CICLO CARLOS CHAGAS DE PALESTRAS

9ª EDIÇÃO

SAÚDE MENTAL E DOENÇA DE CHAGAS: MUITO A DESVENDAR PARA ENFRENTAR

LIVRO DE RESUMOS

IOC Instituto Oswaldo Cruz
Ministério da Saúde
FIOCRUZ Fundação Oswaldo Cruz
MINISTÉRIO DA SAÚDE
PÁTRIA AMADA BRASIL GOVERNO FEDERAL

Ciclo Carlos Chagas de Palestras – 9ª edição

100+12 ANOS DA DESCOBERTA DA DOENÇA DE CHAGAS: O TEMPO NÃO PARA

"Saúde Mental e Doença de Chagas: muito a desvendar para enfrentar"

Webinar – CanalIOC do Youtube
https://www.youtube.com/canalioc

Organizadores: Josefa Oliveira Silva e Joseli Lannes

Prezados participantes,
Neste ano, em que celebramos 121 anos do Instituto Oswaldo Cruz e da Fundação Oswaldo Cruz, o Ciclo Carlos Chagas de Palestras (CCCP) realiza sua 9ª Edição com o tema **"100+12: o tempo não para: Saúde Mental e Doença de Chagas - muito a desvendar para enfrentar",** sendo pelo segundo ano presentado de forma *online*. Na saudade, nos encontramos e difundimos nosso evento que conta com a participação de resumos de trabalhos desenvolvidos em diversos estados do Brasil, em Unidades da Fiocruz e em instituições de Ensino e Pesquisa.
Criado em 2013, o CCCP objetiva apoiar o calendário de eventos internacionais na "Semana de Chagas", da Federação de Portadores da Enfermidade de Chagas – FINDECHAGAS e manter uma pauta viva de discussão sobre a doença de Chagas diante dos desafios a serem enfrentados. Este ano, celebramos o "**Dia Mundial das Pessoas Acometidas pela doença de Chagas -** 14 de abril", criado pela Assembleia Mundial de Saúde da Organização Mundial de Saúde, 2019, com atividades intensas visando maior visibilidade e enfrentamento das necessidades dos portadores da doença de Chagas.
As reuniões anuais do CCCP têm sido oportunidades para reunir pesquisadores da Fiocruz e de outras Instituições, nacionais e, muitas vezes, internacionais. Refletimos sobre os desafios da pesquisa na doença de Chagas e criamos ambiente propício a interações entre pesquisadores e destes com portadores da doença de Chagas. Em 2016, lançou-se no CCCP16 a ***RioChagas***, Associação de Portadores da Doença de Chagas do Rio de Janeiro, desde então presente em nossas reuniões. Este ano, a presidente da ***RioChagas*** faz parte da organização científica do nosso evento, a Sr Josefa Oliveira, quem inspirou em sua fala de abertura do CCCP20.
No segundo ano da pandemia de Covid-19, mantemos o espírito resistente em nome da ciência e da formação de nossos estudantes e pesquisadores. Agradecemos aos participantes pelo interesse em nosso evento e aos palestrantes pela generosidade de compartilharem seu conhecimento. Agradecemos, também, aos avaliadores de resumos que contribuíram para a indicação das apresentações orais (CE-IOC em 09 de julho, aniversário de Carlos Chagas). Todos os resumos estão disponíveis *online,* na *página do IOC,* no *Campus Virtual da Fiocruz* e no *Research Gate*. Agradecemos, de forma especial o essencial apoio logístico do Núcleo de Eventos e do Jornalismo do IOC.
Aqui repetimos o que dissemos em 2020: "Nestes momentos em que lidamos com tantas incertezas, vislumbramos a oportunidade de fortalecer a solidariedade, conhecer a resistência e a resiliência. Renovamos uma vez mais as esperanças na força da democracia institucional e para mudarmos a nossa sociedade através da educação, da cultura e da ciência e tecnologia. Reafirmamos a necessidade de fortalecimento do nosso Sistema Único de Saúde (SUS), uma necessidade de resposta aos desafios de saúde atuais e futuros." Uma vez mais recorremos à frase mote de Oswaldo Cruz "***Não esmorecer para não desmerecer***", que nos guia.

Muito obrigado a todos Josefa Oliveira e Joseli Lannes

Ciclo Carlos Chagas de Palestras - 100+12: O tempo não para

Webinar – CanalIOC do Youtube
https://www.youtube.com/canalioc

Organizadoras: Josefa Oliveira Silva – Associação Rio Chagas
Joseli Lannes – IOC/Fiocruz

Evento de Ciência e Arte: Organização de oficina com portadores da RioChagas
Rosane Assis e Christiane Moreira

08/07

9:00h – **Abertura** (falas de 3 minutos)
Presidente da Fiocruz Dra Nísia Trindade Lima
Vice-Presidente de Pesquisa e Coleções Biológicas Dr Rodrigo Correa-Oliveira
Diretora do IOC Dra Tânia C. de Araújo-Jorge,
Presidente da Associação RioChagas Sra Josefa de Oliveira
Organização do CCCP Dra Joseli Lannes

9:30h
Dr José Eymard Homem Pittella – UFMG - "Reconhecimento da forma nervosa da doença de Chagas. Importância e Desafios."
Debatedora: Dra Andrea Alice da Silva – UFF

10:30hs
Dra Rosane de Assis Barbosa – FAV-RJ, PG-EBS/IOC - "Saúde Mental do portador da doença de Chagas na pandemia de Covid19: experiência de enfrentamento".
Debatedora: Dra Danielle Grynszpan – IOC

09/07

9:00-10:00h
Mini-palestras por jovens pesquisadores – 4 trabalhos selecionados dos resumos recebidos (10 minutos apresentação e 5 minutos de discussão)

10:00h – Centro de Estudos do IOC
Dra Glaucia Vilar-Pereira – UNESA e Prefeitura do Rio de Janeiro - "Alterações comportamentais (ansiedade, depressão e perda de memória) na doença de Chagas: o que modelos experimentais nos ensinam?

Dr Wilson Oliveira Jr – PROCAPE/UPE - "Alterações comportamentais (depressão, ansiedade, perda de memória) e qualidade de vida do portador da doença de Chagas."
Debatedora: Dra Luciana Garzoni – VDPq/IOC

Comissão Avaliadora de Resumos

André Roque / IOC

Andrea Alice da Silva / UFF

Anissa Daliry / IOC

Catarina Macedo Lopes / IOC

Claudia d'Avila / IOC

Cleber Galvão / IOC

Constança Britto / IOC

Daniel Adesse / IOC

Daniel Gibaldi / IOC

Isabela Resende Pereira / UFF

Jacenir Mallet / IOC

Joseli Lannes / IOC

Katia Calabrese / IOC

Kelly Salomão Salem / IOC

Marcelo Alves Ferreira / CDTS

Maria da Gloria Bonecini / INI

Maria de Nazaré Correia Soeiro / IOC

Mariana Waghabi / IOC

Marli Lima / IOC

Michelle Barros / IAM

Natalia Nogueira / UERJ

Otília Sarquis / IOC

Roberto Saraiva / INI

Rubem Menna-Barreto / IOC

Samanta Xavier / IOC

Samara Latgé / IOC

Virginia Maria Barros de Lorena / IAM

Muito obrigado a todos e todas!

Resumos Selecionados para Apresentação Oral

09 de julho - 9:00hs – Centro de Estudos Especial

A avaliação dos resumos, considerando relevância temática, coerência título/conteúdo, clareza, originalidade e qualidade, foi feita por 3 avaliadores independentes especialistas na temática. Eles receberam o título e o texto (omitiu-se autores e filiações), cada avaliador deu as notas e poderia indicar 1 resumo (1 estrela). A síntese dos dados, levou à indicação de **Menção Honrosa** (que receberam 1 estrela – ver Livro de resumos). E à seleção de resumos para o **Prêmio Ciclo Carlos Chagas de Palestras, como Apresentação oral** (que receberam 2 ou 3 estrelas), listados abaixo:

#7 Area: Cell Chemotherapy (drugs and etiological treatment scheme)

Experimental combination therapy using benznidazole and amiodarone in mouse model of Trypanosoma cruzi acute infection.

Juliana Magalhães Chaves Barbosa, Yasmin Pedra Resende da Silva, Tatiana Galvão de Melo,Gabriel de Oliveira, Anissa Daliry and Kelly Salomão Salem

#13 Area: Diagnostic

Development of molecular methodologies for detection and quantification of viable Trypanosoma cruzi in açai samples from oral Chagas disease endemic areas.

Amanda Faier Pereira, Paula, Finamore Araujo, Carlos Ramon do Nascimento Brito, Eldrinei Gomes Peres, Klenicy Kazumy de Lima Yamaguchi, Renata Trotta Barroso Ferreira and Otacilio Cruz Moreira

#15 Area: Education, Information

Playing with Portinari and health: dialogical workshop of Artscience to promote health with joy

Erik Jonilton Costa, Tania Araujo-Jorge and Roberto R. Ferreira

#30 Area: Therapy (immunotherapy, cellular therapy and others)

Treatment with suboptimal dose of Benznidazole and Pentoxifylline regulates microRNA transcriptomic profile in murine model of Chagas chronic cardiomyopathy

Priscila Silva Grijó Farani, Khodeza Begum, Glaucia Vilar-Pereira, Isabela Resende Pereira, Edith A. Fernández Figueroa, Roberto A. Cardenas-Ovando, Igor C. Almeida, Sourav Roy, Joseli Lannes-Vieira and **Otacilio Cruz Moreira**

CICLO CARLOS CHAGAS DE PALESTRAS
9ª EDIÇÃO

SAÚDE MENTAL E DOENÇA DE CHAGAS:
MUITO A DESVENDAR PARA ENFRENTAR

Resumos

Abstracts

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#1 Area: Cell biology and parasite/host cell interaction; Chemotherapy (drugs and etiological treatment scheme)

Myosin-1: a key player for *Trypanosoma cruzi* successful infection

Mylla Spirandelli da Costa, Isabella Teixeira Marques, Bruna Cristina Borges, Rayane Cristina de Oliveira, Thaise Lara Teixeira, Julia de Gouveia Santos, Claudio Vieira da Silva

Department of Immunology, Biomedical Sciences Institute, Federal University of Uberlândia, Rua Piauí, Bloco 2B, sala 200, Campus Umuarama, Uberlândia, 38400-902, MG, Brazil

Myosins are motor proteins expressed by both mammalian cells and *Trypanosoma cruzi*. Pentachloropseudilin (PCLP) is a reversible and allosteric inhibitor of type 1 myosin. Here, we addressed the impact of myosin-1 from both parasite and mammalian host cell, during the invasion process. For that purpose, we treated parasite and mammalian cells with PCLP in order to evaluate parasite motility, adherence and invasion of C2C12 cells. To assess C2C12 myosin, we also checked lysosome exocytosis. We observed that PCLP was not toxic to either *T. cruzi* or C2C12. However, parasite myosin-1 inhibition altered its motility, ability to adhere to and invade the host cells. When myosin-1 from C2C12 cells was inhibited not only parasite invasion but also lysosome exocytosis was impaired. Therefore, myosin-1 from both parasite and host cell present a fundamental role in the infection progression by *T. cruzi*.

Financial support: CAPES, CNPq e FAPEMIG.

#2 Area: Cell biology and parasite/host cell interaction; Chemotherapy (drugs and etiological treatment scheme)

Trypanosoma cruzi multiplication in triple-negative breast cancer cell line

Anna Clara Silveira, Cassiano Costa Rodrigues, Rayane Cristina de Oliveira, Samuel Cota Teixeira, Bruna Cristina Borges, Claudio Vieira da Silva

Instituto de Ciências Biomédicas, Universidade Federal de Uberlândia

In 1946, the international community of cancer researchers was inspired by the announcement that two Soviet scientists, Nina Kliueva and Grigorii Roskin, had discovered anticancer properties in culture extracts made from the South American protozoan, *Trypanosoma cruzi*, and had produced a preparation, which showed therapeutic effects on cancer patients. This discovery pursued research teams from various countries to this line of investigation. Breast cancer is the most common invasive cancer in women and the second leading cause of cancer death in women after lung cancer. Triple-negative breast cancer (TNBC) is characterized by a tumor subtype void of hormone receptors, such as the estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2); thus, this tumor is associated with poor prognosis. Poor prognosis involves a distinct metastatic pattern involving regional lymph nodes, bone marrow, the lungs, and liver and ineffective treatments owing to the lack of therapeutic targets. Here, we aimed to verify the ability of *T. cruzi* to multiplicate in triple-negative breast cancer cell line in comparison to normal breast cells. For this porpoise, we used tissue cultured trypomastigotes from Y strain. Our results showed that although MCF-10A (non-tumoral cell line) had a greater number of multiplying parasites, MDA-MB-231 (tumoral cell line) had a greater number of infected cells per field. Our data suggested that both cells are highly permissive to *T. cruzi* infection. However, MDA-MB-231 appeared to be more susceptible once most cells were infected by the parasite. We will further investigate the formation of lysis plaque and the viability of cells during the kinetics of parasite multiplication.

Support: CNPq

#3 Area: Cell biology and parasite/host cell interaction; Chemotherapy (drugs and etiological treatment scheme)

Repurposing strategy for novel Chagas disease drug candidates

Gabriela Rodrigues Leite[1], Flávia Teixeira Masson[1], Denise da Gama Jaén Batista[1], Patrícia Bernardino da Silva[1], Alan Talevi[2], Lucas Alberca[2], María Laura Sbaraglini[2] and Maria de Nazaré Correia Soeiro[1]

[1]Laboratório de Biologia Celular IOC-Fiocruz [2] Laboratorio de Investigación y Desarrollo de Bioactivos, Facultad de Ciencias Exactas | Universidad Nacional de La Plata.

Neglected tropical diseases (NTD), such as Chagas disease (CD), are associated with poverty and lack of basic sanitation, furthermore, are endemic mainly in underdeveloped countries and responsible for causing thousands of deaths per year. Chagas disease is due to the infection of the protozoan *Trypanosoma cruzi* that may induce severe heart and/or digestive alterations as major clinical manifestations, resulting in loss of organ functionality and death due to a progressive and silent chronic inflammation. The treatment of CD is still limited, restricted to the use of two old drugs, benznidazole (Bz) and nifurtimox, which have better efficacy when administered in the initial stage of the illness (acute phase). Both drugs also require long periods of administration and cause severe side effects, which reinforces the seek for novel therapeutic alternatives. Therefore, new approaches have been studied by our group, including drug repositioning and combined therapy. In this context, phenotypic assays were performed with different compound classes that were reported as anti-microorganism agents, including tetracycline, imidazole, benzimidazole and riminophenazine derivatives (series LIDEB) provided by the team of Dr Alan Talevi and Dr Lucas Alberca. I*n vitro* approaches demonstrated that the studied derivatives have low to moderated cytoxicity profile *in vitro:* LIDEB 6 (riminophenazine derivative), LIDEB 10 (tetracycline derivative), LIDEB 1 (benzimidazole derivative) and LIDEB 5 (imidazole derivative) displayed LC_{50} values of >400µM, >75µM, > 27 and >23 µM upon L929 cell lines, respectively. Following anti-*T. cruzi* screens under a fixed concentration (10 µM against intracellular forms of the Tulahuen strain, DTUVI), the most active were: imidazole>benzimidazole>riminophenazine>tetracycline, exhibiting 98-44% of reduction in the parasite load *in vitro*. These results encourage further studies that are underway to verify the potential of these compounds for the treatment of CD in mono and/or combined therapy with Bz.

Supporting by CNPq, FAPERJ, Fiocruz and Universidad Nacional de La Plata.

#4 Area: Cell biology and parasite/host cell interaction; Chemotherapy (drugs and etiological treatment scheme)

Physical exercise promotes a reduction in cardiac fibrosis in chronic indeterminate form of experimental Chagas disease

Yasmin Pedra-Rezende[1,2], Juliana M. Barbosa[1], Ana Cristina S. Bombaça[1], Luiza Dantas-Pereira[1,2], Daniel Gibaldi[2], Glaucia Vilar-Pereira[2,3], Hílton Antônio Mata dos Santos[4,5], Isalira Peroba Ramos[6], Natália Lins Silva-Gomes[7], Otacilio Moreira[7], Joseli Lannes-Vieira[2,*], Rubem F. S. Menna-Barreto[1,*]

[1] Laboratório de Biologia Celular, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil, [2] Laboratório de Biologia das Interações, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil, [3] Instituto Brasileiro de Medicina de Reabilitação, Rio de Janeiro, Brazil, [4] Faculdade de Farmácia, Universidade Federal do Rio de Janeiro, Rio de Janeiro,Brazil,[5]Laboratório de Análise e Desenvolvimento de Inibidores Enzimáticos e Laboratório Multiusuário de Análises por RMN, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, [6]Laboratório de Cardiologia Celular e Molecular, Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil,[7] Laboratório de Biologia Molecular de Doenças Endêmicas, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil

Chagas disease (CD), caused by the protozoan *Trypanosoma cruzi*, is a neglected illness endemic in Latin America. The mechanisms related to disease progression are still unknown. The etiological treatment has limited effectiveness in chronic CD, thus new therapeutic strategies are required. In this context, the practice of physical exercise has been widely advocated to improve the quality of life of CD patients. In the chronic indeterminate form (CIF), the most frequent clinical CD manifestation, the effect of exercise on disease progression is unknown. In this work, we aimed to evaluate in a CIF model, the effect of physical exercise on cardiac tissue. To establish the CIF model, BALB/c and C57BL/6 mice were infected with 100 and 500 trypomastigotes of the Y *T. cruzi* strain. Compared with BALB/c mice, C57BL/6 mice showed lower parasitemia peak, mortality rate, and less intense myocarditis. Thus, C57BL/6 mice infected with 500 parasites were used to the subsequent analysis. At 120 and 150 dpi, reduced heart rate and slight prolonged corrected QT interval were detected, which were normalized at 180 dpi, characterizing the CIF. Thus, Y-infected mice were submitted to an exercise program on a treadmill for 4 weeks (from 150 to 180 dpi), with a gradual increase in speed from 6 to 20 m/min five times per week with a 30-60 min daily training session. At 180 dpi, the physical exercise neither worsen clinical parameters of infected mice nor impacted cardiac mitochondrial (n= 8) and oxidative metabolism (n=5), compared with sedentary mice. At 120 and 180 dpi, no differences were observed in the serum cytokine levels (n=8), supporting that a crucial biomarker of systemic inflammatory profile (n=8) was absent and not impacted by exercise. Trained Y-infected mice (n=5) showed similar parasite load and inflammatory foci but reduced cardiac fibrosis ($p<0.0001$), in comparison with sedentary Y-infected mice (n=6). Therefore, our data support that physical exercise promotes beneficial changes, suggesting that this intervention may prevent cardiac changes induced by *T. cruzi* infection.

Supported by: FAPERJ, CNPq and FIOCRUZ.

#5 Area: Chemotherapy (drugs and etiological treatment scheme)

A preliminary study of new triazoles with action against *Trypanosoma cruzi* and as inhibitors of P2X7 receptor

Caroline de Souza Ferreira Pereira[1,2], Robson Xavier Faria[2]

[1]Universidade Federal Fluminense – Programa de Pós-graduação em Ciências e Biotecnologia.
[2]Laboratório de Avaliação e Promoção da Saúde Ambiental - Instituto Oswaldo Cruz.

Background: Chagas disease (CD) is a neglected disease caused by the protozoan *Trypanosoma cruzi* and affects millions of people, according to the World Health Organization (WHO). Currently, in Brazil, only benznidazole is available to treat this disease. However, this treatment causes adverse effects that induce interruption of treatment. There is a search for new treatments to CD, for example, triazoles because they demonstrate trypanocidal and anti-inflammatory activity. In CD, purinergic signalization (ATP and adenosine) actives an inflammatory response. Adenosine triphosphate (ATP) is found in millimolar levels extracellularly caused by rupture of infected cells by a parasite. These elevated levels stimulate the purinergic receptor-mediated pore formation, especially the P2X7 receptor involved in activation and release of inflammatory cytokines, cellular damage, and cell death. There are several selective antagonists to this receptor; however, they were not effective in clinical trials, which justify the search for new drugs.
Methods: *In vitro* cell cytotoxicity was tested using peritoneal macrophages of *Swiss Webster* mice plated on transparent 96 wells plates and kept 24 h at 37 ºC with a 5% CO_2 atmosphere. The cells were then incubated with 100 µM triazole derivatives, and cell-only wells were maintained as a control. After 24 h, the resazurin colorimetric assay was performed, and the cytotoxicity was expressed in percentage, with the aid of the program GraphPad Prism 5. The experiment was performed in triplicate on three different days.
Results: In the test evaluating the metabolic action we obtained: TD1, TD2, TD3, TD4, TD5, TD6, TD7, TD8, TD9, TD10, TD11, TD12, TD13, TD14, TD15, TD16 and TD17.The compounds TD6, TD8, TD9, and TD12 reduced, respectively, 5%, 7%, 10%, and 6% of the cellular metabolic activity. However, the other compounds did not interfere with the peritoneal macrophages' metabolism, even at their maximum concentration.
Conclusions: Triazole prototypes demonstrate the possibility of presenting low toxicity in peritoneal macrophages. However, new tests about toxicity will be realized in mammalian cells and against *T. cruzi.*

Financial support: CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) and CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico).

#6 Area: Chemotherapy (drugs and etiological treatment scheme)

Phenotypic evaluation of novel purine nucleoside analogues through *in vitro* and *in vivo* approaches

Ludmila Fiuza[a], Cai Lin[b] Camila Cardoso Santos[a] Daniela Ferreira Nunes[c] , Otacílio Cruz Moreira[c] Jakob Bouton[b] Izet Karalic[b] Louis Maes[d], Guy Caljon[d], Fabian Hulpia,[b] Serge Van Calenbergh[b], and Maria de Nazaré C. Soeiro,[a]

[a] Laboratório de Biologia Celular, Instituto Oswaldo Cruz (FIOCRUZ), Fundação Oswaldo Cruz, Rio de Janeiro, Avenida Brasil 4365, Manguinhos, 21040-360 Rio de Janeiro, Brazil, [b]Laboratory for Medicinal Chemistry (Campus Heymans), Ghent University, Ottergemsesteenweg 460, B-9000, Gent, Belgium and [c]Plataforma de PCR em Tempo Real RPT09A-Laboratório de Biologia Molecular e Doenças Endêmicas, Instituto Oswaldo Cruz (FIOCRUZ), Fundação Oswaldo Cruz, Rio de Janeiro, Avenida Brasil 4365, Manguinhos, 21040-360 Rio de Janeiro, Brazil, [d]Laboratory of Microbiology, Parasitology and Hygiene, University of Antwerp, Universiteitsplein 1 (S7), B-2610, Wilrijk, Belgium.

Chagas disease (CD) or American trypanosomiasis, discovered by the Brazilian doctor Carlos Chagas, is caused by the kinetoplastid parasite *Trypanosoma cruzi*. The treatment is based in old drugs, the nitroderivatives benznidazol (Bz) and nifurtimox. Both were empirically introduced in clinical use for more than 5 decades ago and display several limitations regarding efficacy and safety profile, justifying the search for new therapeutic alternatives. As trypanosomatids are auxotrophic, being dependent on the uptake of host nucleoside substrates, this metabolic pathway represents a promising target for CD drug discovery. Our group previously demonstrated that some purine nucleoside derivatives exhibit promising anti-*T. cruzi* activity *in vitro* and *in vivo* [1, 2]. Then, our present goal was investigated the effect of novel 6-methyl-7-aryl-7-deazapurine nucleosides as anti-*T. cruzi* candidates. Our data showed that several analogues presented high activity (submicromolar) against intracellular forms of the parasite. One of them, the 7-(4-chlorophenyl) analogue (named **cpd 14**), displayed high potency (EC_{50} = 0.77 ± 0.05 µM), low toxicity against mammalian cardiac cells (CC_{50} >480 µM), and sustained a high activity upon *T. cruzi*-infected cardiac spheroids, reaching 77% of parasite reduction (by qPCR) using 10 µM for 96 hours of drug incubation, similarly as Bz. Because of these phenotypic *in vitro* results and its metabolic stability (in microsomes), **cpd 14** was moved to *in vivo* studies using an acute mouse model of *T. cruzi* infection (Swiss male mice infected with 10^4 bloodstream forms, Y strain). We found that the oral administration of **cpd14** (at 25 mg/kg b.i.d.) suppressed parasitemia peak and protected mice from infection-related mortality, giving similar efficacy as Bz. However, the blood parasite analysis by qPCR showed therapeutic failure, for both **cpd14** and Bz, possibly due to the short time-period of drug exposure (only 5 days). New assays will be conducted following longer periods of drug administration as well as with co-administration of Bz aiming to contribute for the identification of novel drug therapies for CD.

Supported by Fiocruz; CNPq; CAPES, FAPERJ, and Flanders Research Foundation; Hercules Foundation

1. Hulpia F, Van Hecke K, da Silva CF, *et al.* (2018) Discovery of novel 7-aryl 7-deazapurine 3'-deoxy-ribofuranosyl nucleosides with potent activity against *Trypanosoma cruzi. Journal of Medicinal Chemistry. d*oi:10.1021/acs.jmedchem.8b00999.
2. Lin C, Hulpia F, da Silva CF, *et al.* (2019) Discovery of pyrrolo[2,3-b]pyridine (1,7-dideazapurine) nucleoside analogues as anti-*Trypanosoma cruzi* agents. *Journal of Medicinal Chemistry.* doi:10.1021/acs.jmedchem.9b01275.

★★**#7 Area: Chemotherapy (drugs and etiological treatment scheme)**

Experimental combination therapy using benznidazole and amiodarone in mouse model of *Trypanosoma cruzi* acute infection

Juliana Magalhães Chaves Barbosa[a], Yasmin Pedra Resende da Silva[a], Tatiana Galvão de Melo[b],Gabriel de Oliveira[a], Anissa Daliry[c] and Kelly Salomão Salem[a]

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[b] Laboratório de Ultraestrutura Celular, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Av. Brasil 4365, Manguinhos, 21040-360 Rio de Janeiro, Rio de Janeiro, Brazil.
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Chagasic cardiomyopathy (CC) is the most relevant clinical manifestation of Chagas disease (CD), caused by *Trypanosoma cruzi*, and has high rates of morbidity and mortality. The etiological treatment of CD is restricted to Benznidazole (**Bz**) and Nifurtimox; however, they have high percentages of therapeutic failure. Among the drugs used for CD treatment, amiodarone (**AMD**) is the safest and most efficient antiarrhythmic available. The BENEFIT (2015) showed a reduction in hospital admissions and risk of death associated with cardiovascular events in chronic CD patients treated with **AMD** in association with **Bz.** However, the effect of **AMD** on CC is still poorly studied, as well as its interaction with drugs used in the etiological treatment of CD. In this study, we tested the *in vitro* interaction of **Bz** and **AMD** in blood trypomastigote and intracellular amastigote, using a fixed-ratio isobologram method. Additionally, the ability of **Bz** and **AMD** to reverse the *T. cruzi*-induced cytoskeleton damage of cardiomyocyte cells (CM) was assessed by immunofluorescence and scanning electron microscopy. The *in vivo* trypanocidal effect of **Bz** and **AMD** treatment was evaluated in an acute murine model of CD. Parasitemia was evaluated by the Pizzi-Brener method, cardiac function by electrocardiogram, inflammation, and fibrosis in cardiac tissue through histopathology and quantification of cytokine levels by flow cytometry. In the *in vitro* assays, we observed that the interaction of **Bz** and **AMD** was classified as additive. Infected CM treated with the combination **Bz/AMD** or **Bz** monotherapy showed a similar phenotype, with partial reversal of *T. cruzi*-induced cytoskeletal damage. *In vivo*, the **Bz/AMD** combination was more effective in reducing the peak of parasitemia compared to the monotherapy treatments. Additionally, **Bz/AMD** treatment reduced (a) IL-6 levels in the cardiac tissue, (b) P wave duration; (c) frequency of animals affected by arrhythmias, as well as increased the gap junction integrity. Therefore, our study indicates that **AMD**, in monotherapy or in combination with **Bz**, has additional effects other than its anti-arrhythmogenic property that could be further explored for CD treatment.

Financial support: FAPERJ, CAPES e CNPq.

#8 Area: Chemotherapy (drugs and etiological treatment scheme)

In silico analysis of pharmacokinetic profile of Imatinib derivatives with anti-*Trypanosoma cruzi* activity *in vitro*

Luca S. F. N. de Freitas[1], Loredana Salerno[2], Sebastiano Intagliata[2] and Maria de Nazaré Correia Soeiro[1]
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Chagas disease (CD), a neglected illness caused by the protozoan *Trypanosoma cruzi*, affects over 6 million people worldwide but still lacks an effective therapy. Our previous assays provided valuable insight regarding the promising effects of imatinib (IMB) and its derivatives against this parasite. This data motivated us to perform bioinformatic investigations into their drug-like properties to support further molecule optimization as well as additional *in vitro* and *in vivo* studies. Some positive characteristics of *in silico* analysis include the low-costs and reduced time to predict drug-like properties (such as ADME: absorption, distribution, metabolism, and excretion). The algorithms take the molecule's structure as an input to their mathematical models and compare it to a diverse database of experimental data on similar molecules. *In silico* assays can also perform 3D simulations at the various potential parasite targets to predict binding sites. These predictions, however, can vary depending on the mathematical program and the nature of the studied compound class, demanding the identification of the most accurate model for each chemotype. This prompted us to use a free and robust platform, SwissADME (http://www.swissadme.ch/), which offers multiple models for several PK parameters, to evaluate the drug-like profile of 8 novel IMB derivatives previously assayed against *T. cruzi in vitro*. In parallel, the same was done with the reference drug (IMB). This computational program gave an accurate PK pattern for IMB compared to the experimental data available in the literature. When the derivatives were assessed, it predicted that they would likewise be inhibitors of CYP enzymes. Of the models used to predict the n-Octanol/Water partition coefficient, XLogP3, referenced for IMB in Pubchem, and the iLogP descriptor, the SwissADME in house model, provided the most coherent IMB values according to the existing literature data. Regarding atomistic properties, the derivatives violated only the first of Lipinski's rules of five, which is related to molecular weight, but displayed favorable XLogP3 values, desirable for oral bioavailability. Considering Veber's rules, all compounds exceeded (≈20%) the rotatable bonds limit and one debased (≈9%) the total polar surface area limit, predicting low gastrointestinal absorption (GIA). On the other hand, IMB had high GIA prediction and violated none of the aforementioned rules, as expected for this licensed medication. The bulk of our *in vitro* and *in silico* analysis motivated the optimization and synthesis of new imatinib-based analogues of benznidazole that will be screened in future phenotypic assays aiming to contribute for the identification of new therapeutic options for CD.

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#9 Area: Chemotherapy (drugs and etiological treatment scheme)

Antiparasitic Potential of Aqueous Extract obtained from a Cyanobacterium

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Chagas disease (CD), caused by the hemoflagellate protozoan *Trypanosoma cruzi*, is one of the 20 neglected tropical diseases according to World Health Organization – WHO. In general, these neglected diseases are characterized by high mortality rates and affecting, especially, regions with precarious social and economic conditions. As a result, these diseases do not receive attention from the pharmaceutical industry, as they are not profitable enough. In addition, the drugs available for the treatment of CD, namely, benznidazole and nifurtimox, are toxic, causing several side effects and, probably, many times, patients' evasion of therapy. Furthermore, these medicines do not demonstrate efficacy in the later chronic phase of the disease. Thus, the development of new alternative anti-*T. cruzi* that are produced at a low cost, have low toxicity and present high efficacy is necessary. Therefore, the bioprospecting of natural products, especially photosynthetic microorganisms, has gained prominence since they are rich in bioactive molecules with several biotechnological applications. In this study, we investigated the antiparasitic activity of a cyanobacterium extract against trypomastigote forms of *T. cruzi*. Aqueous extract from Arthrospira sp. from the University of Texas collection was obtained through Tris-HCl buffer (0.2 M and pH 7.3), under magnetic stirring for 9 hours. Vero cells were infected with trypomastigotes and maintained in culture with RPMI 1640 medium supplemented with 5% fetal bovine serum and antibiotic (100 µg/ml streptomycin). The cyanobacteria extract showed inhibitory activity against the trypomastigote forms of *T. cruzi*, compared with the negative control, containing only cells and trypomastigotes. At 1000 µg/ml, the highest concentration tested, the extract showed a considerable percentage of inhibition, affecting the parasites' viability in 86.1%. At the second highest concentration, 500 µg/ml, the microorganism extract was able to inhibit trypomastigote viability by 52.0%. However, despite the observation of the inhibitory activity of the aqueous extract, additional tests such as the cytotoxicity tests on human cells and purification of compounds must be carried out to prove the potential use of compounds obtained from extract of photosynthetic microorganisms and presenting biological activity.

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#10 Area: Chemotherapy (drugs and etiological treatment scheme)

Synthesis and evaluation of trypanocidal activities of arylboronic acids

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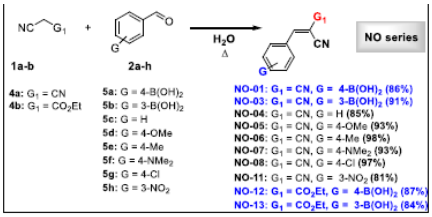
Keywords: *Chagas disease, vinyl nitriles, Knoevenagel condensation, tyrphostins*

Introduction. *Trypanosoma cruzi* (T. *cruzi*) is the protozoan parasite responsible for a widespread endemic neglected disease in Latin America: the Chagas disease (CD), a great challenge to public health, especially when it comes to the economically vulnerable population that has little or no access to a good health system. Nifurtimox and benznidazole are the only drugs used worldwide in the treatment of CD, being effective only in the acute phase and almost impotent in the chronic phase, responsible for about 90% of the associated mortality. They are old medicines that cause several adverse effects for which some patients abandon the treatment.[1] For all the reasons already mentioned, the development of new, safer and potent chemotherapy for CD is imperative. Souza and co-workers[2] reported that tyrosine-kinase, a protein involved in the activation of signal transduction cascades, had an essential role in the *T. cruzi* invasion of primary resident macrophages and that trypomastigote uptake was inhibited by some tyrphostins (**ty**rosine **phos**phorylat**i**on **in**hibitor). Boronic acids have recently emerged as an important class in the tool box of medicinal chemistry. Bortezomib, for example, is a boronic acid available in the pharmaceutical market for treating multiple myeloma.[3] In this work, tyrphostins were prepared by Knoevenagel condensation to evaluate the role of the $B(OH)_2$ units characteristic of boronic acids in their trypanocidal activities against epimastigotes (*T. cruzi* Y strain).[4]

Results. Tyrphostins were prepared through Knoevenagel condensation (**Scheme 1**) and their trypanocidal activities were evaluated. Three of the tested tyrphostins can be highlighted due to the antichagasic activities presented **NO-03** (EC_{50} = 14,5 µM); **NO-04** (EC_{50} = 10,2 µM); **NO-12** (EC_{50} = 0,795 µM), two of which (**NO-03** and **12**) are boronic acids (**Figure 1**). **NO-12** showed an EC_{50} value ten-fold lower than benznidazole (EC_{50} = 40 µM) against epimastigotes of *T. cruzi* (Y strain). Further investigations will be conducted to understand the targets involved in the trypanocidal activities and to better plan new boronic acids using **NO-03** and **NO-12** as prototypes. **Conclusions.** These results indicate boronic acids as effective platforms upon which new molecules with improved actions against *T. cruzi* can be designed.



Scheme 1 - Tyrphostins by Knoevenagel reaction

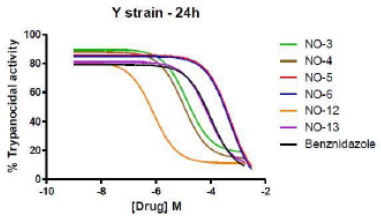


Figure 1 - Trypanocidal activity in 24 h

Support: CAPES, CNPq, FAPERJ (E-26/210.242/2019), UFF.
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#11 Area: Chemotherapy (drugs and etiological treatment scheme)

Benznidazole combined therapy with cardioprotective improves the electrocardiographic profile in chronically *Trypanosoma cruzi*-infected mice

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Chagas Disease (CD) affects approximately eight million individuals in Latin America. A few years or even decades after infection with the *Trypanosoma cruzi* protozoan, 30% of patients progress to chronic Chagas cardiomyopathy (CCC), with electrical alterations and development of heart failure (HF). It is suggested that the severity of CCC is related to (i) parasite persistence, (ii) histopathological and functional changes in the heart, and (iii) systemic inflammatory profile. Moreover, alterations in the expression of the renin-angiotensin-aldosterone system components have been shown in CCC. Benznidazole (Bz) is the first-choice therapy in the acute phase of infection. However, the use of this drug in chronic patients is controversial. Studies show a lower clinical evolution and others show a reduction in the parasite load, but without influence on clinical progression. Therefore, the aim of the present study is to evaluate the influence of combined therapy of Bz with renin-angiotensin system-modulating drugs (Losartan and Captopril) on the electrocardiographic profile of chronically *T. cruzi*-infected mice. For this, C57BL/6 mice were infected with 100 trypomastigotes of the Colombian strain of *T. cruzi* and after establishment of CCC (120 days post-infection) they were submitted to the following treatment regimens for 30 days: (i) captopril (n=4), (ii) losartan (n=3), (iii) Bz (n=5), (iv) captopril and Bz (n=8) or (v) losartan and Bz (n=7). Our preliminary data show that the combined treatment of Bz with losartan, which is an AT1R (angiotensin II receptor) antagonist, after the establishment of experimental CCC had a beneficial and distinct effect from isolated therapies with Bz or the cardioprotective drugs, regarding the electrocardiographic profile at the end of therapy use (150 days post-infection). Based on these data, we intend to investigate the effects of these drugs on the parasite load and molecular mechanisms involved. Next, we going to explore the molecular mechanisms underlying the beneficial effects of the combined treatment of Bz with losartan.

Financial support: CAPES, CNPq, FAPERJ.

★ **#12 Area: Clinical Aspects**

The association of echocardiographic changes with heart disease progression and death in patients with chronic Chagas disease and normal electrocardiogram

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Introduction: In the chronic phase of the Chagas disease (CD), most patients present with the indeterminate form (IF), characterized by absence of clinical findings with a normal electrocardiogram (ECG). The IF has a good prognosis that is similar to the general population with normal ECG. The guidelines that address Chagas' heart disease (CHD) do not consider individuals presenting an altered echocardiogram (ECHO) with normal ECG. These cases in particular, despite showing signs of heart disease, are not classified as CHD. This condition has an impact on CD prognosis assessment. Currently, there are studies that demonstrate the prognostic value of echocardiographic changes in patients with IF.

Objective: To compare the progression rates to CHD and death between patients with normal and altered ECHO with the IF of CD.

Method: Retrospective observational study, including patients with IF followed at the outpatient center at INI-Fiocruz, from Jul 1986 to May 2021. Unadjusted and adjusted by age, sex, and previous benznidazole treatment logistic regression models were fitted to evaluate the association between altered ECHO with progression to CHD and death.

Results: Among 2194 patients (1154 [52.5%] women and 1040 [47.5%] men), 1085 (49.4%) IF were identified (554 [51%] women and 531 [49%] men) with a mean age of 44.8 years. Most patients were born in Bahia (21.38%) and Minas Gerais (18.4%) states. Fifty-eight patients without ECHO were excluded. Sixty-six (6.4%) had altered ECHO with segmental dysfunction of the left ventricle. Two hundred (19.5%) progressions and 147 (14.3%) death were identified. Among those with altered echo, 12.5% (n=22) progressed while 5.0% (n=41) did not progress (p<0.001 chi-squared test), and 11.6% (n=17) died while 5.6% (n=46) survived (p=0.006 chi-square). Logistic regression models demonstrated an important association between altered ECHO with progression to CHD in both unadjusted (OR 2.7 95%CI 1.6 to 4.6; p<0.001) and adjusted (OR 2.8 95%CI 1.7 to 4.8; p<0.001) analysis. Similarly, altered ECHO was also associated with death in both unadjusted (OR 2.2 95%CI 1.2 to 4.0; p=0.007) and adjusted (OR 1.9 95%CI 1.1 to 3.4; p=0.04) analysis.

Conclusion: Patients usually classified as IF (that only considered normal ECG) but with an altered ECHO had a greater odds of progression to CHD and death in comparison to those without ECHO abnormalities. The current classification of Chagas' heart disease based on an altered ECG should take into account the possibility of an altered echocardiogram in the presence of a normal ECG.

★★**#13 Area: Diagnostic**

Development of molecular methodologies for detection and quantification of viable Trypanosoma cruzi in açai samples from oral Chagas disease endemic areas

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In the North of Brazil, about 70% of new cases of Chagas disease (CD) have been associated with consumption of contaminated food, such as açaí berry pulp, bacaba wine and sugarcane juice. Because of that, controlling oral transmission of CD is becoming relevant from public health perspective. The evaluation of CD oral transmission is mostly determined by parasite isolation or inoculation of food in experimental animals. Although some studies about *T. cruzi* DNA detection and quantification in açaí samples have already been described in the literature, it has not yet been possible to evaluate the viability of parasites through molecular methodologies. Instead, RNA was previously reported as a marker of viability in eukaryotic and prokaryotic cells. Therefore, this study aims to develop a qPCR and a RT-qPCR to determine total and viable *T. cruzi* parasites in açai pulp samples. For this, we standardized DNA and RNA extraction methods based on silica-membrane spin columns and using a Guanidine-EDTA solution with açai samples (GEA), what enabled nucleic acids stabilization and preservation. Regarding qPCR and RT-qPCR assays, both reactions were designed for TaqMan duplex systems, targeting *T. cruzi* and, concomitantly, an exogenous internal control (FAM and VIC, respectively). In relation to DNA, the methodologies have already been standardized, showing high sensitivity (0.01 Parasite Equivalents/mL). Currently, we have developed a simple and reproducible methodology for RNA quantification. So far, assessing *T. cruzi* viability in açaí through RT-qPCR singleplex assays are showing good sensitivity (0.1 Viable Parasite equivalents/reaction). Then, we will carry out standardization of a multiplex RT-qPCR One-Step assay, analytical validations and with samples collected from the municipalities with a history of oral outbreak of CD (Coari-AM and Belém-PA), following international guidelines recommendations and using reference samples from different *T. cruzi* DTUs. Thus, we expect to obtain a simple and reproductible methodology to assist the investigation of oral CD outbreaks by the consumption of açai juice.

#14 Area: Diagnostic

Sensitivity and Specificity of rapid tests used at INI-Fiocruz for the diagnosis of Chagas disease

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Introduction: The diagnosis of chronic CD is essentially based on serological methods that must be performed using a high sensitivity together with another high specificity test. Both tests must be reactive to confirm the diagnosis. Conventional reactions such as the enzyme-linked immunosorbent assay (ELISA) test, Indirect Immunofluorescence (IFI), Indirect Hemagglutination (IHA) and, Chemoluminescence (ChLIA) are the most commonly used tests. More recently, the use of Rapid Diagnostic Testing (RDT) is indicated to provide access to diagnosis in remote areas in which the conventional serological tests are not available.

Objetive: To evaluate the sensitivity and specificity of RDTs for Chagas disease used at INI-Fiocruz.

Methods: CD patients with previous confirmed diagnosis and people under suspicion of disease were evaluated in the immunodiagnostic sector of INI-Fiocruz, using ELISA, ChLIA and RDT tests. CD diagnosis was confirmed when both Elisa and ChLIA were reactive.

Results: From July 2018 to December 2020, 1182 CD serological tests were performed. Three hundred ninety-nine patients simultaneously underwent ELISA, ChLIA, and RDT. Of those, 308 presented both Elisa and ChLIA reactive, and 91 non-reactive. Among individuals with reactive tests, 293 presented a RDT positive (95.1% sensitivity). Among individuals with non-reactive tests, 88 presented a RDT negative (96.7% specificity).

Conclusion: The findings of the present study showed that the RDTs used in the diagnosis of CD at INI-Fiocruz have lower sensitivity and specificity when compared to Elisa and ChLIA.

★★**#15 Area: Education, Information**

PLAYING WITH PORTINARI AND HEALTH: DIALOGICAL WORKSHOP OF ARTSCIENCE TO PROMOTE HEALTH WITH JOY*

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*Summary of the MSc Dissertation
Laboratório de Inovações em Terapias, Ensino e Bioprodutos – LITEB / IOC / FIOCRUZ.

Portinari's work is full of images of playing that complement each other with health promotion through the ArtScience approach: a transdisciplinary concept that allows the reintegration of contemporary knowledge, disciplined fragmented. The present work developed a reflexive dialogical practice: “Playing with Portinari & Health”. Based (i) on the theories of Donald Winnicott, a psychoanalyst and pediatrician, which relates the act of playing with creativity and health, (ii) on the methodological assumptions of Paulo Freire's dialogue, (iii) on the couple's 13 cognitive categories Root-Bernstein to promote and stimulate creativity, and (iv) in the dialogue of laughter by Marcus Matraca. We created the educational workshop based on images that present scenes of playing and of the social determinants of health that provide the transmission Chagas disease and we implemented them with adults participating in the Rio Chagas Association and residents of endemic areas for this parasitic disease. This work presents three interconnected activities: 1. Exhibition of 09 replicas of Portinari to observe, make thematic drawings and create titles for each work; 2. Installation of toys and games to exercise play and free drawing, ever with musicalization by voice and guitar; and 3. Creating mural graffiti collectively. The fieldwork was carried out in 5 cities in the state of Minas Gerais between July 17 to 30, 2019. The more than 200 participants who passed through the workshop, experienced artistic and scientific practices and contributed to broaden the discussion on science, art and health. The results are presented here in the form of articles. 1: Playing with Portinari: dialogic workshop with reinterpretations of the artist's works; 2: “Chagas Express XXI”: a new ArtScience social technology for science and health education in Chagas disease e; 3: Portinari and Health to talk about Chagas disease in an endemic area. We report the dynamics of the educational workshops “Brincando com Portinari”, which generated quali and quantitative evidence that allow us to conclude that they are proposals that promote health through creativity, in a dialogue between Science and Art, contributing positively to the participants, mainly in the way they understand the concept of health and its relationship with playing. Thus, the present work contributes directly to teaching practices in the basic education segment, whether in formal or non-formal spaces. Due to the emphasis given to playing in the whole process of building work, we believe that playing can have a decisive influence on people's health.

Keyword: Science in the Arts, Health Promotion, Social Determinants Health, Portinari, Play, Games and Toys.

Support: CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior).

#16 Area: Education, Information

Scientific Dissemination For Society On Infectious Neglected Diseases Such as Chagas Disease Via Social Media (Instagram)

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Funding: CNPq/PIBIC, Faperj

The SarsCov-2 syndemy declared by the WHO in March 2020 led to the adoption of several universal guidelines including physical distance, hygiene policies (such as soap washings and 70% alcohol to decontaminate hands and surface), and home office (non-essential activities) aiming to mitigate the risks of infection. In this context, scientific communication has become crucial for knowledge dissemination besides fighting against fake news. Social media are facilitating bridges in the learning process. Among the available platforms, Instagram has a greater diversity of resources for posts, such as feeds, stories, and long and short videos through IGTV and REELS, respectively. Thus, an Instagram profile named Ciência *Press* (@ciencia.press) was conceived aiming to spread science in small bulletins (few minutes), being also a forum for scientific debate and information, aiding to fight against false “science”, known as fake news. Through this widespread media using different tools such as Canva, Pixlr, InShot and ShotCut, the scientific content may be quickly updated, reaching all society and allowing to access information built on scientific evidence disclosed by official databases. Also, our videos are publicized via Whatsapp to increase the society audience. Among the different public health subjects, Chagas disease, this neglected illness caused by the protozoan *Trypanosoma cruzi*, has been divulged in our media through posts using subtitled videos to increase an inclusive and accessible approach about this severe disease. Currently, Ciência *Press* has 105 followers and 18 publications and hopefully it will increase as part of our contribution to the science network and dialogue with society with playful, interactive and technological educational tools.

Supported by CNPq, FAPERJ (CNE), IOC/Fiocruz

#17 Area: Education, Information

Health Promotion with PICS: the workshop “Knowing Reiki in Expresso Chagas 21”

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Introduction: Integrative and Complementary Practices in Health were introduced in the Unified Health System (SUS) in 2006, expanding to 29 practices by 2018. We highlight the second Ordinance of the Ministry of Health No. 849 of 2017, introducing 14 therapeutic practices into the National Policy of Integrative and Complementary Practices in Health (PNPIC) in the SUS, including reiki. Reiki channels vital energy through the Reiki's hands to promote the energy balance necessary for physical, mental and spiritual well-being. In one of the six imaginary wagons of the Expresso Chagas XXI called 'Health Promotion with ArtScience', we carried out the educational action that presented reiki as a health care practice for visitors to the São Cristóvão Fair, in Rio de Janeiro, on 09/29/ 2019.
Objective: Disseminate the Integrative and Complementary Practices in Health (PICS) with application of Reiki in the “Health Promotion with ArtScience” wagon of Expresso Chagas 21, an itinerant and educational exhibition created by the Oswaldo Cruz Institute to talk about Chagas disease with the community.
Methodology: A portable massage bed, a sound of mantras software, sweet orange essential oil and water flavored with lemon were used. All materials were sanitized with 70% alcohol between each participant. The application time by the Reiki patient lasted 20 minutes and, at the end, the sweet orange essential oil was used in the region of the participant's forehead chakra to awaken them, with the suggestion of drinking a glass of flavored water. At the end of the practice, the participant was asked how he felt.
Results: A patient with Chagas disease from Rio Chagas Association reported “recovery of his mind and body”, feeling of “rejuvenation, calm and relaxation”. In two other cases, an IOC researcher and health manager reported having felt a “great relaxation”, as if he had “renewed energy and eliminated tensions”. A bus driver professional informed that due to his activity he presented “tension and discouragement” and after reiki, reported improvement in “physical health”, “more animated”, feeling of “well-being and calm”. All those attended conveyed a feeling of gratitude and happiness with the reiki care.
Conclusion: In the action described in this work, the benefits of reiki for physical and mental well-being and energy balance were reported. Description of feelings such as relaxation, lightness, gratitude, happiness, "recovery of mind and body", rejuvenation, cheerfulness, well-being and calm were reported. Everyone who was assisted felt better after the reiki application.

Support: POM Fiocruz

#18 Area: Education, Information

Use of audiovisual material for education and information on Chagas Disease: Experience report of a dialogic workshop

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In the Americas, Chagas disease (CD) is found in 21 countries where difficulties in accessing diagnosis and treatment are unresolved issues. According to the World Health Organization (WHO), CD is considered neglected due to the inefficiency of global policies that involve research, drug production and the availability and access to information and education for the population in an endemic region. Currently, it is estimated that there are between 7 million people infected with *T. cruzi* in the world and more than 70 million live at risk of contracting the infection. Therefore, this work aims to present a teaching proposal centered on the use of an audiovisual resource for the approach of CD. To this end, we present an experience report of a pilot workshop carried out with a class of Lato sensu Postgraduate in Science, Art and Culture in Health, from the Oswaldo Cruz Institute. The practice was carried out within the scope of "Special Topics in Health Promotion". For the activity we used an audiovisual material, a Live-Action from a Japanese Manga, called In Hand by Ao Akato. In Hand is a medical suspense in which its protagonist is Dr. Tetsu Himokura, a researcher specialized in infectious and parasitic diseases, where the symptoms and the cause of the disease are involved in a suspense and action plot. CD appears as a theme in the first episode. After the presentation of key excerpts from the film, a conversation circle was held in which issues such as: facilitated teaching, interesting material for adolescents, explanation of the disease with animation, possibility of dealing with various themes, innovative were some points mentioned and discussed. Then it was proposed the collective construction of a Fanzine addressing CD. We emphasize that for the discussion of the theme of CD in audiovisual resources and educational materials it is important to consider the place where the work was produced, the socio-cultural and anthropological aspects, since the representations of Chagas disease may be different. Workshop participants highlighted the potential of employing the activity, especially with young people and schoolchildren. In addition, we report the active participation of the subjects in the elaboration of the collective fanzine, encouraging group work. Thus, we conclude that the material chosen for the workshop presents a powerful resource to be used in education and health promotion activities, covering different approaches and aspects involving Chagas disease.

★**#19 Area: Education, Information**

FluorArte Workshop in Expresso Chagas 21: An ArtScience strategy to discuss Chagas disease using fluorescent images

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Chagas disease (CD) is a neglected disease caused by *Trypanosoma cruzi* and transmitted by a Reduviidae bug. The absence of symptoms in 70% of infected people make it an invisible disease. Strategies that reach affected people, empowering them about the disease knowledge and to fight for their rights, are powerful. In this context, “Expresso Chagas 21” (EC) was created as an itinerant social technology that integrate art and science for education in non-formal teaching spaces, health promotion and active search of infected people. Here, we described the FluorArt workshop that integrated the activities of EC during the expedition for five cities in Minas Gerais (Brazil). FluorArt workshop is based on ArtScience strategy, was inspired by the fluorescence microscopy technique and promotes the observation of images related to the CD obtained from scientific papers, discussion and creation of “fluorescent” paintings by the participants. The FluorArt was carried out in steps: i) personal presentation; ii) dice game followed by the question “What do you think this image might be?”; iii) painting of the image interpretation with fluorescent ink; iv) observation of painting in a booth with black light; v) final dialogue about the painting, its relationship with CD and a brief presentation of original fluorescent images in posters. In our results, we found that 20% of the participants of EC participated in the FluorArt workshop (434 people) and we consider this number a good indicator due to the wide variety (41) of activities offered at EC. Concerning the gender of the workshop participants, 64% were female and 36% were male, as for age, the workshop was attended by the public of all age groups with participants from 1 to 86 years old, which demonstrates its versatility. Regarding the participants answers about what they were observing in the data, the most used words were: *Trypanosoma* (60), cell (47), egg (45), and blood (36), which suggests that most participants in the FluorArt Chagas workshop had some degree of knowledge about Chagas disease and /or understood the context of the EC exhibition. Related to paintings, we classify as reinterpretations, those that reproduced the data image and, free paintings, as those that did not reproduce it. We identified that 83.5% represent reinterpretations and 16.5% represent free paintings. The workshop was validated when the relationship with ArtScience was verified by aligning it with the ArtScience method and with the thirteen cognitive categories for the development of creative ability. The FluorArt workshop was well accepted by the participants and presented enormous potential for education and health promotion, contributing to EC in the awareness and empowerment of vulnerable population exposed to CD.

Financial Support: FIOCRUZ / CNPq

★**#20 Area: Education, Information**

Chagas Express: Breaking Barriers of Information and Communication to Life in COVID-19's Pandemic

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At Oswaldo Cruz Institute, the Laboratório de Inovações em Terapia, Ensino e Bioprodutos (LITEB) has a multidisciplinary profile acting in 3 main subjects: novel therapies, education and bioproducts prospection, ranging from basic research in cell biology, microbiology and immunoparasitology to translational research, resulting in several products, in addition to biomedical and social technologies. To spread the LITEB products and thus providing updated knowledge and scientific communication with society at large, different social technologies and medias have been produced, including those related to Chagas disease, a severe illness caused by the parasite, *Trypanosoma cruzi*. Our present goal is to transform the results of LITEB's projects into media objects – videos, images, interactive websites – related to neglected health problems, such as Chagas disease. Among the LITEB products, we highlight the Expresso Chagas Online version, now founded by a Fiocruz Inova project. It consists in an expansion of the Expresso Chagas, an itinerant, interactive experience themed after Carlos Chagas's cabinet that was adapted from a train wagon, in which he made the discovery of Chagas disease in 1909. In 2019, a crew composed of Rio Chagas association members, researchers from various academic levels from Fiocruz and local health professionals organized an expedition to endemic cities in Minas Gerais. Visitors could engage in various ArtScience activities in the 6 wagons, including testing for Chagas, identifying possible sources of contamination, observing the protozoan through the microscope, and then drawing what they saw with fluorescent paint, participating in musical activities, among others. A second expedition is expected to visit Rio de Janeiro, Minas Gerais, Goiânia and Pernambuco in 2022, with added COVID-related materials throughout the wagons, to present transversally contents dealing with the efforts to face COVID-19 living with Chagas disease. A website for the Expresso Chagas is currently being developed, translating the wagon activities into interactive digital experiences. In addition to the videos already produced for the first Expresso Chagas, translations of foreign pedagogical videos and new ones based on archival material will also be posted on the website. The bulk of our products aim to provide society awareness and interest in scientific development about this silent and neglected disease that affects more than 6 million individuals.

Support: Ministério da Saúde, CNPq, FAPERJ, FIOCRUZ, IOC

#21 Area: Education, Information

Chagas Disease in times of COVID-19: Reports from the presidents of the Chagas disease Associations in Brazil

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On March 2020, the world faced the COVID-19 pandemic and health safety measures were adopted, one of them was the social isolation. The pandemic leads us to reflect on how a global disease affects, not only health, but human values and social layers, and it brings us to the concept of syndemic, created by Merrill Singer. The syndemic designates this combination between health and the social, economic, and cultural contexts of a population. To identify the impact of COVID-19 on Chagas disease patients, we interviewed the Presidents of the Chagas disease Associations of in Brazil. The interviews were conducted by Zoom or WhatsApp and all interviewees signed the informed consent form. Six presidents of Chagas disease Associations were enrolled in our study (Associação Rio Chagas, Associação Goiana dos Portadores de Doença de Chagas, Associação dos Portadores de Doença de Chagas de Campinas e Região, Associação dos Portadores de Doença de Chagas de Pernambuco, Associação dos Portadores de Chagas do Estado da Bahia and the Associação dos Chagásicos da Grande São Paulo). All the participants reported that the COVID-19 pandemic directly affected their lives: (1) the hospital care rules suffered alterations, for example the change in the logistics of the cars that brought Chagas disease patients from the interior of the state to the reference centers; (2) The shift to virtual care during the COVID-19 pandemic was also pointed and; (3) they also reported the sadness and pain caused by the death of Chagas disease patients friends . Moreover, they highlighted the important role of the Associations during the pandemic, emphasizing the need to pay attention to health care, exercising dialogue, the exchange of experiences, the place to remove COVID-19 doubts and also be a to be a site affection, laughter and emotional support. They elucidated a existing groups in WhatsApp, a virtual environment chosen by the ease of use. Some presidents also emphasized the need of to promote the Chagas disease patients mental health. Besides that, some presidents of associations highlighted the insecurity related to COVID-19: "I am afraid to go out in the street, because I don't know where it comes from and how it is caught, some people say it is through the air, another one says from another person and you don't really know where this little thing that knocks you down comes from". Thus, we could conclude that the associations played an important role during the COVID-19 pandemic and that there is a need to increase the dialogue between the academy and the associations to overcome COVID-19 misinformation.

Keywords: COVID-19; Chagas disease; Associations of Brazil.

Funding: CAPES; FAPERJ.

★**#22 Area: Education, Information**

Chagas Express XXI: a new social technology for health and science education

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Chagas disease (CD) affects 6 million people worldwide and is related to poverty-promoting conditions. Aiming (1) to translate CD discoveries into education/information practices leading to increase alertness and empowerment of affected people; and (2) to perform an active search of CD cases, we developed and tested under field conditions a new social technology: an itinerant education interdisciplinary setting named “Chagas Express 21” (CE21). It was unique experience developed in Brazil, that fuses ArtScience practical workshops build about a CD. CE21 articulates workshops, exhibitions, games, practical laboratory activities and conversation/participation rounds, with relevant content for endemic areas with prevalence of chronic cases or risk of acute cases. EC21 was developed by researchers and students at Fiocruz and CD patients who participate at the *RioChagas* Association. The artistic concept configured the EC21 in the format of a train station as an entrance and exit, followed by a set of six “wagons” forming an imaginary train with various education and playful activities. Alluding to the train car adapted as the doctor’s office and laboratory room where Carlos Chagas discovered the CD causing parasite, *T. cruzi*. Identified at the station, participants were sensitized to the exhibition and follow the thematic wagons: (1) CD Associations, (2) Innovations&Laboratory, (3) Discoveries&Play, (4) Home&Environment, (5) Well-Being and (6) Your Voice. Descriptive statistics showed quantitative data collected in the expeditions (CD knowledge and serological results). Qualitative data accessed the public perceptions about the education activities. CE21 was exhibited in local schools in four CD endemic cities (Grão Mogol, Espinosa, Montes Claros and Lassance – Minas Gerais State), engaging 2,117 people that evaluated the 41 activities. Citizens and health professionals enjoyed acquisition of information related to blood, parasites, and vectors of CD. Further, local legacies were 600 participants volunteering for health promotion groups and CD associations, local empowerment to fight for better health conditions and 05 mural paintings. We noticed that 95% of the evaluators loved or liked very much the education activities in all spaces; 81% of the participants ignored the possibility of treating CD; 52% asked for CD blood testing and seropositivity was 20%. CE21 acts as an educational social technology that emerged from an integration of research, education and extension disseminating information through dialogic message between academia and society.
Key words: Chagas disease; education; active search and ArtScience.

Financial support: CAPES; CNPq; FAPERJ and Fiocruz-MS.

#23 Area: Education, Information

Education actions as prevention and control of triatomines in locality of epidemiological surveillance in the state of Piauí, Brazil

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Health education is the field of practice and knowledge in the health sector that has been more directly occupied with creating links between medical action and the population's daily thinking and activities. Therefore, it is essential that the population in areas where triatomines occur is always informed about the insect and Chagas disease, so that they can take the necessary measures, aiming at prevention and better living conditions. This study aggregated educational actions contributing to the fortification of epidemiological surveillance in the municipalities of Simplício Mendes and São João do Piauí, both located in the southeastern mesoregion of the state of Piauí. The actions were aimed at actors involved in health activities, responsible for passing on knowledge to the population: health agents, agents of endemic and doctors, in the form of training courses lasting 40 hours a week, with theoretical and practical classes. Theoretical classes addressed the themes of biology and ecology of triatomines, their relationship with the transmission of Chagas disease, field collection techniques and prevention and control measures. Based on theoretical knowledge, in practical classes, students identified the species of triatomines, most common in the region, using the dichotomous key. To understand the cycle of the parasite in the insect vector and recognize the internal structures, they performed the triatomine dissection, following biological safety protocols. As a result, the project reinforced partnerships between the Health Secretariats of the municipalities of Simplício Mendes and São João do Piauí, and Fiocruz Piauí, as well as serving as a model for other projects, contributing to the improvement of living conditions in the community, improving services of municipalities with regard to neglected diseases and generating relevant results becoming "self-sustainable". The actions continue to be articulated with other municipalities in the state of Piauí, maintaining the goals advocated by Fiocruz Piauí work plan, since education is an important tool to guarantee success in health prevention programs.

Support: CAPES and Fiotec

#24 Area: Epidemiology

Epidemiological and clinical profile of *Trypanosoma cruzi*-HIV coinfection in a cohort of patients followed at the Evandro Chagas National Institute of Infectious Disease (INI) - Fiocruz

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Introduction: Chagas disease (CD) coexist with the acquired immunodeficiency syndrome (AIDS). Patients with CD can become infected with HIV and develop immunosuppression and CD reactivation. In Brazil, the prevalence of coinfection is approximately 1.3%, resulting in 12,558 cases of *Trypanosoma cruzi*-HIV coinfection.
Objective: To identify the prevalence of *Trypanosoma cruzi*-HIV coinfection in the cohort of patients with CD at INI-Fiocruz. The epidemiological and clinical characteristics, the incidence of CD reactivation, mortality, and causes of death were also investigated.
Method: Retrospective observational study, consisting of patients with CD followed up at outpatient center at INI-Fiocruz, from July 1986 to April 2021. Clinical forms of patients were classified according to the 2nd Brazilian Consensus on CD.
Results: Among 2194 patients (1154 [52.5%] women and 1040 [47.5%] men), 11 (0.5%) co-infected Trypanosoma cruzi-HIV were identified (7 [63.6%] women and 4 [36.4%] men) with a mean age of 50.1 (ranging from 38-66). Five patients were originated from Minas Gerais, 4 from Bahia, 1 from Ceará and 1 from Paraíba. Two had the indeterminate form (18.2%), 6 the cardiac form (54.5%), 2 the digestive form (18.2%) and 1 the cardio-digestive form (9.1%). In term of cardiac form classification, two had stage-A (28.5%), two stage-B1 (28.52%), two stage-B2 (28.5%) and one stage-C (14.5%). Eight patients had a CD4 count at HIV diagnosis with an average of 286.3 (50-591) and received antiretroviral therapy. During a median follow-up of 7.3 years (IQR 25%-75% 0,9-10,5), there was 1 (9.1%) reactivation due to myocarditis (patient who did not use antiretroviral), which occurred 1.07 years after the diagnosis of HIV, and 6 (54.5%) deaths, with a median follow-up time of 2.0 years (IQR 25% -75% 0.9-10.5), of those 1 being directly related to CD (sudden death), 3 to AIDS (neurotoxoplasmosis, atypical mycobacteriosis and unidentified respiratory failure), 1 to ischemic heart disease and 1 to esophageal neoplasia. The deaths related to immunosuppression occurred in 2 patients who did not receive antiretroviral therapy and in 1 due to low adherence to treatment. One (9.1%) patient lost follow-up
Conclusion: HIV infection and CD reactivation was a very reserved prognosis before the advent of antiretroviral therapy. Early diagnosis of CD reactivation and prompt treatment dramatically reduces mortality. Therefore, identifying the co-infected *Trypanosoma cruzi*-HIV carrier is extremely important to offer antiretroviral treatment, measure CD4 levels, monitor parasitological status and start trypanocidal therapy early in case of CD reactivation.

★**#25 Area: Epidemiology**

Chagas' disease mortality and the COVID pandemic: experience of the Evandro Chagas National Institute of Infectious Diseases (INI), Fiocruz

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Introduction: The first cases of the new coronavirus (SARS-CoV-2) infection were identified in Brazil at the end of February 2020. Since then,1.3 to 3.2 million Brazilian patients with Chagas disease (CD) are at risk to be exposed to this viral infection. There are no studies on how this pandemic affected patient with CD and whether the cardiac involvement, that is present in 30% of these individuals, may interfere the evolution of the COVID-19.

Objective: To describe the mortality rates (all-cause and by COVID-19) during pandemic period and to investigate the relationship between Chagas heart disease (CHD), presence of comorbidities and death.

Method: Retrospective observational study, consisting of patients with CD followed at the outpatient center at INI-Fiocruz, from March 2020 and May 2021. CHD was classified according to the 2nd Brazilian Consensus on CD.

Results: A total of 909 records were reviewed, 58.1% women, with an average age of 64.5 ±11,3 years. Most patients were born in Bahia (24.8%) and Minas Gerais (20%) states. CD classification was as follows, 532 (58.5%) had the indeterminate form, 222 patients (24.4%) were at CHD stage-A, 93 (10.2%) at CHD stage-B1, 28 (3.1%) at CHD stage-B2, 33 (3.6%) at CHD stage-C and 1 (0.1%) at CHD stage-D. Thirty-five deaths were identified (3.9% all-cause mortality rate), of those 13 related to CD, 16 not related to CD, 11 due to COVID-19, and 6 from unknown causes. Therefore, 31.4% of the deaths were related to COVID-19. Of the 11 patients who died from COVID-19 (mean age 72.5±10,1 years), most were women (n=8), 2 had the indeterminate form (18.2%), 4 were at CHD stage-A (36.4%), 1 at CHD stage-B2 (9.0%) and 4 at CHD stage-C (36.4%). All of them had comorbidities (most three or more) with a predominance of arterial hypertension (100%) and dyslipidemia (81.8%). Comparing deaths from Covid and deaths from other causes, regarding cardiomyopathy, there were no differences between patients with normal echocardiogram (n=13 [44.8%]) and patients with altered echocardiogram (n=16 [55.2%]) (chi-squared p-value=0.41). However, regarding comorbidities, there were differences between those who had three or more (n=7/29 [24.2%]) and those who did not or had one or two (n=22/29 [75.8%]) (chi-squared p-value<0.001).

Conclusion: COVID-19 represented one-third of deaths in CD patients during the pandemic period. The presence of multiple comorbidities seems to make CD population highly susceptible to an ominous prognosis in COVID-19.

★ **#26 Area: Immunology**

CX3CL1/Fractalkine: A potential inflammatory mediator in experimental *Trypanosoma cruzi* myocarditis

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Trypanosoma cruzi is a flagellated protozoan capable of triggering a mammalian immune response, prompting progressive inflammatory mechanisms through activation and recruitment of leukocytes and release of inflammatory mediators, which leads to *T. cruzi*-induced myocarditis. The chemokine CX3CL1 has been highlighted for its potential to control parasite replication in the end-clinical status of infected hosts. This study aimed to investigate the systemic and local (heart) release of CX3CL1 in experimental *T. cruzi* infection by establishing an inflammatory axis with endothelin-1 and TNF (tumor necrosis factor) production. Male Fisher rats (n=20) were placed into equal-sized uninfected and *T. cruzi*-infected (Y strain) groups, and parasitemia and mortality were evaluated for 15 days. Immunoassays were performed in the cardiac tissue macerated supernatant and in serum to evaluate CX3CL1, endothelin, and TNF production on days 5 and 15 of infection. The results showed that *T. cruzi* infection induced a higher serum and cardiac macerate production of all investigated mediators during the peak of parasitemia (5 th day) and after 15 days of infection. In addition, on day 15, CX3CL1 showed a positive correlation with TNF ($r = 0.723$, $p < 0.001$) and endothelin-1 ($r = 0.857$, $p < 0.001$). Together, these data reinforce a direct positive correlation between CX3CL1 and the classic mediators TNF and endothelin-1 on the *T. cruzi* – inflammatory signaling axis. Even considering evidence that CX3CL1 release might be partially controlled by the parasite, endothelin-1, and TNF during myocarditis development, further studies are needed to precisely determine the role of CX3CL1 during *T. cruzi* pathogenesis and to investigate this chemokine as a promising therapeutic target.

Keywords: CX3CL1; *Trypanosoma cruzi*; inflammation; endothelin-1.

Support: UFOP; CNPq; CAPES; FAPEMIG; PEPROTECH US/Brazil.

★**#27 Area: Parasite (genetic, molecular, biological and morphological diversity)**

Identification of *Trypanosoma cruzi* ribose-5-phosphate isomerase inhibitors for Chagas disease chemotherapy: from an *in vitro* approach into the wilderness of exploring protein sequence-structure-function diversity

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The enzyme ribose-5-phosphate isomerase of *Trypanosoma cruzi* (TcRpi) might be a suitable drug target for Chagas disease chemotherapy, since it is essential for parasite survival and share no significant sequence and structural similarity to its human analog, HsRpi. In the present work, we aim to clone, express and purify recombinant TcRpi and HsRpi enzymes to test their inhibition profiles with compounds previously identified by virtual screening. However, while cloning the TcRpi gene of Y and CL Brener strains, we found six TcRpi protein sequences displaying several amino acid substitutions compared to the reference TcRpi sequence of CL Brenner. Preliminary results suggest that one of these variants is less efficient than what has been reported in the literature, raising questions concerning the sequence and functional diversity of TcRpi in *T. cruzi* populations. To address these issues, we BLAST searched TcRpi sequence variants deposited in GenBank, UniprotKB and TriTrypDB, identifying four different sequences. Additionally, we uncovered 133 TcRpi sequences of *T. cruzi* parasites isolated from naturally infected organisms by examining genomic sequencing reads deposited in the Sequence Read Archive (SRA). Some observed substitutions are at or near sites previously reported as implicated in enzymatic properties. Thus, we used homology modelling to generate 3D models of the non-redundant sequences found. The models will be used in molecular dynamics simulations to evaluate if the amino acid substitutions could change protein-ligand interaction. Ultimately, we hope to contribute to the understanding of the relationship between the genetic and functional diversity observed in TcRpi, and any impact on its use as a therapeutic target.

★**#28 Area: Parasite (genetic, molecular, biological and morphological diversity)**

Comparative structure analysis by homology of Murein Endopeptidase in *Rhodnius prolixus*

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INTRODUCTION: *Rhodnius prolixus* is a triatomine with a hematophagous habit. This insect is important in the area of public health as it is a high-capacity vector of *Trypanosoma cruzi* in Latin America. *T. cruzi* is the etiological agent of Chagas Disease or American Trypanosomiasis, a neglected endemic disease according to the World Health Organization (WHO) that mainly affects the population with low socioeconomic status. Studies of the insect midgut microbiota and intestinal enzymes are very important to understand the physiology of the vector and its relationship with the trypanosomatid. Murein endopeptidase is an enzyme reported in gram-negative bacteria related to bacterial wall cleavage. This enzyme was incorporated into the genome of *R. prolixus* probably by the horizontal transfer process and is expressed in the midgut of the insect, possibly acting in the digestion and control of intestinal bacteria. **GOAL:** Analyze a three-dimensional structural model of *Rhodnius prolixus* murein endopeptidase in comparison with its homologous partner from *Escherichia coli*. **METHODS:** The insect protein structure was developed by modelling using the inactive *E. coli* enzyme (without the zinc cofactor) as a scaffold, using the *PHYRE2* bioinformatics program. The two structures (*R. prolixus* and *E. coli*) were compared using the *PyMOL* tool. **RESULTS:** Homology modeling of the murein endopeptidase from *R. prolixus* has a confidence of 100.0 – confirming a true homology – and a high identity percentage of 69%. Surface charges were analyzed by looking positively charged polar (arginine, histidine, lysine) and negatively charged polar amino acids (aspartic acid, glutamic acid) from the two models and no significant differences were found in charge distribution. The distances between the amino acid residues that coordinate the zinc ion (H110, H113, D120, H211) were also analyzed, with no difference between the two structures. **CONCLUSIONS**: There is a similarity in the structure of the two models studied, which reveals that the preservation of the murein endopeptidase in *R. prolixus* may have a functional value for the insect. The analysis of the three-dimensional structure of the enzyme showed great similarity for the surface charges and distance between active site amino acids. A better functional and catalytic understanding will contribute to elucidate physiological and evolutionary aspects, in addition to being able to contribute to the expansion of knowledge of the relationship between the vector and its intestinal microbiota, which is essential to the development of strategies for the control of *T. cruzi.*

Key Words: *Rhodnius prolixus*, murein endopeptidase, bioinformatics tools.

Support: CNPq, Faperj, and Fiocruz.

#29 Area: Therapy (immunotherapy, cellular therapy and others)

Effect of selenium treatment on cerebral alterations observed during acute experimental chagas disease

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Chagas disease (CD) affects 7 million people worldwide and in Brazil approximately 3 million people are infected by *Trypanosoma cruzi*. The main clinical manifestation in the chronic phase is cardiomyopathy. However, central nervous system changes can also occur including stroke, meningoencephalitis, and cognitive damage. Studies show that 25% of stroke cases in patients with CD are not related to cardioembolism and could be associated with alterations of cerebral microcirculation. Recently our group demonstrated that *T. cruzi* acute infection (Y strain) leads to cerebral microvasculopathy in Swiss Webster mice as consequence of endothelial dysfunction, capillary rarefaction and increased leukocytes rolling and adhesion. Currently, treatment options are benznidazole (BZ) or nifurtimox, drugs with trypanocidal effects that presents a cure rate of 80% in the acute phase and 20% in the chronic phase. Therefore, it's necessary to develop therapeutic strategies that contribute to the improvement of clinical manifestations of CD both in acute and chronic phases, regardless of the trypanocidal effect. Selenium (Se) is a trace element with antioxidant properties, essential for the control of oxidative stress. Studies showed that Se is capable of reducing risks of cardiovascular and neurodegenerative diseases, and present beneficial effects in the treatment of cardiomyopathy in acute and chronic phases of CD. In this study, we evaluated in experimental model of acute CD, the effect of Se in monotherapy or in association with BZ on cerebral alterations. Male Swiss Webster mice were inoculated intraperitoneally with 10^4 *T. cruzi* trypomastigote forms (Y strain). After 24 hours, the animals were treated orally with 4 ppm sodium selenite, 50 or 100 mg/kg/day BZ and 4 ppm Se associated with 50 mg/kg/day BZ for 14 consecutive days. Since our group observed increased leukocyte-endothelium interaction in cerebral venules of infected animals, and presence of leukocyte and monocytes in cerebral tissue, we intended to observe if the adhesion molecules involved in diapedesis process were VCAM-1 and ICAM-1. In addition, since we observed a decrease in cerebral blood flow during the *T. cruzi* infection, we investigated if this event were related with change in oxidative stress in the brain tissue. Our previous results demonstrate that treatment with BZ alone or in combination with Se were able to prevent the reduction of parasitemia and mortality. At this point we observed a tendency of increased VCAM-1 expression in the brain of infected animals, also we noted no difference in malonaldehyde levels in the brain tissue of these animals.

Support: CNPQ, FAPERJ, FIOCRUZ.

★★★**#30 Area: Therapy (immunotherapy, cellular therapy and others)**

Treatment with suboptimal dose of Benznidazole and Pentoxifylline regulates microRNA transcriptomic profile in murine model of Chagas chronic cardiomyopathy

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Chagas disease (CD) is caused by the protozoan parasite *Trypanosoma cruzi*. The cardiac form of CD, also called chronic chagasic cardiomyopathy (CCC), is one of the main causes of morbidity and mortality due to cardiovascular disorders in endemic areas. CCC, characterized by persistence of parasite and inflammatory response in the heart tissue, occurs in presence of microRNAs (miRNAs) alterations. miRNAs are a class of small, single-stranded non-coding RNAs that act by preventing transcription or inducing degradation of target mRNA, being involved in several cellular and molecular functions and pathological processes. Here, we investigated the miRNA transcriptome profiling in the cardiac tissue of chronically *T. cruzi*-infected mice, under vehicle control, suboptimal dose of benznidazole (Bz), the immunomodulator pentoxifylline (PTX), and the combined treatment with Bz plus PTX (Bz+PTX), for 30 consecutive days. At 150 dpi, Bz, PTX and Bz+PTX treatments improved electrocardiographic (ECG) alterations, with reduction of the percentage of mice afflicted by sinusal arrythmias and 2-degree atrio-ventricular block (AVB2), compared to vehicle administration. Compared with non-infected mice, miRNA transcriptome profiling revealed alteration as follows: 221 miRNAs in vehicle-treated group, 236 miRNAs in Bz-treated group and 226 miRNAs in Bz+PTX-treated group. Vehicle-treated infected group showed important regulation of pathways related to “organismal abnormalities”, “cellular development”, “skeletal muscle development” and “cardiac enlargement” and “cardiac fibrosis”. The Bz-treated group showed 68 regulated miRNAs, affecting important signaling pathways related to “cell cycle”, “cell death and survival”, “tissue morphology” and “connective tissue function”. Finally, Bz+PTX-treated group showed 58 regulated miRNAs controlling pivotal signaling pathways related to “cellular growth and proliferation”, “tissue development”, “connective tissue development”, “cardiac damage”, “cardiac necrosis/cell death” and “cardiac fibrosis”. The analysis of miRNAs shown to be altered in the acute infection and in *in vitro* studies, when assessed individually the *T. cruzi*-induced miR-146b-5p upregulation was reversed upon Bz and Bz+PTX therapy. The results found here could pave the way for further understanding CD cardiomyopathy onset and progression and allow the evaluation of the efficacy of *T. cruzi* therapeutic strategies. Moreover, identified candidate miRNAs may serve as drug targets alone or combined to other therapies.

Keywords: Chagas disease, microRNA, Benznidazole, Pentoxifylline, Chagas chronic cardiomyopathy. Funding: CAPES, CNPq (311539/2020-3, BPP 306037/2019-0) and FAPERJ (JCNE, E-26/203.031/2018, CNE, E-26/ 210.190/2018).

#31 Area: Therapy (immunotherapy, cellular therapy and others)

From in vitro to in vivo: transforming growth factor beta neutralization reduces *Trypanosoma cruzi* infection and improves the cardiac performance

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The anti-inflammatory cytokine transforming growth factor beta (TGF-beta) plays an important role in Chagas disease, a parasitic infection caused by the protozoan *Trypanosoma cruzi*. The aim of this study was to investigate the effect of 1D11, a neutralizing antibody to all three isoforms of TGF-beta, on *T. cruzi* infection: *in vitro* and *in vivo*. To this end, cardiomyocytes were seeded for 24h, incubated with trypomastigotes and treated with 1D11 (100µg/ml). C57BL/6 mice were also infected with *T. cruzi* (10^2 parasites from the Colombian strain) and, after 120 dpi, treated with 1D11(10mg/kg). In the present study, we show that the addition of 1D11 greatly reduces cardiomyocyte invasion by *T. cruzi*, *in vitro*. Further, the treatment significantly reduces the number of parasites per infected cell. In a murine experimental model, the *T. cruzi* infection altered the cardiac electrical conduction: decreasing the heart rate, increasing the PR interval and the P wave duration. The treatment with 1D11 reversed this process, improving the cardiac performance and reducing the fibrosis of the cardiac tissue. Taken together, these data further confirm the major role of the TGF-beta signaling pathway in both *T. cruzi* infection, *in vitro* and *in vivo*. The therapeutic effects of 1D11 are promising and suggest a new possibility to treat cardiac fibrosis in the chronic phase of Chagas' heart disease by TGF-β neutralization.

Key words: Chagas disease; TGF-beta and 1D11.

Financial support: CAPES; CNPq and FAPERJ.

★**#32 Area: Vaccine**

Needle-free vaccine induce neutralization antibodies against T*rypanosoma cruzi*

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Chagas disease is caused by the intracellular pathogen *Trypanosoma cruzi*, and it is estimated that 8 million people are infected by this parasite. There has been an increase of cases in recent years due to contaminated food (oral infection) and congenital transmission. Needle-free vaccine has the advantage of being painless, easy, fast and safe application. With that in mind this work proposes developing a needle-free immunization protocol via intranasal route using transalidase (TS) as antigen. BALB/c mice were immunized via intranasal route (10 µL per nostril) with Human Adenovirus 5 containing TS gene (AdTS) or b-galactosidase as control (Adb-gal). The protocol used in this work was prime-boost homologous immunization with 14 days apart from prime to boost. Parasitemia, survival rate, ELISA, ELISpot and neutralization assay were used to evaluate the protective response. The mice immunized with AdTS intranasally presented lower parasitemia compared with Adβ-gal ($p = 0.04$) and greater survival (log-rank $p = 0.02$). The Adβ-gal group didn't present antibody of any class or spots in ELISpot. The mice immunized with AdTS present high levels in the serum of specific IgG1, IgG2a e IgGb after prime, but not after the boost. The AdTS group present specific IgA after boost in the serum and mucosal tissue. Specific IgG ASC cells were found in spleen and submandibular lymph node. After 20 days after boost the ASC cells were found in bone marrow producing specific IgG and IgA. *In vitro* neutralization assay showed that serum from mice immunized intrasanal can neutralize *T. cruzi* invasion in VERO cells. This data suggest intranasal vaccination with AdTS can protect against *T. cruzi* infection. Further investigations are needed to evaluate the protective immunity of this vaccination protocol during oral infection and congenital transmission.

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#33 Area: Vector, transmission cycles, ecology and biodiversity

Comparative Antennal Characterization of *Triatoma brasiliensis brasiliensis* and *Triatoma petrocchiae*

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Triatoma brasiliensis complex has eight species with different levels of epidemiological importance, and all are vectors of the protozoan *Trypanosoma cruzi*. This protozoan, when in contact with the human being's organism, causes Chagas disease, a neglected disease that has affected thousands of people in the world, mainly in Latin America. The study and characterization of the antennal phenotype has been carried out in triatomines in order to detail genera, species and different populations. However, there are few analyzes focused on the antennal structures of the species in the aforementioned complex. Thus, this work aimed to carry out comparative morphological characterization between two species of the complex: *Triatoma brasiliensis brasiliensis* and *Triatoma petrocchiae*. Scanning electron microscopy images of the antennae of males and females of the two species mentioned were used, where it was possible to show the different sensillae present in each of the four antenna segments. The preliminary results of this study show that bristles type sensilae with mechanoreceptor function - were found in both analyzed species and in abundance (100%) in all antennal segments, only appearing in a smaller quantity (10-20%) in the flagella, which corroborates with the literature for other species already studied. Trichoid sensillae, which are chemoreceptors, Trichoid sensillas, which are chemoreceptors, were found in the two flagella (100% occurrence in each segment) of both species, in addition to also occurring in the pedicel of *T. b. brasiliensis*. Species of triatomines that can live in different habitats have many chemoreceptors on their antennae. In *T. b. brasiliensis* coeloconic sensillae, with thermohydroreceptor function, were observed in the exhaust of all analyzed antennas, both in males and females. In *T. petrocchiae*, this sensilla was present only in the female's left scap, this sensilla being the main responsible for responding to varied thermal stimuli. Campaniform sensilae (mechanoreceptors) were seen in the scap and pedicel of the males of *T. b. brasiliensis*, with occurrence of 1-3 of this sensila in each observed segment, and in *T. petrocchiae*, this sensila was evidenced only in the male scap with an amount of 1-2 per segment. Studies show that this sensilla works as a proprioceptor that monitors cuticular stress, in addition to detecting temperature, humidity and Co2 concentration. The results evidenced confirm the proximity of these species at the morphological level. The presence of a greater number of chemoreceptors in *T. b. brasiliensis* may be related to the greater adaptive potential of this species not only when compared to *T. petrocchiae* but also to the other six members of this species complex.

Support: CnPq, Fiocruz, FAPESP.

#34 Area: Vector, transmission cycles, ecology and biodiversity

Epidemiological importance of species of the subcomplex *Triatoma rubrovaria* through the analysis of vector competence and food source

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The control of Chagas disease, which is caused by the protozoan *Trypanosoma cruzi*, focuses mainly on the eradication of vectors with proven adaptation to human dwellings. Although domiciled insect vectors are the most important epidemiologically, autochthonous vectors of secondary epidemiological relevance are constantly collected in anthropic environments, providing a risk of transmission of the parasite to humans. This study proposed to identify species of the subcomplex *Triatoma rubrovaria* through molecular taxonomy and to analyze their vector potential on the transmission of the parasite in the Pampa biome. Different aspects related to vectorial capacity were evaluated, such as food source, infection rate and parasitic genotyping. In parallel, bionomic parameters of *T. rubrovaria* after infection by *T. cruzi* were analyzed experimentally. A total of 1.724 triatomines were collected in Rio Grande do Sul, of which 927 were used for molecular analysis. The phylogeny of the subcomplex grouped the 92 samples successfully sequenced for the Cyt b fragment in nine clades. Of the sequenced samples, 19 (20.7%) were identified as *T. carcavalloi*, 17 (18.5%) as *T. circummaculata* and 12 (13.04%) as *T. rubrovaria*. We observed an infection rate by *T. cruzi* of 2.8% (26/927) in the field, with parasitic load variation ranging from $1.5 \times 10_1$ to $2.3 \times 10_7$ parasite equivalents/intestine and the presence of TcI, TcV and coinfection by TcI + TcIV. Twelve species of mammals were identified, in addition to birds and insects, being *Homo sapiens* the most frequently detected food source (73.5%), followed by *Gallus gallus* (33.1%). For vector competence analyses, N5 nymphs of *T. rubrovaria* and *T. infestans* were fed on mice infected with *T. cruzi* (TcVI), in laboratory conditions. We compared the presence and number of evolutionary forms of the parasite in the excreta of both species of triatomines at 30, 60 and 90 days post-infection. *Triatoma rubrovaria* and *T. infestans* presented similar results in infection rates and of *T. cruzi* TcVI metacyclogenesis. Regarding vectorial behavior, we confirm that the triatomine tends to move away from the bite site after the blood meal. Interspecific differences were observed in the volume of ingested blood and in the proportion of individuals who excreted after blood feeding, revealing the higher feeding efficiency and rate of *T. infestans* dejection. The volume of blood ingested and the bite behavior of *T. rubrovaria* seem to be influenced by TcVI infection. Infected specimens tend to ingest ~25% more blood and to bite more frequently the host's head. Furthermore, us analyzes show that *T. rubrovaria* is a potential vector of *T. cruzi*, having bionomic parameters associated with its vectorial capacity similar to the primary vector *T. infestans*, especially when infected, thus alerting to the importance of constant entomological surveillance in the studied areas.

Support: CAPES, CNPq, PAEF (Fiocruz/FIOTEC)

★**#35 Area: Vector, transmission cycles, ecology and biodiversity**

Machine learning applied to the selection of environmental variables in the distribution pattern of *Triatoma vitticeps* infected by *Trypanosoma cruzi* in Espirito Santo, Brazil

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Trypanosoma cruzi presents a complex life cycle and its transmission occurs in different enzootic scenarios. In the Espírito Santo (ES) state, adult triatomines of the species *Triatoma vitticeps* with high *T. cruzi* infection rates are frequently found in the domiciliary environment. However, little is known about the biotic and abiotic variables involved on this transmission. Machine learning is an artificial intelligence approach that was not applied in *T. cruzi* transmission studies. In this case, it was decided to use a machine learning technique to predict the importance of biotic and abiotic variables that influence *T. cruzi* infection in *T. vitticeps* in the Atlantic Forest of ES state. *Triatoma vitticeps* infected or not infected by *T. cruzi* occurrence data were obtained between 2010 to 2019 (n=2508) in different ES state municipalities. From this dataset, the following variables were obtained: wind speed; mammal species richness; NDVI (vegetation index); maximum and minimum temperatures; steam pressure; rainfall; land cover, altitude, and palm trees abundance, through the Google Earth Engine and MapBiomas platforms. The analysis was made using two groups: dry (May to September) and rainy period (October to April) and for the whole dataset (dry + rainy period), analyzed using the Random Forest algorithm (80% of samples for training and 20% for testing) and the importance of the dataset variables was evaluated. Comparing the results between dry and rainy periods and the whole data, the precision values varied between 63% and 83%. From the best model, the variables that influence the transmission were wind speed, mammal species richness, NDVI and palm trees abundance. In conclusion, the machine learning algorithm was capable to model the environmental variables that influence*T. vitticeps* infected by *T. cruzi* occurrence, calculating the statistical importance of the environmental variables, thus making it possible to assist in future studies of *T. cruzi* transmission.

Keywords: *Trypanosoma cruzi*, artificial intelligence, Random Forest, Triatomine, Atlantic Forest
Financial support: Fiocruz, Faperj, CNPq, Sesa/ES and IME

#36 Area: Vector, transmission cycles, ecology and biodiversity

Occurrence of *Trypanosoma cruzi* in triatomines captured by the Epidemiological Surveillance in the municipality of Barra, Bahia

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Triatomines are insects belonging to the Reduviidae family, popularly known in Brazil as "barbeiro". These hematophagous insects have a hemimetabolous development that is characterized by three distinct stages: the egg, nymph and adult stage. All of these stages, except the egg, have the potential for transmission of *Trypanosoma cruzi* to vertebrate hosts. *T. cruzi* is a flagellated protozoan causing Chagas disease (CD). After the implementation of the Chagas Disease Control Program with the eradication of vectorial transmission by *Triatoma infestans*, other species of secondary importance with high potential for *T. cruzi* transmission have emerged. The objective of this study was to perform the taxonomy and parasitological diagnosis of feces of triatomines captured through active and passive search conducted by endemic agents in households in the municipality of Barra, Bahia, upon population notification. Between September 2019 and September 2020, the capture of triatomines was performed in the rural and urban areas: intradomicile and peridomicile. A total of 255 triatomine specimens of two species were collected: 253 specimens of *Triatoma sordida* and 2 specimens of *Triatoma pseudomaculata*. *T. sordida*, endemic to the region, was the most frequent, being 99.2% (253/255), this is a common and frequent species in human habitations. 84 specimens were submitted to direct investigation for *T. cruzi* by stool smear, the remaining specimens were unviable for examination. In the rural peridomicile, 81 females, 31 males and 77 nymphs were collected, while in the rural intradomicile, 12 females, 3 males and 6 nymphs were captured. In the urban peridomicile 8 females, 7 males and 11 nymphs were captured, while in the intra-household only 16 males and 3 females were collected. The natural infection rate was 1.1% (01/84). Thus, infestation and colonization by triatomines was higher in the peridomicile, and the only positive triatomine was from this environment, showing how vectors of secondary importance can become infected and have access to the household. It is worth mentioning that the municipality of Barra has been considered high risk for Chagas disease vector transmission since 2006. The presence of positive vectors in the community suggests the immediate action of public agencies, through preventive and educational actions, making the population aware of the importance of passive search and the epidemiological relevance of triatomines, avoiding exposure of residents to the protozoan parasite, requiring the continuous work of community workers through active searches and educational activities.