diversity of infecto parasitic agents and its impact on the diagnosis, epidemiology and evolution.

2016

Microorganisms Molecular Genetics Laboratory (LGMM)

The highlights of the LGMM embodied in publications involve genomic analyses, metagenomic and phylogenomic of infectious agents and parasitological endemic and emerging in our country, such as: Oncocerca volvulus, human Lymphotropic Virus type 1 (HTLV-1) and Chikungunya virus. Our group has generated and analyzed the first full genomes of HTLV-1 and the first African isolates of Chikungunya in Rio de Janeiro, as well as the first mitogenoma of the Amazon focus volvulus. Brazilian.



Laboratory of Functional Genomics and Bioinformatics (LAGFB)

Leadership: Wim Maurits Sylvain Degrave wim.degrave@fiocruz.br

The lab has comprehensive performance, with projects in the following lines of research: computational biology and bioinformatics in health and environment, functional genomics of Mycobacteria, new therapeutic approaches for Chagas disease and cancer and biotechnology and biodiversity. The first line includes annotation of genomes and evolutionary aspects, development of tools for computational analysis of genes, genomes, transcriptomes and proteomes, search of biomolecules with biotechnological applications and identification of potential therapeutic targets. The second line is due to the determination of the complete genome sequence of the Brazilian vaccine strain, Mycobacterium bovis BCG Moreau, performed in the lab. The current challenge is to associate the mutations identified through comparative genomic analysis to specific phenotypes and its possible impact on vaccine characteristics. The third line is

aimed at testing of new therapeutic approaches for neglected diseases and cancer. Innovation is based on (i) the therapeutic approach focused on cardiac fibrosis reversal in the case of Chagas disease and (ii) in the search for new methods of diagnosis and therapy for cancer, aimed at increasing specificity and avoiding the serious side effects of existing therapies. The fourth line is focused on the characterization of environmental bacteria with impact on health and evaluation of its potential biotechnological use. Evaluate the microorganisms living on interaction can provide parameters for assessing the degree of pollution and environmental recovery and offer access to tools of (bio) remediation that can generate important restorative intervention solutions. The methodological basis and the fundamental issues analysed by the group become the Foundation of a central thematic axis, by integrating the expertise of its components in its different areas of expertise.

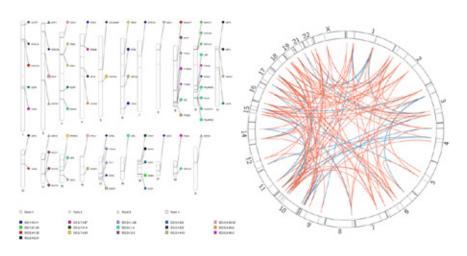


Diagram showing the location of genes encoding enzymes similar to intragenomic in human chromosomes. Enzyme activities in which evidence was found of intragenomic analogy are represented by different colors. The genes encoding enzyme distinct forms are represented by different symbols (A); circular diagram representing the chromosomal distances between the genes encoding alternative forms (red lines) and genes encoding enzyme homologous forms (blue lines) (B).

Laboratory of Functional Genomics and Bioinformatics (LAGFB)

In the line of functional genomics and evolutionary research of similar intragenomic enzymes in humans, developed by the bioinformatics group of the LAGFB, Dr. Ana Carolina Guimarães gained prominence with the work Detection of functional analogous enzymes in the human metabolism, awarded at X-Meeting 2016 — 12th International Conference of the AB3C. Another highlight is the student Pamela Barbosa, a student of the State University of Rio de Janeiro and in stage curriculum (Enterprise Integration Center-School in LAGFB) and co-guided by Dr. Teca Galvão and Dr. Caetano **Antunes (Helium Teacher reference center Fraga** - National School of public health). This student has developed the project on transcriptional regulator EthR Polymorphisms as determinant of Ethionamide resistance in Mycobacterium tuberculosis and has obtained two awards for best poster: a in an International Congress (Brazilian Society of Genetics) and another at the fourth Symposium of Science, health and sports of the Biomedical Institute of the Federal University of Rio de Janeiro State (UNIRIO). The

student Juliana de Souza, directed by Dr. Leila de Mendonça and Dr. Teak Galvão, developed the project Impact of BCG Moreau-specific mutation in the Histidine kinase activity its PhoR and won the 24TH annual meeting of the scientific research of the IOC and 1st place prize for poster presentation on IX Week of Biomedicine of UNIRIO. Finally, we highlight that the line of LAGFB research on the effect of treatment with inhibitors of the activity of TGF-B in experimental murine model of chronic Chagas disease has obtained two awards in conferences, in 2016: Satiety Brazilian of Protozoology 2016/Zigman Brener Award, by Oral administration of GW788388 works reverses cardiac damage during chronic phase of Chagas disease and Evaluation of cardiac regeneration after inhibition of TGF-β pathway in chronic Chagas disease model of experimental, considered in the lab by the relevance and consistency of the data obtained. The work was developed by Roberto Ferreira (PhD) and Chidi Abreu (undergraduate) and directed by Dr. Mariana Waghabi.

Leprosy Laboratory (LAHAN)

Leadership: Milton Ozório Moraes milton.moraes@fiocruz.br

The LAHAN combines basic and applied research in various areas of knowledge applied to disease (Immunology, Pathology, Genetics, Dermatology and Neurology, amongst others). The LAHAN houses the Souza Araújo Ambulatory, the Ministry of health reference for diagnosis and treatment of patients, as well as accompanying family members of patients, and is internationally accredited by the International Joint Commission, American oldest institution of

accreditation. The LAHAN develops projects of basic research, translational and clinical innovation, aiming to better diagnostic tools, more efficient treatments and surveillance actions for the control of the disease, assisting the construction of public policies with the Ministry of health. To this end, has a multidisciplinary team of researchers from various fields of knowledge who work with common goals in attention to the patient and their family members.



External view of Souza Araújo Outpatient Clinic, health attention unit of the Laboratory.

Leprosy Laboratory (LAHAN)

Basic and applied research to clarify the pathological mechanisms that define the markers of progression to leprosy and to facilitate the understanding of the processes of deterioration of the clinical picture are priority. The research is oriented so that it can be quickly adapted in the clinical context and transform into public policy. In this sense, there are two projects (in progress) and two published articles that represent the type of research that the LAHAN develops. The project of chemoprophylaxis of leprosy in contacts, randomized, double-blind and placebo-controlled, is coordinated by Nadia **Duppre and Euzenir Sarno and is underway since** September 2015. This project is the result of many years of research, showing the importance of surveillance of contacts, which is the population at greater risk of developing the disease, in which the second dose of BCG vaccine has protective role relevant. Currently, the project aims to test whether a dose of the antibiotic rifampin increases protection of the vaccine. The design uses the tools of molecular biology and Immunology to monitor the immune response and the presence of Bacillus in contacts over the chemo-and immunoprophylactic intervention. The project,

for the determination of a molecular system ultra sensible for diagnosis of the disease, is supported by Novartis Foundation and coordinated by Milton Matthews and was approved in November 2016. There are currently developing a prototype diagnostic kit in cooperation with the Institute of Molecular Biology of Paraná and technical details for enhancement of this product are in progress on this project which aims to increase the accuracy of early diagnosis with use of tools for DNA detection. Finally, two publications which involve three doctoral theses (two defended in 2016 and one in progress) reflect the research. The studies had the participation of young researchers trained in LAHAN, Bruno Andrade e Mayara Barbosa (guided by Roberta Olmo Pinheiro) and Thiago Toledo-Pinto (directed by Milton Moraes). Studied mechanisms of subversion of the immune response by Mycobacterium leprae interfering in restrictive capacity of the host cell for the growth and spread of the Bacillus. The M. leprae inhibit Autophagy, whitening effector mechanism of Bacillus. The research defines the pathways that underpin infection and therapies that could be used to reverse this process.

Hantaviroses and Rickettsial Infections Laboratory (LABHR)

Leadership: Elba Regina Sampaio de Lemos elemos@ioc.fiocruz.br

Since its creation, the LHR has excelled in training human resources and developing research in the areas of laboratory diagnosis, epidemiology and assessment of animal participation in the cycle of Rickettsial infections, bartonelosis, Q fever and robovirosis (hantavirosis and arenavirosis). Notwithstanding the technical advice and support to the actions of the Ministry of health and health of their peers in the State and municipal spheres, through reference laboratories allocated, the LHR has contributed significantly to the knowledge of these zoonoses, considering the following research projects that are in development: (i) clinical laboratory diagnosis of Rickettsial infections

with emphasis on differential diagnosis and syndromic surveillance feverish; (ii) investigation of rickettsiae *lato sensu* in domestic and wild animals in Brazil with emphasis in the State of Rio de Janeiro; (iii) technological innovation, aiming at the development of alternative systems of diagnosis of Rickettsial infections; (iv) clinical laboratory diagnosis of roboviroses with emphasis on differential diagnosis with dengue fever, yellow fever and malaria; (v) robovirus and ecoepidemiologic studies with wild animals in different biomes in Brazil; (vi) technological innovation, aiming at the development of alternative systems of diagnosis of robovirosis.



Male of Amblyomma rotundatum (Koch, 1844) parasitizing green iguana (Linnaeus) 1758, Amazon.

Hantaviroses and Rickettsial Infections Laboratory (LABHR)

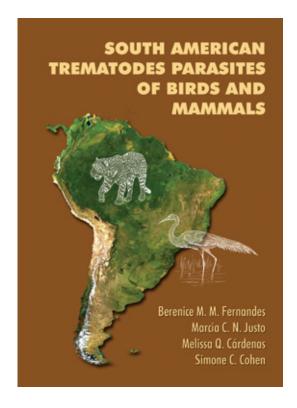
Partnerships with the Institute of Biophysics of the Federal University of Rio de Janeiro and Bio-Manguinhos have enabled, respectively, the generation of recombinant protein for different genotypes of hantavirusis aimed at provision of diagnostic kit for surveillance network and acquisition of alternative serological test based on aptamers. Worth mentioning both articles on Q fever generated by the Group: (i) in Am J Trop Med, in which suspected cases of dengue fever were confirmed as Q fever by molecular analysis, and (ii) on PLoS Neglect Trop D, which confirms the lack of knowledge of this zoonosis in South America. As recognition for the research activities carried out in indigenous community Seemed, in Mato Grosso, granted mention to Elba Lemos and Ana Claudia Terças, by the municipality of Campo Novo dos Parecis. After more than 18 months trying to retrieve the journal of Brazilian Society of Virology, Virus Review, it has been possible to make available in Virus Review & Research, the single volume of this journal, in December 2016. In addition to the articles with the theme of mass events, virus

generated by the students of the postgraduate Committee of Tropical Medicine (CPGMT), are published abstracts submitted by students in the advanced Symposium Virology Hermann Schatzmayr (2015). In the field of scientific dissemination, besides the participation of one of the members as a columnist of VIVERBEM website, which is available students 'text of viral and bacterial Diseases – pelvic inflammatory disease of the CPGMT, the creation of distance education (EAD) entitled *Tourism*, mass events and health: what a hospitality professional should know in partnership with the EAD of the National School of Public Health, Municipal **Health and Municipal Secretary of Tourism of Rio** de Janeiro. Finally, more recently established, also as part of the evaluation of the discipline of Virology of CPGMT and under the coordination of two members of the lab, the elaboration of texts by the students, aiming at the dissemination on the blog Doctor is virus, organized by the students of the IOC Jorlan Fernandes, Natalia Lanzarini and Alexandre Silva.

Laboratory of Helminth Parasites of Fish (LHPP)

Leadership: Simone Chinicz Cohen scohen@ioc.fiocruz.br

LHPP team is dedicated to research in taxonomy, systematics and Ultrastructure of helminth parasites of fish, with emphasis on (i) cataloguing and morphology of Digenea, Monogenea and Nematode parasites of fish, amphibians, reptiles, birds and mammals of South America; (ii) morphological studies, taxonomic and ecological helminth parasites of fish in coastal basins of Brazil, in natural environments and dammed, and (iii) systematics, taxonomy, morphology and biology of Digenea, Monogenea, Nematoda, Acanthocephala and Cestoda of marine fishes of economic interest of the coast of Rio de Janeiro. The fish may be parasitised by a large number of species belonging to several phyla. In recent years, the parasites have been recognized as important components of global biodiversity. The presence of helminths in fish can cause high mortality rates, reduction of capture or decrease the commercial values of the host, as well as cause damage to public health, due to the zoonotic potential of some species of helminths. Become, then, required monitoring and the study of these pathogens, through its morphological characterization, relationships between parasites and their hosts and the influence on the vital conditions of the host.



Laboratory of Helminth Parasites of Fish (LHPP)

Published a catalog updated with information about all species of Trematoda parasites of birds and mammals described in South America, in celebration of 115 of the IOC, and the third in the series that began in 2007, about fish parasites and flukes, in 2014, about parasites of amphibians and reptiles. The information gathered in the book range from the first descriptions flukes species found in birds and mammals in Brazil, in 1819, going through numerous descriptions and redescriptions of species, by Lauro Travassos and collaborators. Published two chapters in the book Parasites of marine fish of South America – Monogenoidea and Trematoda, checklists on the species of these groups of parasites. Is in the process of publishing a catalogue of Cestoda parasites in different host groups. The laboratory is responsible for the integration of data on species of helminth parasites of the taxonomic Catalogue of Brazilian fauna, which has as main objective to create an online taxonomic tool containing all species of Brazilian fauna. Advisory work was carried out, with the technicians of the Fundação Instituto de Pesca do Estado do Rio de Janeiro, in order to identify changes in Loricariidae

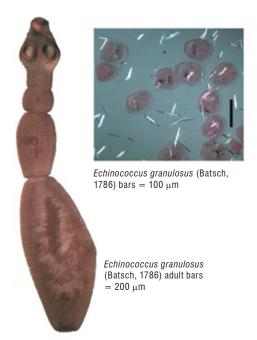
caused by parasites in the Muriaé River; this action is coming from the demand of the own professional fishermen. Continuing the work on diversity of helminth parasites of tuna and the like, being a master's thesis, with molecular approaches of the flukes of the family Didymozoidae. Are being completed doctorate thesis on fish parasites of the Rio Juruá, Acre, for knowledge of the biological wealth of the Amazon, bringing information that will guve input to the sanitary inspection of fish sold, and another on the effect of vitamins on the parasitism by Monogenoidea in fish cultivation, thus contributing to the development of diets that can better meet the nutritional demands of the fish. The Group has guided the Scientific Vocation program students, undergraduate and graduate, in addition to teaching and coordination in postgraduate courses and course of the IOC, participation in scientific events, with lectures and presentation of papers, and reviewers of articles in scientific journals, doctoral qualifications stalls, undergraduate monographs, dissertations and theses of postgraduate courses.

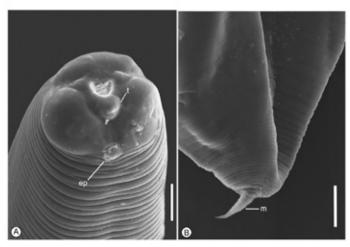
Laboratory of Helminth Parasites of Vertebrates (LHPV)

Leadership: Delir Correa Gomes Maués da Serra Freire dcgomes@ioc.fiocruz.br

The LHPV has, like competence, the development of research for the correlation between helminth infections and different vertebrates. Currently, researchers of the LHPV give continuation to the work

already established, with which we are recognized by our peers, but keeping the concern on modernizing the research, making them competitive with international standard.





Anisakis sp. (L3) in Plagioscopic squamosissimus observed by MEV, Ventrolateral view. (A) anterior extremity showing larval tooth (t) and excretory pore (ep). (B) posterior extremity showing striated tail with terminal mucromus (m). Bars: A = 20 μm e B = 10 μm .

Laboratory of Helminth Parasites of Vertebrates (LHPV)

With very promising results and comprehensive in the lines of research proposals, with approaches to biology, morphology, taxonomy and molecular, develop investigations so as to contribute to the better understanding of the different mechanisms that modulate the parasitic infection by helminthes, with emphasis on the interaction between hosts, parasites and environment, taking into consideration the possible zoonosis, in order to contribute to the improvement of the quality of life of individuals living in endemic areas for hydatidosis In addition to facilitating the use of these

techniques by public health services. We can highlight the presence of helminths with zoonotic potential, like *Echinococcus Calodium hepaticum* and *vögeli*, parasitizing pacas Acre forest areas and, for the first time, the State of Mato Grosso do Sul, as well as report the first case of *Echinococcus granulosus s.s.* (G1) in feces of dogs in the northern region of the country. Another parasite with reflexes in infection in humans, the anisaquidosis, acquired by ingestion of fish, had relevance, with published works, increasing the knowledge of that zoonosis that occurs in Brazil.

Laboratory of Viral Hepatitis (LAHEP)

Leadership: Elisabeth Lampe elampe@ioc.fiocruz.br

(i) evaluation of mutations associated with resistance to antiviral drugs used in the treatment of hepatitis B virus infection (HCB) and hepatitis C (HCV); (ii) evolutionary history and dynamics of dissemination of HCV subtypes circulating in Brazil; (iii) investigation of outbreaks of hepatitis through nucleotide sequencing followed by phylogenetic analysis of sequences of samples obtained of outbreaks, primarily of dialysis units for clarification of nosocomial transmission; (iv) study of prevalence of viral hepatitis in different population groups; (v) studies related to humoral and cellular immune response during the acute phase of HCV infection and implications of immune response on viral evolution; (vi) standardization and validation of methodologies applied to laboratory tests for viral hepatitis; (vii) hepacivirus research in mammals; (viii) gene silencing of HCB via RNA interference.

HIGHLIGHTS

Laboratory of Viral Hepatitis (LAHEP)

We can mention the study in which has been optimized, qualitatively and quantitatively, the method of detection of HCV in dried blood spots. We show that optimized methodology, it is possible to determine the viral load and genotype of the virus, which can contribute, so important in molecular epidemiology studies (J

Clin Wreath 2016 Sep: 82:139-44). In addition to this study, we also publish evidence that, regardless of the IL-28B genotype, the CD4+ specific lymphocyte response for HCV in patients with infections spontaneously resolved is similar (J Viral Hepat Oct 2016; 23:831-2).

Immunopharmacology Laboratory (LIMUNOFAR)

Leadership: Patricia Bozza pbozza@ioc.fiocruz.br

The laboratory has, as its main mission the development of research and human resources training in Immunopharmacology. The laboratory is focused on understanding the cellular and molecular mechanisms of the inflammatory process of infectious, degenerative or allergic origin. The proposed studies seek to contribute to the identification of new therapeutic targets, characterization of prognostic biomarkers, development and/or improvement of clinically relevant models of inflammatory diseases, as well as the development of effective substances in the treatment of inflammatory diseases. The laboratory's research activities are concentrated in four main lines, which

have great interaction and complementarity. All these lines of research include external resources and intra-and inter-institutional partnerships. They are: (i) pathophysiological mechanisms and new therapeutic perspectives in sepsis, severe malaria and dengue; (ii) metabolism and biological function of lipid domains and lipid mediators and their implications in infectious, degenerative or allergic origin; (iii) mechanisms associated with obesity and metabolic changes in the genesis and modulation of the inflammatory response; (iv) development of natural substances with analgesic, anti-inflammatory activity and/or immunomodulary.

Immunopharmacology Laboratory (LIMUNOFAR)

We develop studies demonstrating the role to the Statin in reverse microcirculatory and neuroinflamation dysfunction during experimental sepsis, leading to the prevention of the development of the cognitive decline associated with sepsis. We show also the beneficial effect of supplementation with oleic acid (Omega-9, main component of olive oil) in experimental sepsis. We observed improvement of the clinical signs, decreased liver and renal dysfunction and increased survival rate in septic animals treated with oleic acid. The mechanisms involved include the reduced production of reactive oxygen species (ROS) and plasma levels of fatty acids, increased expression of protein kinase activated by Camp (AMPk), with

consequent expression of enzymes involved in the degradation of fatty acids. The LIMUNOFAR, in conjunction with the Centre for technological development in health (CDTS), led the study for sofosbuvir, repositioning drugs approved for clinical use against hepatitis C and Zika virus (ZIKV). Our group studied the similar effect of chloroquine and Mefloquine against the ZIKV virus. Coordinate clinical and laboratory study of Arboviruses, constituting bio-collection samples of mild and severe cases that are being used in different studies focused on the pathophysiology and development/validation of new diagnostic tests. No less important, and in collaboration with Broad Institute, studied the origins and evolution of the ZIKV in the Americas.

Laboratory of Clinical Immunology (LIC)

Leadership: Rosa Teixeira de Pinho rospinho@ioc.fiocruz.br

The LIC develops research on the immune response to infections with fungus, viruses, protozoa and Mycobacteria and BCG Moreau vaccination. We seek immunological and molecular aspects correlate as modulators of factors infection. We have performed clinical research associated with BCG vaccine in immunological studies in collaboration with the Foundation Ataulpho de Paiva. Also researched natural and synthetic substances with antiretroviral microbicide and activities, in collaboration with the laboratory of Molecular Virology of the Fluminense Federal University. We researched the interaction of

human cells with *Leishmania* and *Trypanosoma cruzi*, using natural or synthetic substances and evaluating immunological aspects and the participation of immune substances on the viability of the parasites. Clinical and applied research in tuberculosis and dengue fever involve the participation of laboratories of the Fluminense Federal University, Hospital Universitário Pedro Ernesto, *the Rio de Janeiro State University and the National Institute of health quality control.* Obtained results have been published in national and international magazines.

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Laboratory of Clinical Immunology (LIC)

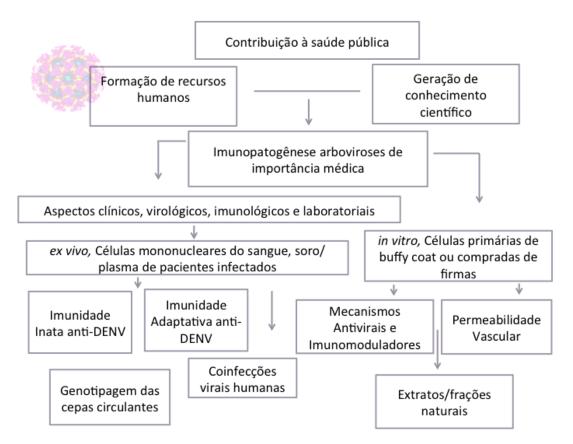
Important studies with opportunistic mycoses line was drawn to examine the *in vivo* immune response infection with *Purpureocillium* front *lilacinum*, one of the causal agents of hialohifomicose, considered, currently, an emerging fungus that affects mainly immunocompromised patients.

Viral Immunology Laboratory (LIV)

Leadership: Elzinandes Leal de Azeredo elzinandes@ioc.fiocruz.br

In biological samples from sick patients for infections caused by dengue, Chikungunya, Zika, other arboviruses and those Coinfected with different arborvirus and HIV, LIV's team is able to quantify the production of mediators related to immune response, such as Cytokines and Chemokines, as well as mechanisms of coagulation of the human host for immunoenzimatic tests. Evaluate the capacity of production of cytokines and cytotoxic activity of T cells and B patients by flow cytometry and ELISPOT assay. A very important aspect discussed in our lines of research is the ability to assess changes in cellular

integrity suffered by endothelial cells grown in the presence of biological samples from patients. Plasmacitoides dendritic cells (pDCs) and *natural killer* cells (NK), important components of the innate immunity and immune cells necessary for the regulation of the immune response exacerbated, as regulatory T cells and cells of Th17 profile, are studied in human infections by Arboviruses. We describe the epidemiological and laboratory aspects of patients infected by dengue fever, Zika, Chikungunha and other arboviruses, beyond the characterization of the infective viral genotypes.



Viral Immunology laboratory is, since its creation, interested in the study of the mechanisms.

HIGHLIGHTS Viral Immunology Laboratory (LIV)

In teamwork, with intra-and Interstate collaborative action of health centres and hospitals, we highlight the collaboration of Fiocruz in Mato Grosso do Sul and the hospital Rio Laranjeiras, Rio de Janeiro. We obtained a cohort of 176 confirmed cases of dengue fever infections, Zika and/or Chikungunha and coinfections for dengue and Chikungunya and/or Zika. Part of this cohort has generated scientific findings — published — that address evolutionary and epidemiological aspects of the virus Chikungunha in the State of Rio de Janeiro. For the proposed studies, we rely on funding from other sources approved: Network 4 — Microcephaly associated to Zika virus infection: a transdisciplinary approach, the Edict Faperj nº 18/2015; Research program in Zika, Chikungunya and dengue fever in the State of Rio de Janeiro, the Edict MCTI FNDCT/ Finep/01/2016; CNPQ universal — Activation of monocytes, NK cells and endothelial hepatocytes, during dengue: membership in the severity and action of natural products in therapeutic targets; Young scientist of our State — Faperj — DENV and HIV Co-infection: antiviral immune response and immunological indicators in Patients Coinfected naturally;

FINEP — Zika virus transmission through different bodily fluids. Other parts of the cohort have been extensively studied and will soon be submitted to scientific journals. In this context, the cohort of patients from 2016 epidemic allowed discuss clinical and laboratory aspects of dengue infections, Zika and/or Chikungunha and the coinfections in Brazil. In addition, in order to identify the immune profile of differential three Arboviruses, have we quantified human circulating immune mediators in the three infections and also in coinfections. We know, currently, the immune response of T cells from patients for infections and coinfections, promoting the understanding of the immunopatogenic mechanisms of the three viruses. With this cohort of patients, researchers from Vaccine Discovery team at La Jolla Institute for Allergy and Immunology in the United States of America, were at the LIV and, with our team, generated important data about the specific T-cell immune response of patients to different regions of polyproteins immunopatogenic peptides of dengue virus and Zika. Analyses of placentas and necropsies of microcephalic babies are being object of analysis by our group and potential results are being generated.

Immune Modulation and Protozoology Laboratory (LIMP)

Leadership: Kátia Calabrese calabrese@ioc.fiocruz.br

The LIMP works in search of alternative therapies for the treatment of leishmaniasis, evaluating the leishmanicide activity and immunomodulatory of several compounds derived from plants such as: Morinda citrifolia, Vanillosmopsis arbórea, Vernonia polysphaera, Garapa guianensis, Arrabidaea chica and Selaginella sellowii, as well as the isolated compound alfa-bisabolol. We studied the genetic and immunological mechanisms involved in resistance/ susceptibility to infection by Leishmania amazonensis from different isogenic mice. We are developing a project to assess the action of Alpha-bisabolol in dogs infected by Leishmania. In collaboration with the laboratory of immunoparasitology, we are evaluating, comparatively, the protective efficacy and immunogenicity of homologous and Heterologous total extracts (of Leishmania amazonensis dead promastigotas and Leishmania braziliensis, respectively), with and without adjuvant CpG-ODN (oligodesoxinucleotídeos rich in CpG motifs) in murine model of experimental cutaneous leishmaniasis

caused by I. amazonians. In experimental infection by *Trypanosoma cruzi*, have developed a project aimed at understanding the mechanisms immunopatologic involved in oral infection by *T. cruzi*. In another project, we are proposing the characterization of fibrocyte's as a model for the study of pathogenesis of *T. cruzi* infection. In collaboration with the laboratory for Toxoplasmosis and other Protozooses, we started the evaluation studies of a possible action to assess their tripanocidal of temporizine and temporizine-1 on experimental infection by T. cruzi. Recently we got involved in a collaboration in the study of maternity care exposed to Zika virus on analysis of placenta and umbilical cord and applicability to the SUS. These projects are developed in collaboration with the Universidade Estadual do Maranhão. Our research group participates as a contributor of papers in the study of genetic markers for the the Dirofilaria immitis resistance macrocyclic lactones, with Fluminense Federal University.

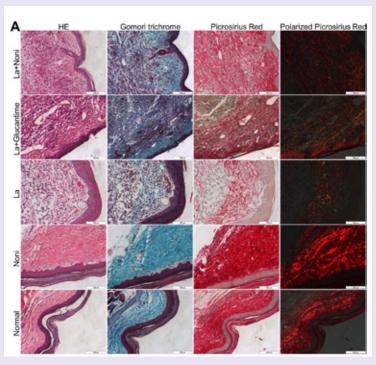
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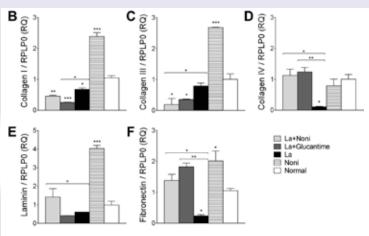
HIGHLIGHTS

Immune Modulation and Protozoology Laboratory (LIMP)

The highlight of the lab was the follow-up of the projects aimed at the search for alternative therapies for the treatment of leishmaniasis. In this line, we publish four articles in indexed journals. The first Ultrastructural changes and death of Leishmania infantum promastigotes induced by Morinda citrifolia Linn. fruit (Noni) juice treatment, appeared on Evid Based **Complement Alternat Med Analyze the** leishmanicide activity caused by treatment with the juice of the fruit of *M. citrifolia* (NONI) in promastigotes of Leishmania infantum and ultrastructural changes observed that indicate the potential use of NONI in the treatment of leishmaniasis. Another article, Morinda citrifolia (NONI) fruit juice Linn induces an increase in *Nitric Oxide* (58: 2016, 51-58) aimed to analyze the activity of NONI against I. Amazon and its action in peritoneal macrophages of BALB/c mice infected with this parasite. It was observed an increase in nitrite production in macrophages infected and uninfected, showing that treatment with the NONI can increase the production of peritoneal macrophages and us that this ability has important role in death of intracellular amastigote L. amazonensis. The third article, Morinda citrifolia Linn. reduces parasite load and modulates cytokines and extracellular matrix proteins in C57BL/6 mice infected with L. amazonenses (PLoS Negl. Trop. Dis. 10: e0004900) showed that the oral treatment of C57BL/6 mice infected with I. further reduces the size of the lesion, as well as the parasitic load, the inflammatory infiltrate and the expression of cytokines and increases the expression of extracellular matrix components. These data show the effectiveness of treatment with NONI. The article Leishmanicidal. cytotoxicity and wound healing potential of Arrabidaea chica Verlot (BMC Complement. Altern. Med. 4, 16:1) showed the potential leishmanicide activity of Arrabidaea chica. In the line of *T. cruzi*, publication *Temporizin and*

temporizin-1 peptides as novel candidates for eliminating Trypanosoma cruzi, in PLoS One, assessing assess their tripanocidal action of temporizina and temporizina-1 on experimental infection by *T. cruzi*.





analysis of the extracellular matrix of the plantar cushion of C57BL/6 infected with *Leishmania amazonensis* and treated with NONI.

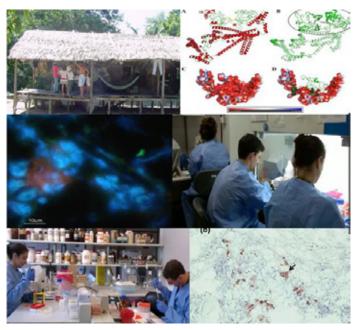
Laboratory of Immunoparasitology (LIP)

Leadership: Fátima Conceição Silva

fconcei@ioc.fiocruz.br

The LIP was organized in 1992 and, since then, has been ruled by the multidisciplinary vision of their projects, staff and students. Our goal is to obtain knowledge in different angles of knowledge in infectious and parasitic diseases (PID) that affect humans and animals. Thus, the LIP is dedicated mainly to the leishmaniasis research, malaria, sporotrichosis, and other fungal infections. We place emphasis on research of immunopathogenic mechanisms that influence the evolution of infections for frames with a tendency to cure self-limited or cases with evolution to the illness, including the presence of comorbidities, generating knowledge applicable to the development of vaccines and new drugs. Aligned with the institutional goals, the LIP has, as its mission, to develop research, education and training of human resources in immunopathogeny, clinic, immunoassay, immunoprophylaxis, therapy and molecular/cellular biology applied to DIP, generating knowledge to contribute to the management of these infections. We have, as an interface feature collaboration with laboratories and research groups at Fiocruz and teaching and research institutions in Brazil and other countries such as United Kingdom (University of Oxford), Spain (Laboratorios Leti), Switzerland (Swiss National Science Foundation) and United States of America (Centers for Diseases Control and Prevention). Act two research platforms, open to multiuser requestors intra and extra Fiocruz: ELISPOT and platform Purifying Cell core flow cytometry platform. Based on the vision of multidisciplinarity, receive students with different backgrounds and expectations, especially biologists, biomedical, pharmaceuticals, doctors and veterinarians (undergraduate/graduate). Despite the

knowledge produced in infections — our studies, fundamental questions have not been answered, making greater efficiency in the management of patients by understanding the mechanisms of illness and protection, including the design of new approaches more effective/less invasive diagnostic drugs easier administration and less toxic, and the consequent development of vaccines/immunotherapy. Thus, the LIP is focused on those evaluations in order to contribute to the improvement of knowledge of the dynamics of infection by *Plasmodium SP., Leishmania SP., Sporothrix SP.* and other mycoses and, to a lesser extent, in infections produced by other protozoa.



Activities of the laboratory of immunoparasitology.

2016

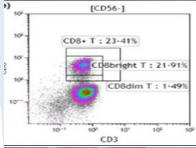
HIGHLIGHTS

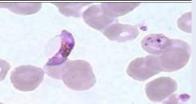
Laboratory of Immunoparasitology (LIP)

The Mission of development of research activities, education and training of human resources in immunopathogeny, clinic, immunoassay, immunoprophylaxis, therapy and molecular/cellular biology applied to DIP, LIP kept the generation of knowledge to contribute to the management of DIP that affect man and animals, in collaboration with the National Institute of infectious diseases Evandro Chagas (INI) and Bio-Manguinhos. The multidisciplinarity of ideas and content was represented on the scientific production of the LIP. In the area of leishmaniasis, evaluate the cytotoxicity on immunopathogeny of American tegumentary leishmaniasis (LTA) (Parasite Immunology), the induction of pancreatotoxicidade by treatment with meglumine antimoniate (Rev. inst. Med. TORP São Paulo) and the influence of coinfections on evolution of cutaneous leishmaniasis (LTA and helminthiasis) (Acta Trop.) and LTA and malaria (Front. Microbiol.), besides the participation in studies on the biology of species in the new world (Biochimie). With regard to malaria, we invest in the development of vaccines with in silico approach (PloS One) and evaluations about the action of chimeric proteins (Sci. Rep.). In the field of mycoses, we contribute in the evaluation of the immune response in human cases, with verification of profile of cytokines in vitro and in situ linked to different clinical presentations (PloS One) and in cats with Sporotrichosis, identifying subpopulations of lymphocytes CD4/ CD8 as markers of severity of infection (Med. Mycol.). Based on our collaboration with the INI, publish study on laryngeal tuberculosis (PloS One) and, with Bio-Manguinhos, the conjugated fluorescent methodology for flow cytometry (PloS One). Also published review articles on immunization in leishmaniasis (Front. Immunol.

and Parasite Vectors) and the Association & malaria-HLA (Front. Immunol.). Orient 32 students (undergraduate, master's or doctorate) and four were completed dissertations/PhD. We're still home to two technological platforms (ELISPOT and flow cytometry). We obtained financial resources in different financial agencies in regional, national and international cooperation, emphasizing the continuity of projects (University of Zurich, Switzerland; Laboratório Experimental de Terapéutica Inmunógena, Spain; Centers for Disease Control and Prevention, United States of America). In summary, the LIP was able, even in a little favorable, keep the academic production, organization and financing of projects.







Activities of the laboratory of immunoparasitology.

Inflammation Laboratory (LABINFLA)

Leadership: Marco Aurélio Martins mmartins@ioc.fiocruz.br

The generation of scientific knowledge, the development of new pharmacological therapies and training staff in the area of Pharmacology of the inflammatory process constitute the central mission of the LABINFLA. The focus of activity of the group is the development of experimental models, aimed at identifying innovative therapeutic targets and the discovery of new drugs and bio-products that can benefit the treatment of pulmonary chronic inflammatory diseases. Are studied, as well, complications with metabolic and neoplastic diseases The allergic, infectious and occupational disorders of the respiratory system are among the most common and disabling diseases of humans. Among them are asthma, silicosis, acute respiratory dysfunction syndrome and chronic obstructive pulmonary disease (COPD). Such diseases typically associated with inflammation, accumulation of extracellular matrix components and plasma proteins, plus remodeling of pulmonary tissue. Lung inflammatory diseases constitute a major challenge to modern medicine, on the basis of high and growing social and economic costs observed in Brazil and in the world. Antiinflammatories (glycocorticoid) and the Bronchodilators (beta-adrenergic agonists and other muscarinic receptor blockers) are the most effective

therapeutic agents in the treatment of asthma, but resistance to steroids and agents the multiple adverse side effects, evidenced by these drugs, limiting its benefits. For patients with silicosis, acute respiratory dysfunction syndrome and COPD, therapeutic difficulties are even more serious, because satisfactory treatments available are nonexistent. Thus, it becomes crucial to search for alternative agents that can bring benefits to patients more effectively and safely. The LABINFLA has different infrastructure for studies of inflammation, mechanical ventilation and pulmonary histopathology, crucial in research of mechanism of action, proof-of-concept and screening of candidate compounds that can inhibit or accelerate the resolution of acute and chronic inflammatory processes. In collaboration with national and international laboratories, the Group has developed several important projects, supported by highly competitive programs, FP-7 (European Union), National Institute of science and Technology-Inofar (CNPg/Faperi), PDTIS (Fiocruz), Fapesp (CNPg/ Faperj), Nanoasma (Capes), Pensa Rio (Faperj), Universal (CNPg), among others.

Inflammation Laboratory (LABINFLA)

Study in collaboration with researchers from the Institute for Research in Biomedicine, Universitá dela Svizzera Italiana (Bellinzona, Switzerland) and Telormedix S.A. (Bioggio, Switzerland) demonstrated the innovative therapeutic potential of TMX-306 compound in the reversal of pathological signs of critical experimental silicosis in rats. This is agonist of toll-like receptor (TLR) 7 which was pegylated to present activity reduced (partial agonist) on this important pathogen recognition receptor. This was the first study involving pegylated ligands for TLR7 in models of acute lung injury, asthma and silicosis and featured four-year funding from the European Commission. The work was published, in 2016, in the journal Frontiers in Immunology, having received more than 1,650 views. Study of about four years of Labinfla, in collaboration with researchers at the Department of organic synthesis of Farmanguinhos and laboratory of cell signalling of the IOC, arrived in term in 2016 with the request, by the Fiocruz, of filing (PCT/ BR2014000266) in various international patent offices, including the North American (US14/911,138), the Japanese (JP 2016-527280) and European (14834562.2-1451). Among about

50 compounds of synthesized, identified potential therapeutics in at least three structurally unique compounds, which showed significant activity dual anti-inflammatory and muscle relaxant. The whole series was planned from the prototype mexiletine, local anesthetic oral clinical use in the treatment of arrhythmias and neuropathic pain. Selected compounds exhibit interesting anti asthmatic activity profile, with local anesthetic activity weakened and can open new perspectives in the treatment of diseases characterized by bronchial obstruction, inflammation, hyperreactivity of the airway and pulmonary remodeling. The work entitled Atypical chemokine receptor ACKR2 contributes to the develpement of lung fibrosis in silicotic mice, presented by doctoral student Davidon Furtado Diasof cellular and Molecular Biology program of the IOC, was selected third by an International Committee that judged the 65 candidates for the Prize José Ribeiro do Vale 2016, Awards of the **Brazilian Society of Pharmacology and Experimental Therapeutics with the support of** the pharmaceutical firm Biolab.

Laboratory of Innovations in Therapies, Education and Bio-products (LITEB)

Leadership: Tania Cremonini Araujo-Jorge taniaaj@ioc.fiocruz.br

Innovation is the central axis of the LITEB, with five groups of research and expertise in three lines that give the name: therapeutic innovations, innovations in education and innovations in bio-products. In 2016, developed 13 macroprojects, contributing to the pursuit of excellence in research in the IOC. This choice is based on our 2003, article in the journal Science & collective health (8: 727-741), Models and conceptions of innovation: the transition of paradigms, the reform of the Brazilian C&T and the conceptions of managers of a public health research institution. In 2016, we kept the production standard above 4000 points total: 17 articles and five chapters of books, as well technical publications and 38 communications in congresses. We put a new patent and kept an earlier. We have strong insertion in education: 614 teaching hours recorded, in addition to 25 coordination of disciplines and courses. The area coordinator of Capes (Tania the-Jorge) and its technical scientific Council Member, the coordinators of the graduate program in the strict sense (Lucia Rocque and Claudia Coutinho, postgraduate-education in biosciences and health) and the PG program coordinators lato sensu (Valeria Trajano and Annunciata Sawada, postgraduate studies-Science art and culture on health). The head

of the lab graduated from September 2016 to participate as a candidate for President in the electoral process to the Fiocruz. The national situation and the crisis at Petrobras, central finance group of innovations in bio-products of LITEB, led to the forced reduction of our team, in 2016, from 34 to 23 professionals (servers and scholars of projects). We also count on Paulo Vasconcellos-Silva, whose renewal of the cooperation agreement with the National Cancer Institute has not yet been finalized, but we received, for relocation, the new researcher, Luciana Garzoni, and so the group will evolve in its dynamic links with professionals. We finish the year with 83 active enrollment (in 2015 were 68), of which 33 of PhD (in 2015 were 32), 10 (in 2015 were seven), 17 lato sensu specialization (in 2015 were eight) and 23 in other levels, undergraduate and high school. In 2016, formed five doctors, three Masters, three specialists and 14 trainees from other disciplines. The student Lorrayne Isidoro Gonçalves of the Colegio Pedro II and Provoc, with Anna Carvalho, won the IV Brazilian Olympiad for Neuroscience and was the international Olympiad, prominently in the mainstream media by overcoming various difficulties.

2016

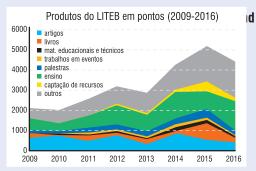
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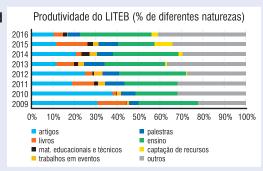
Laboratory of Innovations in Therapies, Education and Bio-products (LITEB)

Therapies: (M01) Selenium in chronic Chagas disease. It's about half the expected number of patients randomized and was presented at the DNDi. TGFB advanced studies (article in Immunobiology); (M02) Accession and adherence of patients to the treatment of tuberculosis (TB). Rocinha study completed, educational materials produced and qualitative studies in progress. We Report TB — Regional observational prospective and Research in tuberculosis in Brazil; (M03) Immune response about Duchene muscular dystrophy (DMD) and the pathophysiology of the liver, with intricate connection between the liver and the immune response of peripheral immune response. Article in J. Immunology describing muscle migration of lymphocytes T delta range, the chemotactic agents for the induction of Cytotoxic Effector activity migration, its site and what are the pathways of cell death used in the destruction of cardiac mieloides cells; (M04) Highly aggressive behavior: biomodel to study pathophysiological mechanisms and of the action of drugs in clinical use in humans.



Intern. J. Mol. Sciences); (M05) Helminths (an article); (M06) Teaching — science, art and educational materials. Eight articles and three chapters of books, educational products and extension activities; (M07) Education and science expeditions. Two expeditions focusing on Arboviruses transmitted by Aedes (Manguinhos-Quixeramobim in Rio de Janeiro, Brazil-Ceará); (M08) Supporting patients with chronic conditions. Courses and events with carriers and family about Chagas, hepatitis, leishmaniasis, tuberculosis; (M09) Community health training strategies for health promotion. The Community health course: a construction of all qualified residents 150 in 50 communities, with a publication. Action in Laje do Muriaé, São Francisco do Itabapoana, Ilha Grande, Rio de Janeiro, Magdalene and Quixeramobim, Ceará; (M10) Dialogia (communication), culture and health. Cooperate with the project by joining the ends of the SUS. Discipline Popular education, culture and health in PG/IOC; (M11) Amazon. An article and a book chapter published and M09 studies in Pará; (M12) Bioproducts — active principles. Deposit, with the PTO, the patent application (confidentiality until June 2018). **URBI** expanded to antiviral activities: two items highlighting antiviral action of natural substances (seaweed) and synthetic substances; (M13) Ulcerative colitis. Completion of a doctoral thesis and a master's degree from the Federal University of Rio de Janeiro.





Productivity developments of the laboratory of Innovations in therapies, education and Bioproducts, of 2009 to 2016.

Cardiovascular Research Laboratory (LICV)

Leadership: Eduardo Tibiriçá

etibi@ioc.fiocruz.br

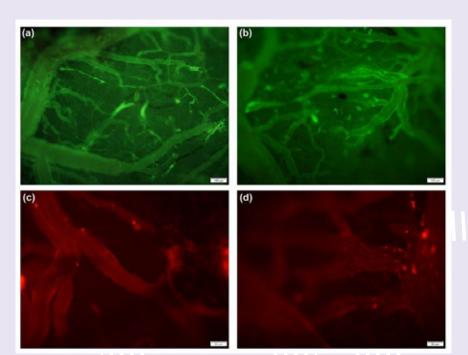
The lab is devoted essentially to the study of cardiovascular and metabolic diseases of relevance in the Brazilian public health, such as hypertension, diabetes mellitus and metabolic syndrome. The experimental research of the laboratory have given emphasis to the investigation of the Microcirculatory disturbances and changes of tissue perfusion characteristics of cardiometabolic care diseases. One of the fundamental scopes is the evaluation of changes of cerebral Microcirculation in hypertension and diabetes. These changes, represented mainly by microcirculatory rarefaction, heart attacks and brain incomplete cerebral perfusion reduction, are involved in the pathophysiology of dementia in elderly patients and in experimental models, with hypertension and diabetes. Have also been studied the effects of antihypertensive medications and medications in the reversal of these changes Microcirculatory disturbances. From the point of view of Cardiovascular Pharmacology, we investigate the pleiotropic effects of Statins that are not related to the actions of these drugs on the plasma cholesterol changes

Microcirculatory disturbances in hypertension. Another line of research aims to clarify the pathophysiology of hepatic changes in experimental model of diabetes and metabolic syndrome. In this project, we investigated the role of advanced glycation end products, important triggers of vascular damage in diabetes. By means of official collaboration agreement with the National Institute of Cardiology, we have developed clinical academic studies that investigate the pathophysiology and treatment of microvascular changes in cardiovascular diseases. In addition to drug treatment, we have studied the effects of cardiovascular rehabilitation and dietary measures in Microvascular changes of patients with ischemic heart disease after myocardial revascularization. We consider, as important, the aspect Integrator between experimental research and clinic featuring the lab. also known in medicine as survey "the bench to bedside" (translational research). The studies developed in the laboratory contribute to the understanding of the involvement of Microcirculatory disturbances changes in the pathophysiology of cardiovascular diseases.

Cardiovascular Research Laboratory (LICV)

In a model of experimental diabetes induced by Streptozotocin, describe changes, including increased liver oxidative stress markers of inflammation and increased deposition of advanced glycation end products (AGEs). Among the changes Microcirculatory disturbances, we highlight the considerable increase of bearing and leukocyte adhesion in sinusoid venules and post sinusoids. In order to evaluate the effect of combined treatment of metformin, hypoglycemic agent, and insulin, if these parameters have been modulated after treatment. We found that the combined treatment showed more pronounced effects on cardiometabolic care changes protection and liver damage when compared to monotherapy with insulin. We develop, also, an experimental model of metabolic syndrome induced by high-fat diet in mice, which is characterized by the presence of

hypertension, insulin resistance, glucose intolerance and visceral obesity. Metabolic syndrome is also associated with increased risk of cerebrovascular disease, including cerebral ischemia. We demonstrate that in this experimental model, there are inflammatory changes and severe cerebral Microcirculatory disturbances associated with greater susceptibility to ischemic events in the central nervous system. In this context, the cerebral microcirculation becomes therapeutic target for the prevention of cerebrovascular diseases in patients with metabolic syndrome. Also demonstrate that the treatment of those animals with aerobic physical training immediately after a cerebral ischemic event reduces the changes brain Microcirculatory disturbances, as well as the cerebral vascular inflammation.



Intravital videomicroscopy images of cerebral microcirculation in mice.

Malacology Laboratory (LABMAL)

Leadership: Silvana Carvalho Thiengo sthiengo@ioc.fiocruz.br

In 2016, continued to research in the areas of systematic morfomolecular, biology of reproduction and other aspects of the biology of the gastropoda, with emphasis on vectors of parasites and their respective host-parasite relations, all guided by institutional guidelines aimed at the generation, advancement, dissemination and application of knowledge in the field of human and environmental health. The experience achieved by the team is allowed to respond to national demands, both in relation to specific identification, ecoepidemiologic information, such as identification and examination of transmitting species of *Schistosoma mansoni*. identification of Chinese slug *Meghimatium pictum* acting as Prague grape plantations in southern Brazil and the participation of the African snail Achatina *fulica*, urban pest, in the transmission of Eosinophilic meningitis emerging zoonotic disease in the country,.

We have responded promptly to the society by means of clarification on the mollusks and the associated parasites, either by spoken and written media, making explantory notes techniques. We have included a new line of research, biodiversity of terrestrial mollusks, especially Veronicellidae, involved or not in the transmission of parasitic infections, resulting in publications with collaborators from Brazil and abroad. The maintenance of 10 different strains of *S. mansoni* fostered research and intra-and inter-institutional partnerships, resulting in formation of human resources (theses and dissertations), in addition to publications. As for the damages arising from environmental changes, have held the comnic malacofauna monitoring in various catchment areas, especially areas impacted by major water projects, contributing to the promotion of human health, as well as the knowledge and biodiversity conservation.

HIGHLIGHTS Malacology Laboratory (LABMAL)

We stress the continuity of research in the areas of biodiversity, systematics and biology of morfomolecular gastropods, with emphasis on vectors of parasites and their respective host-parasite relations, all guided by institutional guidelines aimed at the generation, advancement, dissemination and application of knowledge in the field of human and environmental health.

Cellular Microbiology Laboratory (LAMICEL)

Leadership: Maria Cristina Vidal Pessolani cpessola@ioc.fiocruz.br

The LAMICEL has, as its central theme, the study of leprosy and tuberculosis (TB), harms listed among the priorities of the Ministry of health, since they are endemics of great impact to public health in Brazil. Both diseases are waiting for the creation of more effective tools for its control. Among these, we can highlight the development of tests for early diagnosis, more effective vaccines, as well as alternative therapeutic schemes. More recently, the laboratory has expanded its activities to the study of other bacterial pathogen of great interest for public health, Klebsiella pneumoniae. The general lines of research of the laboratory are: (i) Characterization of the mechanisms of pathogenesis of Mycobacterium leprae. The purpose of this line is to generate basic knowledge, identifying processes and relevant molecules in *M. leprae* interaction with the human being and in the pathophysiology of leprosy. Among the goals, we can emphasize the identification of new treatment alternatives and diagnostic biomarkers and disease progression; (ii) analysis of specific immune response in individuals with different degrees of exposure and susceptibility to M. leprae and Mycobacterium tuberculosis. This line has, as its

objective, identify relevant antigens and characterize the immune response in susceptible groups and resistant to infection by these pathogens. The goal is to define new immunological biomarkers that could be used in the detection of infection, diagnosis and prognosis in leprosy and TB as well as generate subsidies for the development of vaccines for Mycobacterial infections; (iii) transmission mechanisms and other epidemiological studies. This line has as objectives, characterize strains Mycobacterium tuberculosis clinics in selected populations, as well as check the potential involvement of the oniscidea and arthropods in leprosv transmission vectors. Among the goals is to generate knowledge that will enable the introduction of measures of impact on interruption of transmission of these micobacterioses: (iv) Mechanisms of pathogenicity of *K. pneumoniae*. Our group has, as its objective, to characterize virulence factors of this kind, the structural and functional point of view, as well as the metabolic pathways and/or signalling of host cells modulated by such bacterial virulence factors. In particular, we are studying a protein secretion system, the type VI secretion system.

Cellular Microbiology Laboratory (LAMICEL)

(i) identification of the mannose receptor, a molecule CD206 as involved in internalization of M. leprae in Schwann cells. In addition, showed a crosstalk between the receiver and the lipogenic transcription factor PPAR and the concomitant formation of lipid bodies in cells infected with M. leprae; (ii) the demonstration of the importance of pentose for successful infection of the bacillus of Hansen in the Schwann cell, as well as your relationship with Leprosy neuropathy; (iii) advances in understanding of the involvement of purinergic receptors and metabolizing enzymes of extracellular nucleotides in the pathogenesis of leprosy; (iv) the development of new models for study of Leprosy neuropathy, as crops of dorsal root ganglia and peripheral neurons cultures, to begin in 2017, the demand for drugs capable of reducing the damage observed during infection by M. leprae to the nerve; (v) progress in understanding the mechanisms of pathogenesis of Erythema Nodosum leprosum through identification of the endogenous DNA recognition by TLR-9 bacterial and as via relevant during this inflammatory reaction episode; (vi) validation of

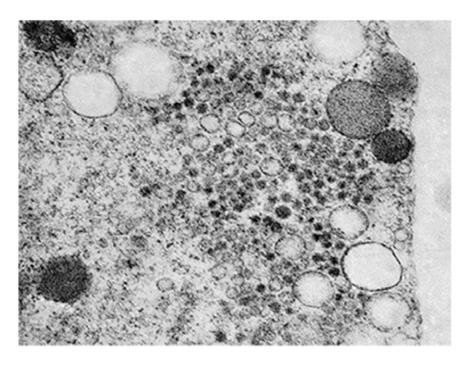
new bookmark, PstS-1 (285-374): CFP10 for latent infection by M. tuberculosis (LTBI) in network in two States of Brazil; (vii) transcriptomic biomarkers study on tuberculosis (TB) and LTBI, in which mRNANPC2 was first identified and validated with high sensitivity and specificity, being associated with the pathogenesis of TB because it has the expression modulated in different stages of the disease; (Viii) Immunodominance of IgA-MPT-6: MT-10 was identified in bacilliferous TB patients, preferably in indigenous patients; (Ix) Analysis of genotypic lines of *M. tuberculosis* in the Bangu Complex, Rio de Janeiro, shows that the then predominant T family is giving way to the LAM family, through microevolution. The Beijing family was found for the first time. Improvements and control of TB in prisons are urgent; (x) the platform of flow cytometry and sorting RPT08A, of the network of Technological Platforms of Fiocruz, linked to the laboratory, he moved to new premises and has incorporated new methodologies, supporting the work plans of several units of Fiocruz and other national and international institutions.

Viral Morphology and Morphogenesis Laboratory (LMMV)

Leadership: Ortrud Monika Barth Schatzmayr barth@ioc.fiocruz.br

The Mission of the LMMV is (i) morphological studies in cellular and tissue level. Ultrastructural studies of viruses and cellular response to viral infection; (ii) study the Morphogenesis in cell culture and viral in virus-infected pathogenic vectors to human and animal health; (iii) carry out rapid diagnosis of viruses and other microorganisms; (iv) develop methodologies applied to viral Diagnostics; (v) perform additional

viral diagnosis techniques such as immunofluorescence, viral isolation, PCR and others; (vi) to train specialized human resources in viral and cellular morphology through stages of training and post-graduate courses. The lab is a member of the IOC's research areas of viral and rickettsial infections diseases, as well as dengue and other arboviruses.



Vero cell containing numerous virus particles Zika (dark spheres) with average diameter of 50 n.

Viral Morphology and Morphogenesis Laboratory (LMMV)

We highlight the publication of several articles related to the morphology of the Zika virus, of fundamental importance to the increased knowledge about this pathogen during the confrontation of public health emergency in the country [Mem. Inst. Oswaldo Cruz 411-413/2016. DOI: 10.1590/0074-02760150433; Mem Inst Oswaldo Cruz 111: 532-534/2016. DOI: 10.1590/0074-02760160104; Studies in Biosciences (IJRSB) 4: 46-54/2016. [ISSN 2349-0357 (print) & 2349-0365 ISSN (online)]. In addition, Honorable mention for the work HPV virus-like particles (VLP): morphological alterations of HPV-positive (SiHa and HeLa)

human cervical carcinoma cell lines as possible prognostic markers of cervical cancer (Simões RSQ, Barth OM) (STD-Brazilian Symposium on Human Papilomavirose (HPV in Rio 2016); the RAIC Award Annual Meeting of scientific initiation (CIWIN)/IOC for Glenford Cardenas Caldas: Morphological and molecular studies of tissues of experimentally infected with murine model virus dengue serotype 3 (Advisor: DF Barreto-Vieira); the CIWIN/IOC Award for Karolina Madruga de Freitas KM: Antiviral activity of synthetic compounds dengue virus interaction front — the host cell in vitro (Advisor: Elen de Mello e Souza).

Hematozoa Transmitting Mosquitoes Laboratory (Lathema)

Leadership: Ricardo Lourenço-de-Oliveira

The Lathema develops research whose goals are fully aligned with those of Fiocruz and the strategic mission of our unit. In addition to the lines of research activities, the Lathema comprises a reference service in malaria vectors and a biological collection institutionalized. Research actions, reference and collection developed in Lathema are often unique in the country. With regard to research, not only seek work at the frontier of knowledge and in line with the policy of science and technology in health, as we seek to generate knowledge applicable to programs of monitoring and control of diseases that are important for the country, in particular dengue, Chikungunya, Zika, yellow fever and malaria. As a result, the Lathema and the quality of its production are recognized as a reference in their areas of expertise.

Our research still cover essentially multidisciplinary scientific investigations that lead to the production of knowledge about systematics, ecology, biology, behavior, distribution timeline and vector competence of mosquitoes to Arboviruses and transmitters of malaria. Such investigations are essential to the understanding of the dynamics of the transmission and the improvement, guidance and assessment of the efficiency and effectiveness of alternative control methods of Arboviruses mentioned above, such as, for example, the use of obligatory endosymbiont Wolbachia bacteria. Equally important is the research that develop on the risk of emergence and expansion of the Chikungunya virus and yellow fever and malaria from border, peri-urban areas and indigenous people in the country.

Hematozoa Transmitting Mosquitoes Laboratory (Lathema)

As featured in Lathema research, we have, in this year, the definition of Zika virus in the country, which left the experimental evaluation of vector competence for this virus, followed by the detection of naturally infected mosquitoes in Rio de Janeiro and, finally, demonstrating that the genus *Culex* of these locations does not transmit the virus, while the *Aedes* transmits with great skill.



Award-winning photo of the antenna of a male mosquito genus Uranotaenia.



Pathology Laboratory (LABPAT)

Leadership: Marcelo Pelajo Machado mpelajo@ioc.fiocruz.br

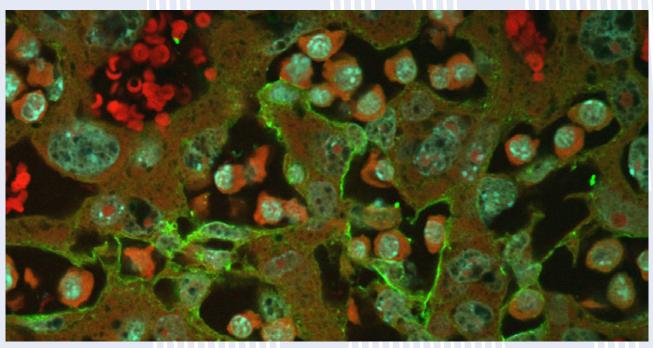
The laboratory operates in two lines of research: one on themselves the pathology of infectious and parasitic diseases and another on the lympho hematopoietic system morphobiology. At first, the experimental pathology on schistosomiasis mansoni (the lab maintains a laboratory biological cycle of Schistosoma mansoni, cepa BH, since 1984), abdominal angiostrongiliasis (the same does for Angiostrongylus costaricensis in rodents since 1994 Cotton hispidus) and flaviviruses (especially yellow fever and Zika). On Monday, are projects related to the physiology of normal and pathological hematopoiesis, especially under the prisms of the ontogeny of the lympho hematopoietic system and comparative hematopoiesis. The LABPAT is also responsible for curating the collection of yellow fever (CFA), which is institutionally recognized by Fiocruz and Depository of Genetic Heritage is faithful. This collection is composed of 498,000 human liver samples obtained from patients who came to death suspected of yellow fever between 1930 and 1970 and preserved in formalin with their respective paraffin blocks and histological slides. In addition to this collection, the

other two are under the Trusteeship of the LABPAT and are in the process of institutional recognition: (i) the collection of Pathological Anatomy section (CSAP), which gathers 854 anatomical parts and histological slides, you had its home in 1903, as a Museum of Pathology, and was built from the material reviewed by several researchers who passed by the IOC; and (ii) the collection of the Department of pathology (CDEPAT), that containing the experimental pathology material produced by LABPAT since 1984. when the departmental structure was created. In addition to the own lines, the LABPAT collaborates with other laboratories of the IOC and with groups inside and outside the Fiocruz, to the study of other diseases. Although the LABPAT is officially not a referral service, receives eventually demands to support diagnosis, especially human, in the sense that, sometimes, the existing infrastructure for research is useful for elucidation of etiological a particular disease. Part of this infrastructure, notably related to Photonic microscopy (confocal and superresolution), is managed by the lab while institutional technology platform.

Pathology Laboratory (LABPAT)

The laboratory participated in the publication of 11 scientific articles of varied themes in indexed journals. Among them, it is up to the article published in the Placenta, on the hematopoietic activity of placenta of mice in intermediate stage of gestation, and the other, published in PLoS One, on the kinetics of infection of chicken embryos infected with yellow fever vaccine virus, 17DD. In this line of research in arbovirose, the laboratory joined the research networks to confront public health emergency on the Zika virus, seeking, from different animal models, responses to the pathophysiology of ZIKV infection, in particular with regard to vertical transmission mechanisms. The training of human resources, the laboratory participated in the microscopy II LymphoRioMove, international course of lymphocyte motility for graduate students and organized by the laboratory of research on the thymus, in

partnership with the Toulouse Purpan University Hospital, France. Similarly, started a discipline on foundations of Photonic microscopy, also for graduate students. Undergraduate monographs were completed, undergraduate research guidelines and a doctoral thesis. Other levels follow guidelines in progress. With regard to LABPAT managed platforms, in the last weeks of the year was received and installed the LSM 710 confocal microscope, which happens to be the core of confocal microscopy platform RPT07A, which back then to take account of the scientific community in 2017. In addition, the laboratory has installed an automated scanning system prepared in blades, purchased with funds raised by the BNDES in the context of the project Maintain, which went into operation in order to scan material tumbled by nine Biological Collections participating in the project, including the collection of yellow fever.



Murine placenta maze (PNA-FITC, Evans blue, DAPI). Paul et al. Placenta 47, 2016.

Hospital Infection Research Laboratory (LAPIH)

Leadership: Marise Asensi marise@ioc.fiocruz.br

Hospital infections constitute a serious public health problem. Antimicrobial resistance among hospital pathogens has increased at alarming levels, both in the developed countries, as in development. The LAPIH acts as a Collaborating Center in network monitoring of Antimicrobial Resistance of ANVISA and general coordination of Public health laboratories/ SSC/Ministry of health. In this network, the LAPIH serves as a reference of the central public health laboratories and hospitals in the country for phenotypic and genotypic characterization of resistance genes in multidrug-resistant BGN and genotyping by PFGE method of bacteria involved in outbreaks. With this action of molecular diagnosis, we operate in the control of outbreaks of carbapenemases KPC-producing bacteria, NDM, OXA-48, SPM and OXA-23 circulating in several regions in the country.

In addition, it houses the collection of Cultures of bacteria of Nosocomial Origin (CCBH). This diverse and representative material of the country allows the development of research projects, with unpublished results, and serve as an indicator of the prevention and control of multidrug-resistant bacteria in the country. In this way, the LAPIH develops diagnostic studyrelated research, mechanisms of antimicrobial resistance and molecular epidemiology of bacterial species isolated from patients and hospital environments and water collection and community environments associated with the health units. Performs, also, epidemiological and clinical research for the prevention, diagnosis, treatment and control of healthcare-related infections in Brazil, besides developing kits for the diagnosis and detection of genes associated with resistance to carbapenems.

Hospital Infection Research Laboratory (LAPIH)

In research of characterization of resistance genes, we describe the presence of carbapenemase OXA-370 in Rio de Janeiro. This enzyme had been described in 2014 in an isolate in Rio Grande do Sul, and our article is the second account of this enzyme in the country. In another article, we describe the presence of simultaneously transporting samples, genes of the two most important epidemiological carbapenemases (KPC and NDM). In addition, we carry out the sequencing of the genome of different producing total

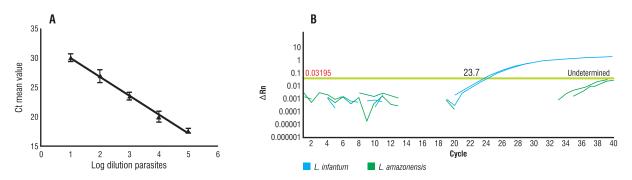
carbapenemases which led to the publication of three drafts of genome. This data allowed the development of several other studies which are being carried out. Through the funding of PDTIS and co-written with Bio-Manguinhos, we are finalizing the development of a real-time PCR for the detection of genes associated with resistance to carbapenems, which will be distributed to the LACENs, which will allow greater agility in the molecular diagnosis of carbapenemases in our country.

Leishmaniasis Research Laboratory (LPL)

Leadership: Renato Porrozzi de Almeida porrozzi@ioc.fiocruz

The complexity ecoepidemiologic of leishmaniasis is reflected in the variety of species of animals and insects vector tanks involved in the transmission cycle, as well as in clinical pleomorphism in humans and diversity of responses to treatment. The disease comes in three main clinical forms: (i) visceral leishmaniasis (VL), which is lethal when not treated, (ii) cutaneous leishmaniasis and Mucocutaneous leishmaniasis, which causes lesions mutilantes. The severity of clinical manifestations in immunocompetent people and the response to treatment depend, among other factors, the species infecting parasite. There are, for example, species and strains responsible for self-resolutive infections that can present themselves in sympatry with more virulent variants, which represents a challenge for clinical diagnosis and treatment. It is likely that the geno-and phenotypic variability of the parasite promotes its survival in the various ecological systems where is described and determine the distribution of observed clinical forms of the disease. Still no safe and efficient vaccine against any form of human leishmaniasis and

the spectrum and the efficiency of drugs are limited. One of the reasons that hamper progress in these areas is precisely the diversity of the parasite itself. The research conducted in the LPL seek understanding the role of the parasite as a causative agent of leishmaniasis, taxonomic and epidemiological aspects, biochemical and molecular as well top the immunopathologic developments. The characterization of parasites is critical step to achieving the objectives of the projects proposed by the laboratory. Thus, we discuss the taxonomic identification, we investigated molecular and biochemical characteristics of parasites and its relationship with the clinical manifestations of the disease and explored molecules which have therapeutic potential. These activities are completely in line with the Mission of the Leishmania collection of the IOC/national reference laboratory typing Leishmania (CLIOC/LRNTL), that support research conducted at the LPL and several other labs at Fiocruz and national and international institutions.



Specific amplification of Leishmania infantum using a Ampliprepobas strategy against a target of kDNA.

Leishmaniasis Research Laboratory (LPL)

One of the goals of the LPL, we propose to identify targets for diagnosis of the different species of Leishmania and develop tools for detecting and identifying particular species of these parasites. In this context, we have developed a tool for quantitative PCR (qPCR) for specific detection of Leishmania. infantum and determination of parasitic load in natural or experimentally infected animals. This study was motivated by the fact that, although several papers report the use of PCR for specific detection of L. infantum in silico analysis of the sequences reported showed that there were cross-amplification of other species of Leishmania. So, we developed a qPCR assay, using Taq-Man on experimentally infected BALB/c, and validate its application using tissues of naturally infected dogs, being the last major urban reservoirs of L. infantum. For this test we have designed a set of primers and probe for the amplification of a region of kDNA and evaluate the efficiency and sensitivity of the qPCR using serial dilutions of L. infantum DNA extracted from a known number of parasites. The default amplification curve indicated a linear correlation between the log of the number of parasites detected and the value of Ct (R2 = 0.9963) and

106% efficiency. Based on the calibration curve, the test has reached the limit of detection of 0.01 pg of DNA of the parasite. The gPCR was evaluated in samples of liver and spleen of experimentally infected BALB/c mice (n = 9), displaying 100% sensitivity; the target was detected in both tissues with variation cross test coefficients of 0.04-0.06 between biological samples. Also assessed DNA samples from naturally infected dogs liver previously characterized as positive for L. infantum. We observed specific amplification of *L. infantum* asymptomatic animals (n = 7) and symptomatic (n = 7) with coefficients of variation between 0.05-0.11 and 100% of sensitivity. In addition, the test detected parasitic load 7.2 times higher in symptomatic animals than in asymptomatic (p < 0.0001). There was no cross-amplification with mouse DNA or dog not with DNA of Leishmania braziliensis, Leishmania donovani, Leishmania major, Leishmania tropica or Trypanosoma cruzi. Thus, the tool developed by the group can be valuable for the specific detection of *L. infantum* in sympatric transmission of parasites that cause visceral leishmaniasis.

Malaria Research Laboratory (LPM)

Leadership: Claudio Tadeu Daniel Ribeiro ribeiro@ioc.fiocruz.br

(i) Mechanisms active in vascular dysfunction in experimental cerebral malaria, involving vasoconstriction, ischemic and hypoxia, nitric oxide deficiency, deregulation of arachidonic acid metabolism and potential interventions based on these targets as adjunctive therapy for cerebral malaria and new drugs against blood and forms against hypnozoites; (ii) diagnosis of malaria infection and the chemoresistance of the Plasmodia and gene diversity of malaria parasites; (iii) involvement of apoptosis in severe anemia erythrocyte experimental malaria and antimalarial effect and apoptosis inhibitors in the course of this anemia; (iv) importance of recruitment and differentiation of cells

of the innate immune system in experimental malaria and the formation of extracellular neutrophil networks (NETs) by neutrophils of patients with malaria; (v) evaluation of gene polymorphism and immunogenic potential of molecules of *Plasmodium falciparum* and *Plasmodium vivax* vaccine and potentially genetic control of specific immune response in individuals exposed to naturally be necessary concomitants of infection; (vi) preclinical evaluation of antigens of *P. falciparum* and *P. vivax* in Neotropical primates *Saimiri sciureus* and *Aotus infulatus*; (vii) evaluation of the interaction of cognitive systems and neural immune in experimental murine model.

Malaria Research Laboratory (LPM)

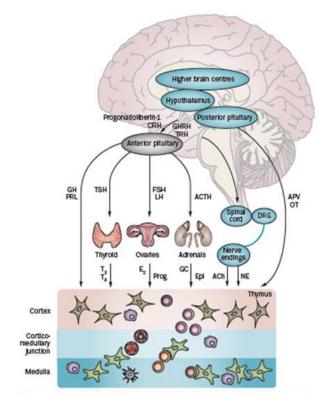
We can cite, as featured in the research lab, the discovery that mutations in portions of a gene of P. falciparum that encodes Kelch domains (K13) are the main determinant of chemoresistance to artemisinin, which provides opportunity to monitor such resistance on a global scale (n. Engl. J. Med. 2016 Jun 23; 374: 2453-64. DOI: 10.1056/NEJMoa1513137). In this work, for the first time in the context of a consortium of the international network of Pasteur Institutes and his associates examined the polymorphism of the K13 in samples collected in 14,037 59 countries where malaria is endemic. Another important highlight occurred in collaboration with researchers of the Faculty of Tropical Medicine Heitor Vieira Dourado fro the Amazon,

where we showed, for the first time in Latin America, artesunate-amodiaquine combination, traditionally used for the treatment of falciparum malaria, is safe and effective therapeutic alternative for malaria vivax ((Clin. Infect. Dis. 2017 Jan 15; 64: 166-174. DOI: 10.1093/cid/ ciw706. EPUB 20 Oct 2016). Finally, also deserves to be highlighted that the Chief of the laboratory was awarded the Medal of the Société Française de Pathologie Exotique during the making of the XIX International Congress for Tropical Medicine and Malaria, in Australia, 20 September 2016, and with the title of *Doutor* Honoris Causa of the Universidade Nova de Lisboa, Portugal, on 29 November 2016.

Thymus Research Laboratory (LPT)

Leadership: Vinicius Cotta vca@ioc.fiocruz.br

Scientific research projects and technological development of the LPT feature as central objective, studying the molecular mechanisms of cellular interaction associated with tissue pathological response niches. In these studies, we address the interactions that result in events of differentiation and cell migration in tissue niches, particularly in immune, endocrine systems, neural and muscular. The interactions include locally produced factors such as cytokines, growth factors, hormones, neuropeptides, extracellular matrix proteins, in addition to pathogens that interact with these tissue sites. Applying broad set of technological approaches, we study the pathological mechanisms and therapeutic intervention possibilities associated with autoimmune inflammatory diseases, neuromuscular, lymphoproliferative, neurodegenerative and psychiatric and even by *T. cruzi* infections, the Zika virus and retrovirus HIV-1 and HTLV-1. These studies seek to contribute to the mecanical actions understanding involved in physiological and pathological processes associated with diseases, in addition to point to ways that allow effective therapeutic interventions.



Immunoendocrine interactions in the thymus.

Thymus Research Laboratory (LPT)

The physiology of the thymus, an organ in which occurs the differentiation of T cells, can be controlled by hormones through endocrine and paracrine pathways and this hormonal control is discussed in one of the research lines of the LPT. The set of this research line was the highlight of the scientific research of the laboratory presented in article Hormonal control of T-cell development in health and disease (Savino W, Mendes-da-Cruz DA, Lepletier A, Dardenne M. Nat. Ver. Endocrinol. 2016 Feb; 12: 77-89. DOI: 10.1038/nrendo.2015.168). The article presents a set of data from our laboratory, and other groups, showing, for example, that growth hormone and prolactin secreted by adenopituitary induce the proliferation and migration of thymocytes. On the other hand,

glicocorticoides secreted by the adrenals induce the death of these cells. in addition hypothalamic hormones act on adeno-pituitary and this, for its time, secretes hormones that stimulate other target organs to secrete other hormones that affect various aspects of the physiology of the thymus, as described above, and shown in the following figure (Figure 2 in the article). Such circuit features the calls neuroimmunoendocrine interactions in the thymus. Finally, it is worth pointing out that the invitation for the preparation of review article in the journal of international impact, as the Nature Reviews in Endocrinology, highlights the recognition by the scientific community, the quality of the work carried out in the LPT in this line of research.

Simulídeos and Onchocerciasis and Sympatric Infections Laboratory: Mansonelliasis and Malaria (LSO)

Leadership: Marilza Maia Herzog mherzog@ioc.fiocruz.br

Promote and carry out actions related to the Simulium, as well as the damages caused and the adult for they transmitted, developing comprehensive and specific research, in addition to the provision of reference service, collection management and training of human resources, with a focus to the medical and veterinary importance of Simulium, considering the environmental and water monitoring, epidemiological surveillance, biodiversity the bio-ecology and the mapping of the species. Above all, develop interdisciplinary knowledge about the Simulium through projects, published works and training programs and professional training, as tools of action, (i) the research on molecular biology of Simulium vectors and of etiological agents; (ii) genetic characterization of Simulium vectors and of etiological agents; (iii) onchocerciasis and mansonelliasis clinical, genetic, immunological aspects, parasitological and vectoring; (iv) control, biology and

ecology of Simulium and associated fauna; (v) epidemiology of the vectors and the etiological agents; (vi) maintenance and development of parasitological diagnostic tools, molecular and immunologic diseases linked to Simulium; (vii) taxonomy, morphology and Systematics of Simuliidae. In addition, the LSO realizes actions of scientific dissemination, through scientific and technical publications, organisation of and participation in scientific events and training of human resources, through the guidance of professionals and students in high school, graduate and PhD. Carries out aid to educational institutions, research and promotion as a teacher, conductor, evaluator and reviewer, meets the demands to participate in technical Chambers and coordination of laboratory interest, inter-ministerial and institutional, and finally helps the SUS institutions, basic care and diagnosis.

Simulídeos and Onchocerciasis and Sympatric Infections Laboratory: Mansonelliasis and Malaria (LSO)

(i) active participation in activities to promote knowledge about the Simulium and the diseases they are related, whether as organizers of courses or participating as panelists or speakers of disciplines, teaching material production and dissemination of knowledge through participation in events; (ii) two PhD theses defended, on the theme of malaria and leishmaniasis/other themes of action strategies in the control of Simulium; (iii) two projects developed in the LSO received awards in different events.



Research activities carried out by the laboratory of Simulium and Onchocerciasis & Sympatric Infections: Mansonelliasis and Malaria.

Laboratory of Taxonomy, Biochemistry and Bioprospecting of Fungi (LTBBF)

Leadership: Aura Maria Lage de Moraes aurea@ioc.fiocruz.br

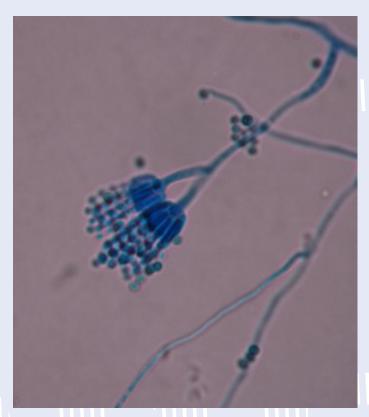
The laboratory of Mycology and the collection of Cultures of Fungi of the IOC were created in 1922. under the leadership of Olympio da Fonseca, from the determination of Prof. Carlos Chagas, then Director of the IOC, due to the big world activity in the field of research on Mycology. Today, with new name, Taxonomy, biochemistry laboratory and bioprospecting of Fungi of the Instituto Oswaldo Cruz keeps its vocation to the taxonomy and different studies on the etiological agents of human mycoses. The lab has always proposed to work with lines of research involving taxonomy, biodiversity and different studies etiological agents of human mycoses, seeking the formation of human resources for the area, as well as new scientific contributions. On the lines of existing research, the molecular, biochemical and morphological characterization of filamentous fungi to identify markers that help the classical taxonomy, potential targets and Diagnostics chemotherapy and the prospect of new fungal bioinsecticides. In addition, studies on fungal air line seek discussion and revision

of the current legislation, as well as fungi that can be used as biomarkers of interior air quality. The researchers also aim the establishment of experimental model for study of the virulence of emerging fungi. In Brazil, there are few research groups dedicated to Mycology. Most of the researchers is concentrated in food technology-related studies and the biological control and diagnosis of human and animal. The lab remains, to this day, and is responsible for curating the collection of cultures of Fungi of the IOC, faithful depository by the genetic heritage management Council of the Ministry of the environment, and develops projects for maintenance, expansion and modernization of its collection, in addition to the provision of service to the scientific and academic communities, public and private, with identification, assignment and deposit of strains of filamentous fungi, as well as human resources training in the identification and preservation of filamentous fungi.

Laboratory of Taxonomy, Biochemistry and Bio-prospecting of Fungi (LTBBF)

We emphasize, in the line of morphological, biochemical and molecular characterization of filamentous fungi, the project studied isolates of Purpureocillium using animal model for lilacinum better understanding of the pathogenic mechanisms of this fungus. The work was awarded at the Congress of the American Society for Microbiology in may 2015, and is the subject of the doctoral thesis by the postgraduate course in Parasitic Biology of the IOC. The Group's experience with this species resulted in the publication of the chapter Paecilomyces: mycotoxin production and human infection no livro Molecular biology of food and water borne mycotoxigenic and mycotic fungi, book published by CRC Press, United States of America. The line closed, air-conditioned environments: epidemiology and assessment of biological hazards, stands out for the new approach, taking into consideration the microbiological analysis of the subject and not the physical and technical aspects, in addition to the proposal of new techniques of evaluation of the interior air, and will guide studies for the improvement of existing regulation in Brazil. The projects in this line have been successively awarded by funding agencies, in addition to providing laboratory partnerships with the different public and private agencies, both for the analysis of environments, as for discussion related to the worker's health, protection, maintenance of collections etc. Due to the production of large amount and diversity of secondary metabolites, fungi are considered valuable source of biological activities and pharmacological products. So, the lab's studies related to new bioactive substances, such as those already underway, with derivatives of citrinin and their biological activities, and aureonitol, as an inhibitor of Influenza. Another line of research aims at (i) biochemical and functional characterization of molecules involved with crucial processes of pathophysiology, such

as microbial enzymes proteases and protein phosphatases and (ii) to study the action of different compounds with antimicrobial potential in biology and virulence of fungal pathogens. Our study aims to identify potential targets for the future development of new drugs to be used in the treatment of neglected diseases, including acanthosis and feo-hifomicose.



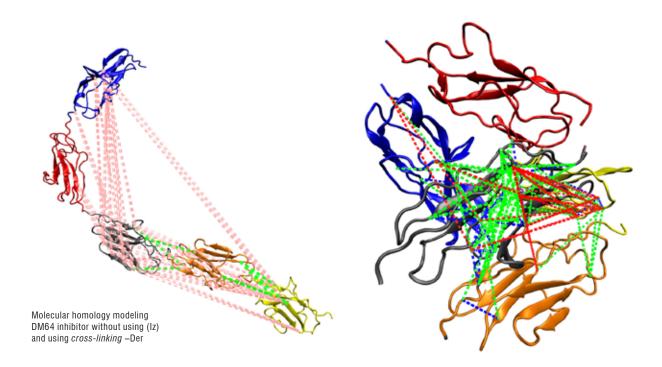
Penicillium waksmanii 100X.

Toxinologia Laboratory (LATOX)

Leadership: Jonas Enrique Perales Aguilar jonasperales@gmail.com

Using biochemical techniques, fundamentally based on Proteomics mass spectrometry of high resolution in the study of different important pathologies, such as cancer, Chagas disease, dengue fever, abdominal angiostrongiliasis, snake poisoning, among others. The scientific-methodological point of view, the last years have brought an important paradigm shift for the Group: in keeping with the world trend, the CATALASE migrated successfully, the emphasis in gel-based Proteomics (protein-centric) for shotgun Proteomics (peptide-centric), most determined and sensitive analytical methodology, current state of the art in the area. The implementation of new analytical approach

was made possible through the acquisition, in 2012, the first liquid nanocromatography system coupled to a mass spectrometer of high resolution with nanospray source (LTQ Orbitrap nESI-nLC-XL), whose purchase was financed jointly and severally, by Fiocruz and by the National Institute of science and technology in toxins and, more recently, a Q-Exactive Plus, also bound to a nanocromatograph. In addition to the classic, LATOX and proteomics has been working on the implementation of structural biology techniques based on mass spectrometry, using the techniques of cross-linking-mass spectrometry (MS) and, more recently, of hydrogen/deuterium exchange-MS.



Toxinologia Laboratory (LATOX)

Initially, we would like to highlight that, in a special issue of the Journal of Proteomics to Brazilian researchers (Brazilian proteomics), our group published four papers, being the group that more works published in this special issue for Brazil (vol. January / 2017 One of the great highlights of our lab was the technical implementation of high resolution mass spectrometry in structural analysis of proteins and their complexes. The technique of crosslinking-MS was used, initially, using as models and DM64 DM43, natural inhibitors of miotoxic and hemorrhagic toxins of botropic snakes, respectively. We were able to determine the regions of the inhibitors involved in interaction with their toxins (third and fifth DM64 and third domain of DM43). The data obtained in these experiments allowed, also, enhance the molecular structures obtained exclusively by molecular modeling and docking, producing structures notably more compatible with its function (Figure). We can also clone and express DM64 with biological activity in Pichia pastoris. We develop new proteomic approach for characterization of venom of Bothrops jararaca. This work revealed that the proteome and the

peptidome of B. jararaca are much more diverse than had previously been reported in the literature. Proteins were detected in that never before poison. In addition, this is the most complete peptidome of snake venom described so far. We use an approach known as a connectivity map for blind scan for biological activities present in the peptidome of the poison of B. jararaca and identify various activities with potential therapeutic or diagnostic use. Already confirmed the activity of anti-interference peptidoma in Chiang forms of *Trypanosoma cruzi* through in vitro assays. Our group, in collaboration with the laboratory of Immunopharmacology, using quantitative Proteomics techniques, demonstrated the involvement of multiple mechanisms involved in Platelet Activation and inflammatory response in infection with dengue, but also of processes not previously assigned to platelets during this infection, including the processing and presentation of Antigen, proteasome activity and expression of histones and its participation in the activation of platelets. Our study represents the first in-depth characterization of the proteome of platelets on dengue.

Laboratory for Toxoplasmosis (LabTOXO)

Leadership: Maria Regina Reis Amendoeira amendoei@ioc.fiocruz.br

The LabTOXO has, as a guiding principle, the application of knowledge acquired in actions to control the protozoosis, making feedback with the population studied. Research lines: (1) epidemiology and immunoprotection of immunodiagnostic infection by Toxoplasma gondii; (2) epidemiology of protozoosis of interest in public health; (3) study of membrane receptors and its participation in the mechanism of infection of Protozoan. (1i) Toxoplasmal Eye infection Assessment of recurrence patterns of eye infection and associated risk factors and analysis of patients with Immunogenetics ocular recurrence [national infectious diseases Institute Evandro Chagas (INI)/ Fiocruz and Universidade do Estado do Rio de Janeiro]: (ii) toxoplasmosis in domestic/wild animals (laboratory and epidemiological study of t. gondii infection in wild and domestic animals of Nhecolândia. Mato Grosso (EMBRAPA/Pantanal); study the use of filter paper and collect the blood of cats to diagnosis, by MAT, of *T. aondii* infection (Université de Limoges): research of Ac against *T. gondii* in cats of Rio de Janeiro and in farm animals in the region of the Triângulo Mineiro, Minas Gerais; (iii) congenital toxoplasmosis (Toxoplasmosis knowledge assessment and implementation of primary prevention measures in the programmes of public health prenatal of Niterói, Rio de Janeiro). (2) Studies on Chagas disease. Patients accompanied in the INI, with isolation and genotyping of *Trypanosoma cruzi* (Tcl). Analysis and elaboration of 11 volumes on the themes of T. cruzi genotype I, T. cruzi genotypes III and IV and trypanosome parasites of bats (epidemiological importance for Chagas disease). Epidemiological, biological and genetic studies of Balantidium coli. (3i) natural and synthetic products (like naphthoguinones and triazoles) against the feasibility of protozoa; (ii) antimicrobial peptides against the feasibility of protozoa: (iii) operating mechanism of P2 receptors. featured the P2X7 receptor; (iv) natural and synthetic products that can play antagonistic action against purinergic receptors (receptor P2X7); (v) participation of purinergic receptor in the mechanism of infection of protozoa. Membrane receptors, such as the purinergic, the transitional potential enabled (TRPs), have stood out for their involvement in the mechanism of infection of microorganisms, namely, namely, meet the functioning, the Pharmacology and the action of the receptors in the Protozoan cycle enables the discovery of new drugs to control/eradication of diseases like toxoplasmosis and Chagas disease.

Laboratory for Toxoplasmosis (LabTOXO)

(i) In collaboration with Dr. M.-Laure Dardé and Paula Borba, of the Institute of Epidemiology and **Tropical Neurology and Neurological University** of Limoges, France, studied for the first time, the effectiveness of using filter paper as a means of transportation and collecting blood of cats for diagnosis of *T. gondii* infection, using the technique of MAT, confirming that this method of storage is reliable alternative. This project has generated a publication accepted international journal Parasites and Vectors; (ii) for the first time, was genotyped B. coli isolated from feces of pigs and non-human primates from Brazil. This study was a collaboration of Dr. Francisco p. Fat, Department of Parasitology at the Complutense University of Madrid, Spain, generating the doctoral thesis of Camilla da Silva Barbosa and an article that is being subjected to an international magazine; (iii) By means of a

> collaborative project between the IOC and the INI, evidenced, in patients with Chagas disease accompanied by this Institute, one of the genotypes of *T. cruzi* (Tcl) less frequent in **Brazil. This study** generated an article

accepted for publication by the journal of the Brazilian Society of Tropical Medicine; (iv) Studying the action of naphthoquinones about the viability of the *T. cruzi*, discovered three naphthoquinones with excellent therapeutic index to continue to in vivo studies, which gave rise to a publication in the New Journal of Chemistry; (v) the temporizine-1 was built by a peptide fusion of amphibian with also for vesicles (used with antifungal). The new peptide showed excellent action against the viability of the T. cruzi, changing the mitochondria of this Protozoan. This study resulted in the article published in PLoS One; (vi) Between the research on purinergic receptors include the study of the use of the pore opening P2X7 receptor associated as a tool of drug entry with hydrophobic properties that would not be used therapeutically, in the light of that limitation, as methylene blue (AM). We note that the opening of the poro made it required lowest concentration and incubation time of AM front its use without activating the pore is associated with the P2X7 receptor. This study is published in the JOBB (DOI: 10.1007/s10863-016-9668-6); (vii) we detected the action of a natural product with action in vitro and in vivo anti-inflammatory based on inhibition of the P2X7 receptor that led to a national patent.



Folder to the distribution in the Pantanal population and students who attend the Nhecolândia, Mato Grosso.

Laboratory of Cellular Ultrastructure (LUC)

Leadership: Mirian Claudia de Souza Pereira mirian@ioc.fiocruz.br

LUC develops studies on cellular and molecular biology of infectious agents, with emphasis on Chagas disease and leishmaniasis. Our research focus on the biological events involved in the early stages of parasite interaction-target cell, including cell recognition and invasion mechanisms, as well as structural changes and modulation of signalling pathways involved in the regulation of cardiac hypertrophy and fibrosis. A combination of biochemical, molecular and cellular approaches is employed to identify signalling pathways used as a strategy of invasion, and biological processes that disregulate the cell homeostasis during the intracellular parasite development. In this way, we intend to contribute with relevant information for understanding the pathogenesis of some infectious diseases. Yet, whereas chemotherapy against Chagas disease comes down the developed compounds in the 60 that feature variable efficacy against *Trypanosoma* cruzi and the persistence of the parasite is implicated in the pathogenesis of Chagas disease, we invest in

search of tripanocidas compounds with potential therapeutic application. We use in vitro and in vivo approaches to screening of prototypes the drugs with activity against t. cruzi, focusing on the development of therapeutic compounds based on molecular targets of parasites, including C14α-demetilase lanosterol (CYP51), essential enzyme in the biosynthesis of ergosterol of the parasite. LUC also develops research on possible changes in protein expression as the determining factor of resistance to treatment with benznidazole (BZ) in the dog, through comparative study on re-isolated of *T. cruzi* sensitive and resistant to this drug. Dissection of protein expression in these re-isolated of t. cruzi from dog in the chronic phase of the disease, with the purpose of exposing likely (eis) protein (s) that had (had) its expression changed by the influence of various factors, we will certainly contribute with significant share in understanding the molecular bases of the complex phenomenon of drug resistance observed in this parasite.

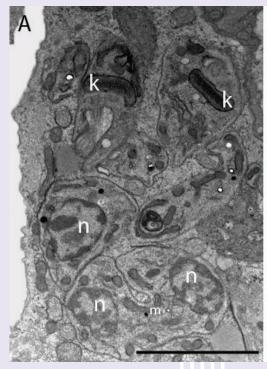
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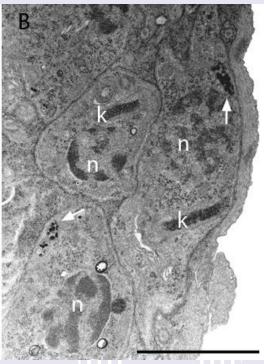
HIGHLIGHTS

Laboratory of Cellular Ultrastructure (LUC)

The projects developed with focus on biology of parasite-host cell interactions have contributed to the understanding of the changes in the blood-retinal barrier (BHR) induced in experimental infection by Toxoplasma gondii. We demonstrate that the damage evidenced in ocular toxoplasmosis can be related to dysfunction of the BHR by amendment of the integrity of joints palatalized (tight junctions). Reduction of electric resistance transepitelial and loss of cell-cell contacts demonstrate the commitment of the retinal pigmented epithelium (EPR), suggesting that the retinopathy is due to access of parasites and inflammatory cells immunologically privileged in this place. In T. cruzi-cardiac myocytes, we highlight that the spatial distribution of receivers (TGFB RII) of the signaling pathway of transforming growth factor beta (TGFB) and co-location with its costemeres of vinculin in cell surface are essential for activation of the signaling cascade of Smads. We describe the differential role of TGFB in infection with *T. cruzi* from different

host cells and the participation of alternative pathways of TGFβ in inducing & of cardiac fibrosis. Still, we advance in the analysis of screening of compounds with activity to assess their tripanocidal. We demonstrate the activity of chemical structures containing hidroxâmico acid, carbonic anhydrase inhibitor against T. cruzi and assess their tripanocidal effect and mechanism of action mediated by the interaction of 4-aminoquinoline and heme. We highlight the import of heme pathway as important chemotherapy strategy, due to the absence of enzymes that promote its biosynthesis in the *T. cruzi*. We demonstrate that the Association quinoline-heme potentiates the activity to assess their tripanocidal in combined therapies and intracellular structures changes essential for homeostasis of *T. cruzi*. The description of this mechanism directs potentially the rational development of drugs and search for new cellular targets that may interfere in the heme metabolism.





Ultrastructure of cardiomiocytes infected with *Trypanosoma cruzi* (the) and treated with quinoline-heme (B). .

Comparative and Environmental Virology Laboratory (LVCA)

Leadership: Marize Pereira Miagostovich marizepm@ioc.fiocruz.br

In 2016, the LVCA fulfilled its mission to generate scientific knowledge, contributing with 12 original publications and keeping its average annual publication for the last six years (13.7 publications per year). The lab, which acts as a Regional reference laboratory of Rotavirosos (LRRR), passed on to the regional laboratory proficiency of Latin America by the PAHO/WHO, with 100% success rate in tests conducted. LRRR also modernized the screening tests for diagnosis of rotavirus and norovirus, the establishment of quantitative PCR reaction in real time. In relation to human resources training, two doctoral theses were defended in the area of food and environmental Virology. During this period, the activities in the area of food Virology gave grants to

the national program support LVCA strengthening of health surveillance Actions in ports, airports and borders, the Anvisa, which is establishing the diagnosis of NoV from water and food in LACENs that are on the route of the cruise season (Amazonas, Bahia, Ceará, Pará, Pernambuco, Rio de Janeiro, Santa Catarina and São Paulo). The teaching activities included participation of servers in different disciplines technical courses and graduate programs of the IOC. The LVCA offered the discipline of Environmental Virology and food and organized the discipline of dynamics of Viral Gastroenteritis in the graduate program in science to the development of the University of Cape Verde, funded by the Gulbenkian Foundation, Lisbon.

Comparative and Environmental Virology Laboratory (LVCA)

The researcher José Paulo Gagliardi Leite, LRRR, was elected a member of the Advisory Committee of Microbiology & Parasitology of CNPq. That same year, the Group of **Environmental Virology participated in the III Latin American Symposium of Environmental** Virology, continuing the I Symposium, held in 2010, in Rio de Janeiro, and organized by the LVCA. In March, he organized the course of Virological Quantitative risk analysis, taught by professors Doctors. Jack Snchijven and Martijn Bowknegt, of the National Institute for Public

Health and the Environment, the Netherlands, held at Fiocruz. The course was attended by 17 professionals, including researchers, technologists and graduate students from different national and international institutions, and aimed to expose the principles of modeling and risk assessment of viral infections for contact with food and water, as well as providing content for the implementation of the process in practice. This course represented important progress for the research in the area of environmental Virology performed in the lab.

Molecular Virology Laboratory (LVM)

Leadership: Christian Maurice Gabriel Niel niel@ioc.fiocruz.br

The survey fits the URBI called study of hepatitis Virus B, C and D with emphasis on Phylogeny, hepatocellular carcinoma and resistance to antiviral drugs, included in the purpose of Fiocruz: Generating knowledge About Viruses and Rickettsial infections. This line of research is of utmost importance when we know that the different types of viral hepatitis reach one-third of the world's population and that most of the carriers are not aware of its state. The infection by hepatitis viruses B and C can lead to chronic hepatitis, liver cirrhosis or even, in certain cases, to hepatocellular carcinoma. There are currently two main lines of research in the lab: (i) molecular epidemiology of hepatitis B virus in Latin America. Three genotypes of the hepatitis B virus, called A, D and F, circulating in Latin America.

Our laboratory studies the prevalence, geographic distribution, phylogeny and phylogeography of the viral strains of the three genotypes circulating in Brazil; (ii) studies of the molecular mechanisms that lead to the development of cirrhosis and hepatocellular carcinoma after infection by hepatitis viruses B and C. Most cases of hepatocellular carcinoma associated with cirrhosis which occurred after chronic infection by hepatitis B or c. certain genotypes and mutations in these viruses are associated with increased risk of developing this cancer. We are studying the hypermethylation promoter region of human genes as epigenetic mechanism of gene silencing and its association with the development of hepatocellular carcinoma.

Molecular Virology Laboratory (LVM)

(i) molecular epidemiology of hepatitis B virus in Brazil and Africa. Identify the high prevalence (15.4%) of current or prior infection by the hepatitis B virus in a group of 522 men who have sex with men, thus demonstrating the importance of the improvement of public health strategies in this population. Also identified cases of hepatitis B hides in patients with HIV and tuberculosis patients, indicating that the hepatitis B diagnosis in these patients must include, in addition to serological markers, the detection of viral DNA. In addition, we investigate the hepatitis B virus infection in 1,323 individuals resident in the Republic of Ghana, Africa. Identify the high prevalence of hepatitis B (8%) and exclusive circulation and

genotype on these individuals; (ii) Studies of the influence of genetic factors in the progression of liver disease. We demonstrate that the single nucleotide polymorphism Tnfalpha-308 G/A is factor associated with the chronicity of HBV infection and, therefore, may have prognostic significance in hepatitis b. Additionally, our studies have shown that hypermethylation in the promoters of human genes and RASSF1A DOK1 is associated with the progression of liver disease and liver cancer development in patients. Therefore, the presence of hypermethylation in these genes could be used as a biomarker for early diagnosis of this type of cancer.

Respiratory Virus Laboratory (LVRS)

Leadership: Marilda Agudo Mendonça Teixeira de Siqueira mmsiq@ioc.fiocruz.br

The LVRS performs research, technological development, innovation and training in topics related to the biology of respiratory viruses, measles and rubella. (1) Influenza. (i) Epidemiology, evolution and phylogeny studies in different Brazilian regions and epidemiological aspects of Influenza virus evolution, aiming to rebuild the phylodynamic viral patterns, understanding the role of Brazil in the dynamics of global dissemination of these viruses and to check the consistency between the strains included in the vaccine and those circulating in the country. A doctoral thesis with results of this study won the incentive Award in science and technology to the SUS: (ii) next generation sequencing (NGS). Pioneered in Brazil, studied the full genome of the Influenza A/H3, featuring internal genes and demonstrating the presence of what species. We detected a variant of Influenza A (H1N2) v, with possible pandemic potential; (iii) Analysis of variants of the Influenza A (H1N1) pdm09 resistant to antiviral oseltamivir (OST). In 2016, by means of a multicenter study, we identified variants resistant to OST in Brazil and we

have detected the presence of permissive mutations found in other countries; (iv) Influenza infection in immunocompromised patients through cooperation with the National Cancer Institute and the Centers for Disease Control and Prevention (CDC), studying the clinical evolution and viral Influenza A (H1N1) pdm09 in patients with cancer and the biomarkers; (v) the Immunopathogenesis and immune modulation. The study of immunopathology in murine model of Influenza infection was developed in cooperation with the Federal University of Minas Gerais. This study won the young scientist Award of the Foundation Mérieux (Lvon, France): (ii) measles and rubella. Measles was considered eliminated from the Americas in 2016. Researches; (a) in collaboration with National Institute of Microbiology, Canada, we initiated a study of molecular epidemiology to identify viral sublines and present the results in meetings of the WHO and the International Expert Committee, for verification of elimination of measles in Brazil: (b) evaluation studies of MMR vaccine with Bio-Manquinhos.

Respiratory Virus Laboratory (LVRS)

(i) As national reference laboratory of Ministry of health and who's regional measles and rubella, participate actively, since 1991, the Measles Elimination Plan of Brazil and the Americas. In 2016, the Brazil and the Americas received the certificate of elimination of measles; (ii) Young Scientist Award of the Foundation Mérieux, in

network GABRIEL, to Cristiana Couto Garcia; (iii) honorable mention award to encourage science and technology of the SUS, to Paola Cristina Resende; (iv) identification of variant strain of Influenza A (H1N2) v derived from pigs infecting a human derived.

Bacterial Zoonosis Laboratory (LABZ00)

Leadership: Deyse Christina Vallim da Silva vallim@ioc.fiocruz.br

The LABZOO is dedicated to understanding the mechanisms associated with the bacterial diseases with zoonotic characteristics, with emphasis on those related to the genus Campylobacter spp., Leptospira spp., Listeria spp. and Yersinia spp. studies have epidemiological character, since bacterial strains are isolated from clinical specimens (humans and animals) and environment and food samples. Identification and characterization of these strains are made using phenotypic and genotypic methods in order to add data on the movement of such pathogens in Brazil and in other countries. As LABZOO research lines are: (i) the elucidation of the factors of virulence of these bacterial groups, using for this purpose, methodologies that allow the identification of genes associated with virulence and survival in certain environmental niches; (ii) the monitoring of

antimicrobial resistance of these pathogens routinely used in the treatment of infectious processes, in order to make a significant contribution to the better management of patients; (iii) characterization of strains deposited in collections through genomics and proteomics methods. Another very relevant focus on research carried out by LABZOO refers to the search for alternative methods faster and sensitive in the diagnosis of illnesses associated with these bacterial genera. It is important to mention that the different approaches of the studies carried out in the LABZOO aim to reflect not only long-term benefits for the population, but also the generation of trained human resources, through the training of laboratory technicians, undergraduate and postgraduate students and in the improvement of professionals from other institutions.

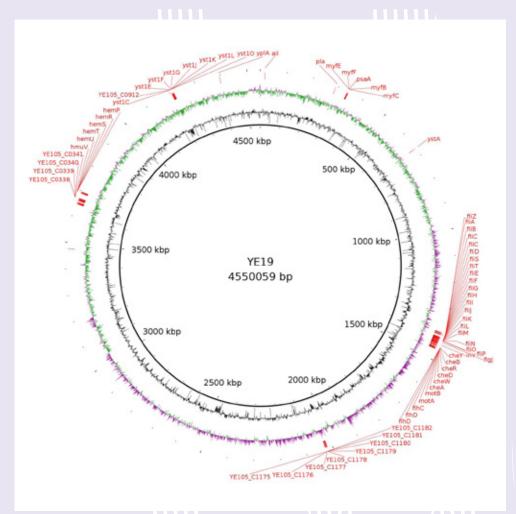
2016

HIGHLIGHTS

Bacterial Zoonosis Laboratory (LABZOO)

The lab expanded its expertise to the fields of genomics and proteomics, in addition to developing its research lines related to epidemiology, virulence and diagnosis of zoonotic bacterial infections. A study using multilocus sequence typing techniques (MLST), next generation sequencing (NGS) and filteraided sample preparation (FASP), respectively, is being developed as part of a PhD project with samples of Yersinia enterocolitica 0:3 and had, as preliminary findings, the determination of two new sequence type (ST) and the characterization of virulence genes and 1,400 103 proteins being analyzed as to the functions performed for

elucidation of the pathogenesis of yersiniosis. It is worth noting the collaborations with research groups Work Magalhães Research Center (Fiocruz-Pernambuco), the Federal University of Viçosa, Fluminense Federal University, Federal University of Rio de Janeiro and the Federal University of Bahia. These partnerships have resulted in published scientific articles throughout the year, addressing the presence of zoonotic pathogens bacteria in samples of foods, animals and the environment, in addition to the molecular characterization of clinical importance species isolated from different backgrounds in the country.



Analysis of the presence of virulence genes of the Y enterocolítica 0:3 YE19 strain through next generation sequencing (NGS).

Interdisciplinary Medical Research Laboratory (LIPMed)

Leadership: Alda Maria da Cruz alda@ioc.fiocruz.br

The LIPMed was created with the Union of three research groups and presents management practices based on a horizontal model of sharing of responsibilities. Our mission is to investigate the biological and molecular mechanisms of pathogenic processes, particularly those caused by infectious agents, in a systemic and multidisciplinary perspective. Our work is focused on two areas that integrate scientific and technological research: (i) the analysis of the biological processes-and neuroimmunoendocrine involved in molecular epidemiology and physiopathogenic mechanisms generated by infectious agents. Currently are investigated the following diseases: leishmaniasis and visceral, Chagas disease, sexually transmitted diseases, coinfections with HIV, intestinal parasitosis. Sporotrichosis and, more recently. Arboviruses; (ii) the technological axis for the development of new vaccine strategies, with a focus on leishmaniasis caused by Leishmania (Viannia)

braziliensis. The strategies involve the use of via mucosa, prime-boost heterologous protocols and use of vaccine candidates associated with adjuvants and bioactive formulations. In parallel, we developed the hamster model of infection by L. (V.) braziliensis, one of the few animals susceptible to this species, which has the highest prevalence in Brazil. The reference Service in Diagnosis of leishmaniasis in molecular diagnostics and pathology of leishmaniasis. The collection of bacteria from the environment and health (CBAS) consists of cultivable bacterial strains of different environmental niches, as well as health impact bacteria, characterized by sequence analysis of 16S rRNA gene. The CBAS acts in the acquisition, preservation, identification and distribution of authenticated microorganisms, to support research, epidemiological studies, as well as the development and production of bio-products for diagnosis, vaccine and medicines, acting also as specialized service providers.

2016

HIGHLIGHTS

Interdisciplinary Medical Research Laboratory (LIPMed)

In the context of molecular epidemiology studies, we identified and genotype of *Giardia lamblia* in 15 children of a community day care center in Rio de Janeiro. As this genotype/assemblage had only been described in cloven-hoofed animals such as horse, ox and pig, our hypothesis is that a new cycle antropozoonotic should be taking place, which may contribute to the high prevalence of *G. lamblia* which has been observed in epidemiological studies. The

possibility of other sources of infection coupled with high frequency of infection with *G. lamblia* brings concern to public health, so much so that our findings were disseminated by various media that stressed the relevance of the results to the population (newspaper O Globo and O Globo online, Newspaper the Day and online day Newspaper, radio CBN, Fiocruz Intranet, IOC, Magazine Crescer). This work was published by the journal The Journal of Infectious Diseases.

Interdisciplinary Laboratory for Entomological Surveillance in Diptera and Hemiptera (LIVEDIH)

Leadership: Elizabeth Ferreira Rangel efrangel@ioc.fiocruz.br

The concept of Entomological surveillance macro, the lab is involved in multidisciplinary approaches in insects of the orders Diptera and Hemiptera, of different Brazilian biomes (Amazon, Cerrado, Caatinga, Atlantic forest), assessing biological indicators associated with the vector competence. through studies of the habits of the vectors in its interrelation with the epidemiologic chain. We carry out the taxonomic identification by means of morphological, ultrastructural and molecular characters, description of new species and of complex critptic species, studies on the biology of the species, with the knowledge of habits associated with vector competence (eating habits and local clearance assessment), in addition to natural infection by pathogens research. Added to these studies, the application of remote sensing and geoinformation, as the implementation of a geographic information system (GIS) that make it possible to correlate climate, environmental and biological information associated to vectors, contributing to the definition of determinants of expansion and installation of leishmaniasis and Chagas disease. Such information can be valuable tools in the definition of surveillance and control measures. You have to consider also the

taxonomic status of the vector species, taking into account the need for proper identification and diagnosis of cryptic species complexes, whose populations may respond differently to chemical insecticides. Are also in the scope of activity of the laboratory, health education activities for leishmaniasis, Chagas disease and dengue fever, as grants to programs of monitoring and control in the context of integrated actions, being continuous training activities of health agents, guards of endemics and Laboratorians, linked to the health system in several States of Brazil. In conjunction with these activities, we conduct the awareness of the population living in the area of risk regarding the importance of the knowledge about the transmission of such diseases, the health and welfare of communities, stimulating the participation of popular groups, in partnership with health professionals. In the control of these diseases, the adoption of a proposal for integrated actions appears to be promising possibility so as to interfere with the population dynamics of the vector, involving not just the chemical control, but mainly in health education and environmental management.

Interdisciplinary Laboratory for Entomological Surveillance in Diptera and Hemiptera (LIVEDIH)

The LIVEDIH was awarded the program National Institute of science and technology-climate change, CNPq, in coordinating the Subarea health, with two post-doctoral fellowships and funding of extrabudgetary funding and capital; international cooperation with the University of Lisbon, Portugal, and with the London School Hygiene & Tropical Medicine, United Kingdom; human resources training: six theses and two dissertations defended, 16 doctoral guidelines and six master's guidelines; 10 published articles.

National and International Reference Laboratory in Taxonomy of Triatominae (LNIRTT)

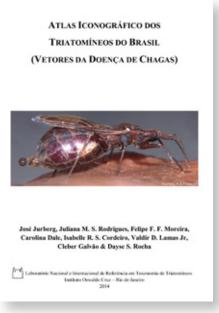
Leadership: José Jurberg jjurberg@ioc.fiocruz.br

The lab is dedicated to broadening the knowledge of the Triatominae based on its external and internal morphology, biological and morphometric parameters, on systematics and phylogeny of Triatominae, in addition to promoting the dissemination of triatominic diversity of Brazil, with the distribution of colored

prints of the five regions of Brazil of the Vectors of Chagas' disease in Brazil e do Iconographic Atlas of Triatominae of Brazil (vectors of Chagas disease), used as a tool of identification by the SSC of the five regions of Brazil, as well as in schools of middle and high level of endemic areas of Brazil.



Iconographic atlas of triatomine of Brazil (vectors of Chagas disease)



National and International Reference Laboratory in Taxonomy of Triatominae (LNIRTT)

We highlight the tool developed by LNIRTT, the collection of five blocks of colored prints with images of Triatominae of Brazil, in its Fourth Edition (2017), which constitutes sweeping approach in the area of education, for ease in identification of Triatominae. About of 6,500 copies were freely distributed to health care agents, teachers, doctors etc, all over Brazil. We wish that around 5,000 municipalities in Brazil are achieved, as well as the third edition of Atlas iconográfico dos triatomíneos do Brasil (free

transition - Iconographic Atlas of Triatominae of Brazil). In addition, we highlight the publication of eight scientific articles on molecular and taxonomic aspects of Triatominae (Afr. Entomol. 24: 257-260; Genet. Mol. Res. 15: 1-10; PLoS Neglect Trop. D; Revista Enfermagem Digital Cuidado e Promoção da Saúde-REDCPS 1: 82-84); Revista de Patologia Tropical 45: 323-326.; Zootaxa 4078: 153-160.; Zootaxa 4171: 586-594; Afr. Entomol. 24: 261-264).











