CICLO CARLOS CHAGAS DE PALESTRAS

7ª EDIÇÃO

110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

LIVRO DE RESUMOS

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

110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Ciclo Carlos Chagas de Palestras – 7ª edição

100+10 ANOS DA DESCOBERTA DA DOENÇA DE CHAGAS: O TEMPO NÃO PARA 110 DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Local: Auditório Emmanuel Dias - Pavilhão Arthur Neiva
Organizadores: Marli Lima e Joseli Lannes
Colaboradora: Raquel Aguiar

Prezados participantes,

Neste ano, o Ciclo Carlos Chagas de Palestras (CCCP) chega à sua 7ª Edição com o tema **"110 anos da publicação do ciclo da doença de Chagas"**. 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, assim como manter uma pauta viva de discussão sobre a doença de Chagas diante dos desafios a serem enfrentados. Nos últimos 6 anos, esta foi uma oportunidade para reunir pesquisadores da Fiocruz e de outras Instituições, nacionais e 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. Foi neste fórum que, em 2016, lançou-se a ***RioChagas***, primeira Associação de Portadores da Doença de Chagas do Rio de Janeiro.

Reafirmamos nossa disposição em continuar fazendo o que acreditamos, em nome da ciência e da formação de nossos estudantes e pesquisadores. Neste ano em que celebramos os 110 anos da descoberta da doença de Chagas, realizamos o CCCP de forma associada ao Centro de Estudos do Instituto Oswaldo Cruz em 4 seções mensais de abril a julho. Agradecemos aos participantes pelo interesse em nosso evento e aos palestrantes por compartilharem conosco seu conhecimento. Agradecemos, também, aos avaliadores de resumos que contribuíram para a indicação das apresentações orais a serem feitas em 17 de maio. 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.

Nestes momentos em que lidamos, particularmente os jovens, com dificuldades e frustrações, de financiamentos e perspectivas para continuidade de nossos trabalhos, vislumbramos a oportunidade de fortalecer a solidariedade, conhecer a resistência e a resiliência. Pensamos ser também uma oportunidade para renovar as esperanças na força da democracia para mudarmos a nossa sociedade através da educação, da cultura e da ciência e tecnologia.

Uma vez mais recorremos à frase mote de Oswaldo Cruz "***Não esmorecer para não desmerecer***", que nos guia.

Muito obrigado a todos

Marli Lima e Joseli Lannes

110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Ciclo Carlos Chagas de Palestras – 7ª edição

100+10 ANOS DA DESCOBERTA DA DOENÇA DE CHAGAS: O TEMPO NÃO PARA
110 DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Local: Auditório Emmanuel Dias - Pavilhão Arthur Neiva
Organizadores: Marli Lima e Joseli Lannes
Colaboradora: Raquel Aguiar

Programa Científico ABRIL / MAIO

12 abril de 2019
Centro de Estudos Especial

08:35h – 09:30h Inscrições

09:30h-10:00h – Abertura
Presidente da Fiocruz **Nísia Trindade**, Vice-Presidente de Pesquisa e Coleções **Rodrigo Corre-Oliveira**, Diretor do IOC **José Paulo Leite**, Representante da Associação de Portadores da Doença de Chagas do Rio de Janeiro e Organizadores do CCCP

10:00 – 10:20hs - Associação Rio Chagas – Avanços e desafios – **Nancy Costa** – Presidente da Associação de Portadores da Doença de Chagas – Rio Chagas

10:20 – 11:00hs - Projeto Selênio - avanços científicos e retorno ao portador da doença de Chagas - **Tania C. de Araújo-Jorge** – LITEB – Instituto Oswaldo Cruz

11:00 – 11:40hs - Impactos do Programa de Exercícios Físicos na capacidade cardiopulmonar do portador da doença de Chagas - **Fernanda Sardinha** - Cardiologia - Medicina do Exercício e do Esporte - Clínica Médica - Instituto Nacional de Infectologia Evandro Chagas (INI/Fiocruz)

17 maio de 2019
Centro de Estudos Especial

09:00h-10:00h
Apresentação dos trabalhos selecionados

1- Resumo selecionado
2- Resumo selecionado
3- Resumo selecionado
4-Resumo selecionado
5- Expresso XXI – **Tania C. de Araújo-Jorge**

10:00 – 10:40hs - Pacientes o actores? Reflexiones en torno al proyecto “Pasa la voz” - **Leonardo de La Torre** - International Health Department at the Hospital Clínic de Barcelona

10:40 – 11:20hs - Agendas inconclusas para doença de Chagas: contextos epidemiológicos e perspectivas em um mundo em rápida transformação - **Alberto Novaes** – Universidade Federal do Ceará

CICLO CARLOS CHAGAS DE PALESTRAS
7ª EDIÇÃO
2019

110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Programa Científico JUNHO / JULHO

~~14~~ junho de 2019
Centro de Estudos

10:00 – 12:00 hs – Mesa Redonda:
Reflexões sobre "100+10 anos da descoberta da doença de Chagas: conquistas e desafios para a próxima década"

Coordenadoras: Joseli Lannes e Marli Lima

Comentaristas (10 minutos por comentário):

1- **Maria de Nazaré Soeiro**
2- **Tania de Araújo-Jorge**
3- **Rodrigo Correa-Oliveira**
4- **Andrea Silvestre**
5- **MSF - representante**
6- **DNDi - representante**

Discussão com plenária

Atenção: devido à programação de greve geral, provavelmente, nosso encontro de junho será **13/06** (confirmação em breve)

12 julho de 2019
Centro de Estudos

10:00 – 10:40hs - A descrição de uma nova doença: reconhecimento e controvérsia - **Simone Kropf**, pesquisadora da Casa de Oswaldo Cruz (COC/Fiocruz)

10:40 – 11:20hs - Joias do acervo iconográfico do Fundo Carlos Chagas - **Aline Lacerda**, chefe do Departamento de Arquivo e Documentação da Casa de Oswaldo Cruz (COC/Fiocruz)

CICLO CARLOS CHAGAS DE PALESTRAS
7ª EDIÇÃO
2019

110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Resumos de Participantes

Comissão Avaliadora de Resumos

Andrea Alice da Silva / UFF
Andrea Silvestre / INI
Claudia Paiva / UFRJ
Cleber Galvão / IOC
Constança Britto / IOC
Cristina Carrazzone / PROCAPE-UPE
Daniel Gibaldi / IOC
Danielle Grynszpan / IOC
Fernando Genta / IOC
Jacenir Mallet / IOC
Joseli Lannes-Vieira / IOC
Juliana De Meis / IOC
Katia Calabrese / IOC
Maria da Gloria Bonecini / INI
Mariana Waghabi / IOC
Marli Lima / IOC
Natalia Nogueira / UERJ
Otacílio Moreira / IOC
Otília Sarquis / IOC
Rubem Menna-Barreto / IOC
Solange De Castro / IOC

Muito obrigado!

CICLO CARLOS CHAGAS DE PALESTRAS 2019 7ª EDIÇÃO

110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Resumos Selecionados para Apresentação Oral

17 de maio 9:00hs – Centro de Estudos Especial

Tema: Biologia celular e interação parasito/célula hospedeira

Farani, P.S.G.; Ferreira, B.I.S.; Gibaldi, D.; Vilar-Pereira, G., Lannes-Vieira, J.; Moreira, O.C. **Regulation of miRNAs in an experimental model of Chagas disease: effects of benznidazole and pentoxifylline therapy on chronic chagasic cardiomyopathy.**

Tema: Educação/informação

Analuz Cunha de Sá Freire Sermarini; Hosana Figueiredo de Athayde; Sheila Soares de Assis; Tania Araújo-Jorge. **Educational approaches of chagas disease: an exploratory analysis.**

Tema: Terapias (imunoterapia, terapia celular e outras)

Roberto Rodrigues Ferreira, Rayane da Silva Abreu, Glaucia Vilar-Pereira, Wim Degrave, Marcelo Meuser-Batista, Nilma Valéria Caldeira Ferreira, Otacílio da Cruz Moreira, Natália Lins da Silva Gomes, Elen Mello de Souza, Isalira Ramos, Sabine Bailly, Jean-Jacques Feige, Joseli Lannes- Vieira, Tania C. de Araújo-Jorge, and Mariana Caldas Waghabi. **Cardiac regeneration after TGF-β inhibitor therapy in a pre-clinical study of chronic Chagas' heart disease.**

Tema: Vetor, ciclos de transmissão, ecologia e biodiversidade

Letícia Paschoaletto, Cauan Antunes, Gabriel A. G. Passos, Jader de Oliveira, João A. da Rosa, Catarina M. Lopes, Teresa C. M. Gonçalves, Jane Costa. **Behavioral and morphometric characterization of sexual selection in males of the triatoma brasiliensis complex.**

CICLO CARLOS CHAGAS DE PALESTRAS
7ª EDIÇÃO
2019

110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Resumo a convite

ASSOCIAÇÃO DOS PORTADORES DE DOENÇA DE CHAGAS DO RIO DE JANEIRO
Fundada em 8 de abril de 2016. Filiada à FINDECHAGAS
CNPJ: 30.381.129/0001-58

Evolução da Rio Chagas de Abril de 2016 a Abril de 2019

Missão: Acolher os portadores da doença de chagas, bem como seus familiares, sem distinção de classe social, nacionalidade, sexo, raça, cor ou crença religiosa.

Visão: promover e desenvolver formas de cooperação entre portadores da doença de chagas, divulgação sobre a doença de chagas, conscientizar e defender os direitos dos pacientes, fazer intercâmbio com entidades afins no âmbito nacional e internacional.

Valores: Acolhimento, proteção a vida, tratamento Humanitário, comprometimento, cooperação, ética, transparência, honestidade, dedicação, competência, respeito, igualdade, democracia, cidadania, liberdade de opinião e expressão.

Na segunda semana de nascida a Rio Chagas foi convidada para participar da Assembleia geral da FINDECHAGAS em Laplata na Argentina.

Como a Associação nasceu em rodas de conversas do **Curso "Falando de Chagas com Alegria",** continuamos neste curso oferecido pela Fundação Oswaldo Cruz e ministrado pelo professor **Marcelo de Oliveira Mendes**, servidor da Fiocruz. Então, em 2016 e 2017 a Rio Chagas não participou de alguns eventos e montou um bazar com o apoio da Fiocruz.

O Brasil tem um sistema complexo na Administração Pública. Então, devido a isso e a falta de recursos financeiros, encontramos dificuldades para registrar a Rio Chagas.

Só em 2018 que conseguimos legalizar de fato a documentação da Associação. Só em 2018 que conseguimos legalizar de fato a documentação da Associação.

Eventos e atividades que a Rio Chagas participou em 2018 e em 2019.

Eventos

1 Participação na sobre a Doença de Chagas da Associação Médicos Sem Fronteiras.
2 Participação no Congresso Fio Chagas em Petrópolis.
3 Participação no Ciclo Carlos Chagas na Fiocruz.
4 Participação na feira de Talentos Fiocruz Saudável e Meio Ambiente.
5 Participação da semana da Doença de Chagas na Cinelândia.
6 Participação no Congresso de Medicina Tropical no Recife
7 Participação no Congresso Internacional FindeChagas no México.

Atividades:

1 Curso básico de Biscuit
2 Curso de Customização de Sandálias
3 Participação com Barraca de artesanato na festa junina dos alunos da FioCruz
4 Divulgação da Associação no Hospital da Universidade Federal do Rio de Janeiro
5 Exposição do bazar no Simpósio Ciência e Arte na Universidade Federal do Rio de Janeiro.

Av. Brasil, 4.365–Pav. Cardoso Fontes, Sala 65 – Manguinhos – Rio de Janeiro – RJ – CEP. 21040-360 Telefone: (21) 2562-1413 E-mail: riochagas@gmail.com.

Aspectos clínicos, estudos de polimorfismos genéticos, biomarcadores
Clinical Aspects, genetic polymorphism, biomarkers

Study association between the parasite *Trypanosoma cruzi* and genetic polymorphisms of cytokines in a cohort of patients with different clinical forms of chronic Chagas' disease

Ana Carolina Bastos de Lima[1], Roberto Saraiva[2], Constança Britto[1], Otacilio Moreira[1]
1-Laboratório de Biologia Molecular e Doenças Endêmicas-IOC/Fiocruz
2-Laboratório de Pesquisa Clínica em Doença de Chagas-INI/Fiocruz

Trypanosoma cruzi is the etiological agent of Chagas' disease (CD), considered one of the main neglected disease in Latin America. CD is characterized by a broad spectrum of clinical outcomes, varying in severity from asymptomatic infection to severe forms related to cardiac damage, as well as digestive tract. Regarding the parasite, its intraspecific heterogeneity has been widely investigated and the correlation of the different genotypes with clinical manifestations of the disease is still a great challenge. The host's genetic profile and immune response to infection are considered important factors in the progression of the disease. This work aims to correlate the parasite load and circulating *T. cruzi* genotype with the genetic profile of patients with chronic CD, by analyzing the profile of SNPs in human cytokine genes. Quantitative Real-Time PCR (qPCR) assays were performed to estimate the parasitic load of *T. cruzi* in blood, with the multiplex TaqMan system. Molecular characterization of *T. cruzi* in DTUs was conducted following methodology based on conventional multilocus PCR reactions. Of the 294 patients analyzed, 133 (45.2%) had positive qPCR, of which 32 presented the indeterminate form of CD, 76 the cardiac form (35 in stage A, 21 in stage B1, 3 in stage B2, 15 in stage C and 2 in stage D), 19 patients with mixed clinical form and 6 with the digestive form. The parasitic load of patients ranged from 0.002 to 72.21 eq. parasites/mL, with a median value of 0.390 [0.0200 - 2.070] eq. parasites/mL. In patients with positive qPCR, it was possible to identify *T. cruzi* genotypes in 72% of them. TcII and TcVI were the prevalent genotypes with 33.3% and 8.3%, respectively. In addition, a single TcV infection was observed in 1 patient (born in Bahia) with chagasic cardiomyopathy (CCC) in stage C, beyond, a TcII+TcV co-infection in 1 patient (born in Paraíba) with CCC in stage A. When comparing the parasite genotypes and parasite load, it was observed a median of 1.065 eq. parasites/mL for TcII genotype and 0.870 eq. parasites/mL for TcVI. Among patients infected with TcII, 71.9% represented CCC cases, whereas for those infected with TcVI, the frequency was 50%. At present, we are standardizing the High Resolution Melting (HRM) protocol for the analysis of SNPs in human cytokine genes. When analyzing the parasite and the host, we hope to find new associations with the potential to be used as biomarkers for chronic CD progression.

Aspectos clínicos, estudos de polimorfismos genéticos, biomarcadores
Clinical Aspects, genetic polymorphism, biomarkers

Influence of angiotensin II type 1 receptor polymorphisms in progression of Chagas' heart disease in a cohort of Brazil

Lucia Elena Alvarado-Arnez[1,2,#], Silvia Marinho Martins Alves[3], Angelica Martins Batista[1], Isabelle de Oliveira Moraes[2], Gloria Melo[3], Cristina Veloso Carrazzone[3], Thayse do Espírito Santo Protásio da Silva[1], Antonio G. Pacheco[4], C. Sarteschi[3], Milton Ozório Moraes[2], Wilson Oliveira Jr[3], Joseli Lannes-Vieira[1]

[1] Laboratório de Biologia das Interações, Instituto Oswaldo Cruz/Fiocruz, Rio de Janeiro, Brazil
[2] Laboratório de Hanseníase, Instituto Oswaldo Cruz/Fiocruz, Rio de Janeiro, Brazil
[3] Ambulatório de Doença de Chagas e Insuficiência Cardíaca do Pronto Socorro Cardiológico de Pernambuco (PROCAPE)/UPE, Pernambuco, Brazil
[4] Programa de Computação Científica, Fiocruz, Rio de Janeiro
[#]Current affiliation: Coordinación de Investigación, Universidad Franz Tamayo/UNIFRANZ, Cochabamba, Bolivia

Abstract

Chagas disease (CD) is a neglected tropical disease caused by infection with *Trypanosoma cruzi*. Ten to thirty years after infection, one-third of the patients present the cardiac form of CD, which may progress to heart failure (HF) with a poor prognosis. However, the factors that determine disease progression remain unclear. Increased angiotensin II activity is a key player for pathophysiology of HF. Angiotensin II type 1 receptor (AT_1R) rs5186 +1166A>C polymorphism has been linked to myocardial infarction and cardiomyopathy. In CD, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor antagonists have beneficial effects supporting commitment of the angiotensin/angiotensin receptor axis in chronic chagasic cardiomyopathy. Here, we evaluated the association of the *AT_1R* rs5182T>C, -119 275653 C>T, rs2131127 A>G and rs5186 +1166A>C polymorphisms towards developing HF, performing a case-control study encompassing 402 patients with positive serology for CD resident in the Northeast of Brazil. Genotyping was performed by PCR. Groups were compared using unconditional logistic regression analysis and adjusted for non-genetic covariates age, gender and trypanocidal treatment Patients were staged as non-cardiopathic (stage A; 109) and mild (stage B1; 161) and severe (stage C; 132) forms of Chagas' heart disease. *AGTR1* rs5186 +1166A>C heterozygotes showed weak association to protection against Chagas' heart disease (A *vs* C: OR = 0.6; *P*-value = 0.07; B1 *vs* C: OR = 0.6; *P*-value = 0.05; A + B1 *vs* C: OR = 0.6; *P*-value = 0.03). Further, the rs275653/rs2131127/rs5186/rs5182 T/A/C/T haplotype was protective against progression to the cardiac form of CD (B1 *vs* C: OR = 0.3; *P*-value = 0.03). Therefore, our data suggest that genetic variants of *AGTR1* may contribute to Chagas' heart disease outcome.

Support: DECIT/MS/CNPq, FAPERJ, Universal-CNPq

Aspectos clínicos, estudos de polimorfismos genéticos, biomarcadores
Clinical Aspects, genetic polymorphism, biomarkers

Imunoproteoma da doença de Chagas: busca de candidatos a biomarcadores de progressão de lesão cardíaca

Marcelle Almeida Caminha[1,2]; Virginia Maria Barros de Lorena[3]; Wilson de Oliveira Júnior[4]; Jonas Perales[2]; Paulo Costa Carvalho[5]; Diogo Borges Lima[5,6]; Maria da Glória Aureliano de Melo Cavalcanti[4]; Sílvia Marinho Martins[4]; Richard Hemmi Valente[2 *]; Rubem Figueiredo Sadok Menna-Barreto[1 *]

[1]Laboratório de Biologia Celular, IOC, Fiocruz, Rio de Janeiro, RJ, Brazil; [2]Laboratório de Toxinologia, IOC, Rio de Janeiro, RJ, Brazil; [3]Laboratório de Imunoparasitologia, CPqAM, Fiocruz, Recife, PE, Brazil; [4]PROCAPE, UPE, Recife, PE, Brazil; [5]Computational Mass Spectrometry & Proteomics group, ICC, Fiocruz, Curitiba, PR.; [6]Mass Spectrometry for Biology Unit, CNRS USR 2000, Institut Pasteur, Paris, France.

Causada pelo protozoário *Trypanosoma cruzi*, a doença de Chagas afeta milhões de pessoas em todo o mundo, sendo endêmica na América Latina. Dada a baixa taxa de diagnóstico preciso na fase aguda, a maioria das pessoas infectadas evolui para a fase crônica, a qual pode persistir como assintomática por décadas. Entretanto, 30% dos casos desenvolvem manifestações clínicas cardíacas e/ou digestivas, geralmente acompanhadas de comprometimento do sistema nervoso. Dado que, frequentemente, os sintomas mais graves estão relacionados à lesão do tecido cardíaco, o objetivo central deste estudo consistiu em pesquisar potenciais biomarcadores proteicos capazes de detectar a progressão da doença para a sua forma cardíaca. Assim, proteínas de tripomastigotas sanguíneos de *T. cruzi* (cepa Y) foram extraídas e submetidas à imunoprecipitação utilizando anticorpos de pacientes com as formas indeterminada (assintomática) ou cardíaca (estágios B1 e C) da doença; anticorpos de doadores saudáveis foram utilizados como controle. As proteínas imunorreativas foram identificadas e quantificadas com base na análise de espectrometria de massa e os perfis de reconhecimento foram comparados. Anticorpos de pacientes com cardiomiopatia precoce (B1) e avançada (C) foram capazes de detectar diferencialmente quatro e uma proteína, respectivamente, em comparação com amostras daqueles com a forma indeterminada. O autoantígeno I/6 (gi | 70878028) foi predominantemente detectado por amostras purificadas de pacientes no estágio C, enquanto as proteínas precursor da diidrolipoamida acetiltransferase (gi|71665855), calpaína cisteína peptidase (gi|71404593) e duas variantes de CAP5.5 (gi |71401694 e gi|71415498) apresentaram maior rendimento quando do reconhecimento de IgG de pacientes B1. Neste trabalho, o reconhecimento da CAP5.5 por anticorpos de pacientes com cardiomiopatia precoce gerou uma variação de abundância de 23 vezes quando comparado a amostras de pacientes assintomáticos, destacando-se essa como um potencial biomarcador para a progressão da forma cardíaca da doença de Chagas.

Palavras-chave: *Trypanosoma cruzi*; tripomastigota sanguíneo; doença de Chagas; cardiomiopatia; biomarcadores; CAP5.5; imunoproteoma; espectrometria de massa.

Biologia celular e interação parasito/célula hospedeira
Cellular Biology and parasite interaction / Host cell

Regulation of miRNAs in an experimental model of Chagas disease: effects of benznidazole and pentoxifylline therapy on chronic chagasic cardiomyopathy

Farani, P.S.G.[1]; Ferreira, B.I. S.[1]; Gibaldi, D.[2]; Vilar-Pereira, G[2]., Lannes-Vieira, J.[2]; Moreira, O.C.[1]

1 Laboratório de Biologia Molecular e Doenças Endêmicas – IOC/FIOCRUZ

2 Laboratório de Biologia das Interações – IOC/FIOCRUZ

Chagas disease is caused by the protozoan *Trypanosoma cruzi*, being estimated that 6-7 million people are infected by *T. cruzi* and about 65 million individuals are at risk of infection. Chronic chagasic cardiomyopathy (CCC) is the most common and severe form of the disease, being one of the main causes of mortality in endemic areas. MicroRNAs are small molecules of single-stranded RNA that act on the regulation of gene expression by inducing destabilization and/or inhibiting mRNA translation. In this study, we propose to evaluate the expression of microRNAs miR-145-5p and miR-146b-5p in mice with CCC, treated or not with Benznidazole (Bz) and/or Pentoxifylline (PTX), and in cell culture of cardiomyoblasts experimentally infected with *T. cruzi*. Female C57BL/6 mice with 5-7 weeks old were infected intraperitoneally with trypomastigote forms of *T. cruzi* Colombian strain (TcI). After 120 days of infection, animals presenting clinical signs of CCC and non-infected controls received apyrogenic saline as vehicle or PTX (20 mg/Kg, intraperitoneally) and/or Bz (25 mg/Kg/day, by gavage), daily for 30 days. For in vitro assays, cardiomyoblasts (H9C2 line) were seeded at density of 5x10 ^{3} cells/well in 24-well plates, or 10^5 in 25cm² flasks. Cells cultures were infected with *T. cruzi* Colombian strain in 5:1, 10:1 and 20:1 ratio, for 4 hours. Trypomastigote egression from cardiomyocytes was detected 48 hours post infection (0.3250 ± 0.0 x10^5 parasites/mL), increasing after 72 hours (0.86 ± 0.05 x10^5 parasites/mL), 120 hours (13.25 ± 2.8 x10^5 parasites/mL) and 144 hours (40.25 ± 11.67 x10^5 parasites/mL), supporting that H9C2 is competent for maintaining the life cycle of the parasite. The *in vitro* infection of H9C2 using different 5:1, 10:1 and 20:1 parasite/cell ratio showed statistically significant values between different MOI and between 24 and 48 hours after infection. In cardiac mice tissues, microRNA expression for miR-145-5p showed statistically significant decrease between control (1.448 ± 0.3392) and infected groups (0.7355 ± 0.1089; P=0.006), but showed no statistically different expression between infected and treated with Bz and/or PTX groups. On the other hand, an increase in miR-146b-5p expression was observed between control (1.481 ± 0.6883) and infected (3.921 ± 0.9736; P=0.007) groups and, also, between infected and the group treated with Bz (1.742 ± 0.6039; P=0.002) and Bz/PTX (1.651 ± 0.4002; P=0.002). Therefore, these results are promising and might suggest the involvement of miR-146b-5p in the cardiomyopathy of the chronic phase of experimental Chagas disease.

Support: CNPq, FAPERJ

Biologia celular e interação parasito/célula hospedeira
Cellular Biology and parasite interaction / Host cell

Role of FAK in *Trypanosoma cruzi* induced cardiac hypertrophy

Amanda R. Tucci[1], Francisco O. R. Oliveira Jr[1], Ana C. P. Eleutério[1], Gabriel M. Oliveira[2], Alanderson R. Nogueira[1], Liliane B. Mesquita[1] & Mirian Claudia. S. Pereira[1]
Instituto Oswaldo Cruz - FIOCRUZ
[1]Laboratório de Ultraestrutura Celular, [2]Laboratório de Biologia Celular
Instituto Oswaldo Cruz, Fiocruz, RJ, Brazil

Chagas disease, an important neglected tropical disease, is the leading cause of heart failure in Latin America. Hypertrophy and cardiac fibrosis are among the main symptoms of chronic chagasic cardiomyopathy (CCC). Hypertrophy can be triggered by a variety of external stimuli through multiple signaling pathways. Focal adhesion kinase (FAK), a non-receptor protein tyrosine kinase, has emerged as a signaling pathway regulating idiopathic cardiac hypertrophy. Endothelin 1 (ET-1), a vasoconstrictor produced by endothelial cells, cardiomyocytes among others, plays an important role in CCC and has been pointed as a modulator of FAK activation. Thus, in this study we evaluated the participation of FAK in the modulation of hypertrophy induced by *T. cruzi*. C57Bl6 mice were infected with *T. cruzi* (Brazil strain) and evaluated for electrocardiographic (ECG) disorders and activation of signaling pathways involved in cardiac hypertrophy, including ERK1/2 and FAK, as well as the expression of hypertrophy markers and extracellular matrix components (fibronectin and collagen), in the different stages of infection development (60 to 180 dpi). Parasitemia was followed up to 40 days post infection (dpi) showing low parasite burden ($7x10_4$/mL) at the parasitemia peak (26 dpi). Arrhythmia, bradycardia and atrioventricular block were alterations evidenced in ECG analysis, which were prominent at 150 - 180 dpi. ECG changes are accompanied by increased expression of extracellular matrix components such as fibronectin. Activation of extracellular signal-regulated *kinases* 1/2 (ERK1/2), a regulator of cardiac hypertrophy, was evidenced in early and late stages of *T. cruzi* infection. Our preliminary results revealed activation of FAK signaling pathway, demonstrated by increased level of FAK Tyr397 phosphorylation (150 and 180 dpi). Together, these results suggest that FAK may be involved in the regulation of heart hypertrophy.

Supported by: Fiocruz, Faperj, Capes, CNPq, PAPES VI

Diagnóstico
Diagnosis

Molecular diagnosis in patients with different forms of chronic Chagas disease that attended to the PROCAPE/UPE

Thayse do Espírito Santo Protásio da Silva[1], Angelica Martins Batista[1], Constança Britto[2], Otacilio da Cruz Moreira[2], Joseli Lannes-Vieira[1]

[1] Laboratório de Biologia das Interações, IOC/FIOCRUZ-RJ
[2] Laboratório de Biologia Molecular e Doenças Endêmicas, IOC/FIOCRUZ-RJ
E-mail: thayseprotasio@gmail.com

Chagas disease (DC) is a neglected endemic disease that affects around 6-7 million people worldwide. DC is caused by the flagellate protozoan *Trypanosoma cruzi* and it is characterized by two distinct phases: the acute and the chronic phase. We aimed to carry out the molecular diagnosis in a group of clinically and demographically characterized chronic CD patients who attended the "Ambulatório de doença de Chagas e Insuficiência Cardíaca do Pronto Socorro Cardiológico de Pernambuco" (PROCAPE / Universidade de Pernambuco). Patients were classified according to clinical criteria in indeterminate, cardiac, digestive and cardiodigestive forms. A peripheral blood sample from each patient was collected in EDTA tubes. Guanidine-EDTA was added 1:1 to the blood sample and DNA isolation was performed using the High Pure PCR Template Preparation Kit (Roche). The kDNA amplification was performed by conventional PCR, using the oligonucleotides 121 and 122, as described by Wincker et al (1994). Out of 345 samples tested by conventional PCR, 127 (36.8%) were positive for the presence of *T. cruzi* kDNA. Preliminary analysis showed a high frequency (70%) of cardiac patients in our study group, which were subdivided into mild heart disease (39%) and severe heart disease (31%). As for the other clinical forms, 16% of the patients presented the cardiodigestive form, 12% the indeterminate form and 2% the digestive form of CD. However, when we observed the percentage of positivity of conventional PCR in these groups, we found a higher frequency of severe cardiac patients (about 37%), followed by the group with mild heart disease (32%). These findings suggest a PCR positivity/severity relationship that needs to be further investigated by the quantification of parasitic load by qPCR. At the end of the study, we sought to contribute to the knowledge of the parasite/clinical outcome relationship, envisaging a possible outcome/prognostic biomarker for these patients.

Educação/informação
Education / Information

EDUCATIONAL APPROACHES OF CHAGAS DISEASE: AN EXPLORATORY ANALYSIS

Analuz Cunha de Sá Freire Sermarini[1]
Hosana Figueiredo de Athayde[2]
Sheila Soares de Assis[3]
Tania Araújo-Jorge[4]
[1]Programa de Vocação Científica – Laboratório de Inovações em Terapias, Ensino e Bioprodutos. Bolsista CNPq.
[2]Programa de Vocação Científica – Laboratório de Inovações em Terapias, Ensino e Bioprodutos. Bolsista CNPq.
[3]Pós doutoranda do Programa de Pós-Graduação em Ensino em Biociências e Saúde - Laboratório de Inovações em Terapias, Ensino e Bioprodutos. Bolsista CAPES.
[4]Pesquisadora chefe do Laboratório de Inovações em Terapias, Ensino e Bioprodutos. Bolsista de produtividade do CNPq.

Chagas disease, American Trypanosomiasis or chaguismo, is a tropical parasitic disease, first described in 1909 by Carlos Chagas. It's a disease caused by the *Trypanosoma Cruzi* and transmitted by the "barbeiro", an insect of the Triatominae subfamily. The transmission cycle occurs from the contaminated barber that stings the human for the ingestion of blood and soon after it defecates. The human scratches the region and the barber's feces come in contact with the wound, transmitting the protozoan *Trypanosoma Cruzi* to the person. This work's objective is to explore the existing approach through the public sphere and the dissemination of the theme. Through this analysis, it is sought to improve the strategies of health education around which directly reflect the control of epidemics and the enlightenment of the population in general. The methodology involved the exploratory analysis of the topic through the analysis of scientific publications hosted in institutional repositories and articles bases, their connection with the production of educational materials and the analysis of official documents that guide the dissemination of Chagas disease to the population in four different countries in Latin America (Brazil, Bolivia, Argentina and Mexico). No studies were found that associate the theme in educational materials and Chagas disease. In addition, it was revealed that educational strategies were not prioritized in the countries' government guidelines in which the official documents were analyzed. However, studies on educational materials involving other health-related topics indicate important clues to the production, analysis, and refinement of those themes. It is reinforced in the literature review that Chagas disease is attributed to poverty, as well as its ignorance. A total of 10 official documents were analyzed and in general they focus on addressing the issue with a focus on health professionals. Thus, no documents were identified that signal an approach close to the population.

Educação/informação
Education / Information

Inovações educacionais e tecnologias sociais para o enfrentamento da doença de Chagas: Analise da experiência da rede interinstitucional e multidisciplinar no Plano Estadual de Intensificação das Ações de Controle da Doença de Chagas por transmissão alimentar no Pará

Borges, Cristina X.A.[1]*; D´Andrea, Paulo S*[1]*; Araujo-Jorge Tania C.*[1]

A Coordenação Estadual de Controle da Doença de Chagas da Secretaria de Estado de Saúde Pública do Pará(SESPA) realizou no período de 05 a 19 de novembro de 2011, no arquipélogo Combu, Região Metropolitana de Belém, a segunda fase da pesquisa de "Protocolo de definição das áreas de risco de transmissão de *T. cruzi* na região Amazônica" estado do Pará contribui com cerca de 90% dos casos de Doença de Chagas Aguda DCA no Brasil. Foi observado pelos pesquisadores possível relação entre o aumento de casos de DCA e a ingestão alimentos in natura produzidos artesanalmente (da mesma forma que surtos orais nos estados da região não-Amazônica).O Protocolo é parte integrante das atividades do **"Plano Estadual de Intensificação das Ações de Controle da Doença de Chagas"** em parceria com o Ministério da Saúde. As atividades compreenderam inquéritos: humano, de reservatórios animais (silvestres e domésticos); entomológico; palestras de vigilância sanitária/educação; aplicação de questionário socioeconômico, étnico e cultural, georreferenciamento das moradias do arquipélago de Combu e inquérito do substrato vegetal. (Relatório Preliminar Protocolo Chagas Combu: 2011) Os estudos preliminares realizados no estado apontam para a gravidade dos casos agudos, mesmo após iniciar tratamento parasitológico específico e oportuno. Além disso, a doença acomete diversos membros da mesma família simultaneamente, em alguns casos culminando na morte; limitação ou incapacidade permanente. O que nos mobilizou a participar da Expedição foi o grande número de profissionais envolvidos e de formação escolaridade variadas, e investigar a motivação destes para participar do trabalho mesmo que os obrigou a conviver com insetos e outros animais, voltar à terra utilizando barco e ausência de suas casas e parentes. Essa a curiosidade no instigou perguntar: Qual a sua motivação para participar desse trabalho? Quem são esses profissionais, da onde vem, escolaridade, porque estão ali, suas críticas, quais os acertos da expedição? Aqui apresentaremos os resultados e análise da pergunta referente aos aspectos motivacionais. Gravamos em telefones móveis durante a realização das tarefas, com espontaneidade, sem elaborações mentais mais profundas, sem passar pelo crivo da autocensura nos deu a noção da grandiosidade da entrega ao projeto "Protocolo de definição das áreas de risco de transmissão de *T. cruzi* na região Amazônica.

Epidemiologia
Epidemiology

ANALYSIS OF CHAGAS DISEASE MORTALITY IN BRAZIL: BAYESIAN CRITICAL OF THE AGE OF THE AGE PERIOD AND COURT OF BIRTH

Lucycleia Bezerra do Nascimento[1].
Aline Baldi Leal[2].
Wagner Nazário Coelho[3].
[1]. National School of Public Health Sergio Arouca. [2]. Oswaldo Cruz Institute. [3]. Institute of Communication and Scientific and Technological Information in Health.

Chagas disease is of great interest to public health, being a serious and largely preventable infection when the conditions of maintenance of the pathological cycle are removed. The present work aims to analyze the indicators of age, sex and death period by Chagas' disease in Brazil between 1988 and 2017 available in the Mortality Information System. Correcting deaths by proportional redistribution for ill-defined causes, age, sex and ignored, allowed us to calculate gross and standardized rates by the direct method, with the population of the last Census of 2010. As a standard, the APC models were estimated under the Bayesian approach, considering temporal effects and random unstructured terms. The deterministic method INLA (Laplace Integrated Approach) was used in the interference of the parameters through software R. It was possible to verify that the temporal effects on the mortality vary according to the sex and geographic region. In general, there was a growing convergence of deaths from Chagas' disease, being widely reached in the age range of 50-54 to 50-64 years. Black men die, on average, five years younger than white men, which is repeated when compared to black and white women. The morality rates over the analyzed period were higher in the Midwest, South and Southeast regions, with progressive reduction in all regions for cohorts born from the 1960s, which may be related to the increase in access to health services after the implantation of SUS in the occupation of the urban space that reduces the exposure of the population

Keywords: Chagas disease. Bayesian models. Neglected Diseases.

Epidemiologia
Epidemiology

MORTALITY PROFILE OF CHAGAS DISEASE IN BRAZIL

Wagner Nazário Coelho[1];
Lucycleia Bezerra do Nascimento[2];
Aline Baldi Leal[3].
[1]. Institute of Communication and Scientific and Technological Information in Health.
[2].National School of Public Health Sergio Arouca. [3]. Oswaldo Cruz Institute.

Chagas' disease still presents as an important endemic notification in Brazil, having a high cost for public health, social and wide impact on mortality. However, there are still incipient studies in the country about the lethality of the disease in the exposed population. The objective of this study was to analyze the occurrence of deaths due to Chagas disease in Brazil, considering the period from 2010 to 2017, indexed in the Mortality Information System (SIM). In the analyzed temporality, 37817 deaths from Chagas disease in Brazil were identified. The lethality of the complaint was higher among men, with 55.70% of the cases possibly related to the standard of living of men. The number of deaths was between elderly individuals aged between 70 and 79 years (25.88%) and 60-69 years (24.65%), which may be associated with chronic non-communicable diseases. The educational variable in the analyzed historical analysis suggests that individuals with low educational level have a greater chance of being negatively impacted; individuals who studied up to 3 years (49.7%) presented higher risk, a factor that negatively impacted the self-care of patients with a positive diagnosis for Chagas. In the analysis of mortality by region, the results showed that the Southeast had the highest number of deaths, with 49.04% of the total, probably due to the Northeastern migratory process, followed by the Central West (22.29%) and the Northeast (21, 93%), the latter due to the process of occupation of rural areas, low effectiveness of vector control measures, and lack of monitoring and assistance strategies in basic health care. Sub-notification during acute conditions and the chronic nature of the disease may justify the slow decrease in mortality rate; which justifies continuous interventions, extension of guidelines on self-care in Chagas disease and timely notification.

Key words: Chagas disease; Mortality; Time series studies.

Parasito (diversidade genética, molecular, biológica e morfológica)
Parasite (genetic, molecular, biological and morphological diversity)

Investigation of biological roles of pseudogenes in *Trypanosoma cruzi*

MAYLA ABRAHIM[1]*, FERNANDO ALVAREZ-VALÍN[2], LUISA BERNA[3], LUIZA PEREIRA[4], PATRÍCIA CUERVO [4], CLAUDIA AVILA-LEVY [5], ANTONIO BASÍLIO DE MIRANDA[6], MARCOS CATANHO[1]

1 Laboratório de Genética Molecular de Microrganismos, IOC/FIOCRUZ, Brazil
2 seccion Biomatematica, Universidad de la República del Uruguay, Uruguay
3 Intitut Pasteur de Montevideo, Uruguay
4 Laboratório de Pesquisas em Leishmaniose, IOC/Fiocruz, Brazil
5 Laboratório de Estudos Integrados em Protozoologia, IOC/Fiocruz, Brazil
6 Laboratório de Biologia Computacional e Sistemas, IOC/Fiocruz, Brazil
***abrahim.mayla@gmail.com**

BACKGROUND: Protozoa of the species *Trypanosoma cruzi* cause annually millions of death and disease in humans and other animals. The genome sequencing of these pathogens contributed to a better understanding of the biology and relevant aspects of the genome and evolution of these organisms. Similarly, transcription profiles offer new opportunities for better understanding of biological processes, such as pseudogenization. Pseudogenes provide a powerful tool to record the evolution of genomes, and experimental evidence suggests that some of these molecular relics are biologically active in process of regulation of gene expression in several distinct lineages. **METHODS:** 4 genome sequences transcripts of human infective *Trypanosoma cruzi* were obtained from public databases. The identification, characterization, and annotation of pseudogenes are undergone based on sequence similarity between intergenic regions of the analyzed genomes measured against a dataset of reference protein sequences dataset, as well as based on the presence of degeneration signals typically associated with the loss of function in these genomic segments, such as insertions, deletions and/or substitutions. **RESULTS:** So far, a total of 29,846 intergenic regions were recognized as putative pseudogenes in the selected group of parasites in this work. **CONCLUSION:** We intend to contribute for a better knowledge of the evolutionary origin and mechanisms of pseudogenes formation in these organisms, as well as to reveal their potential involvement in regulation processes of gene expression, therefore, contributing to the understanding of the mechanisms of post-transcriptional regulation in *Trypanosoma cruzi*, a crucial phenome still mostly unknown in these organisms.

key words: bioinformatic, pseudogenes, evolution, biological processes

Acknowledgments: CAPES, PAPES-FIOCRUZ, CNPq, FAPERJ, and Plataforma de Bioinformática Fiocruz RPT04A/RJ

Parasito (diversidade genética, molecular, biológica e morfológica)
Parasite (genetic, molecular, biological and morphological diversity)

Nutritional and pH stress induce changes in the mitochondrial functionality of *Trypanosoma cruzi* epimastigotes

Yasmin Pedra Rezende da Silva; Michelle Casal Fernandes; Renata Stiebler; Camila Mesquita-Rodrigues; Solange Lisboa de Castro; Rubem Figueiredo Sadok Menna-Barreto

Laboratório de Biologia Celular, IOC, Fiocruz, Rio de Janeiro, RJ, Brazil

Trypanosoma cruzi is the causative agent of Chagas disease, a neglected illness that affects millions of people in Latin America. This protozoan parasite has a complex life cycle, alternating between replicative and infective stages comprising triatomine bugs and mammals. *T. cruzi* has a single mitochondrion, an organelle responsible for ATP production and the main site for formation of reactive oxygen species. During the parasite life cycle, stress conditions such as pH and nutritional changes induce protozoan differentiation: epimastigotes to metacyclic trypomastigotes in insect, and trypomastigotes to amastigotes in mammals. These stress conditions induce physiological and morphological changes in several organelles, such as mitochondria. In this work, we evaluated the role of mitochondrion and the production of oxygen reactive species in *T. cruzi* epimastigotes submitted to nutritional stress and pH variation. After 24 and 96h, only nutritional and alkaline stress induced an important reduction in respiratory rates. On the other hand, when cultivated under nutritional deprivation and pH stress parasites decreased complex II-III and increased complex IV activities in both times. Regarding citrate synthase, only parasites cultivated under nutritional and acid stress for 24 h had a significant reduction in the enzyme activity. In addition, the production of oxygen reactive species was higher in parasites submitted to nutritional and alkaline stress. Our data suggest that reactive oxygen species may alter mitochondrial enzymatic complexes activities reducing respiratory rates in epimastigotes cultivated under stress conditions. The knowledge on mitochondrial functionality in different stress conditions is critical for understanding the molecular mechanisms that occur during the evolutionary cycle of *T. cruzi*.

Keywords: *T. cruzi*, mitochondrion, ROS

Supported by: FAPERJ, CNPq and FIOCRUZ

Patologia / Patogenia
Pathology / Pathogeny

CCL3/Macrophage inflammatory protein-1α (MIP-1α) participates in parasite persistence and induction of a TNF- and IFNγ-enriched inflammatory milieu in the heart tissue of chronically *Trypanosoma cruzi*-infected mice

Daniel Gibaldi[1], Isabela Resende Pereira[1], Glaucia Vilar-Pereira[1], Andrea Alice da Silva[1,2], Ricardo Gazzinelli[3], Joseli Lannes-Vieira[1*]
Laboratório de Biologia das Interações, Instituto Oswaldo Cruz-Fiocruz, Av. Brasil 4365, 21045-900 Rio de Janeiro, RJ, Brasil[1], Departamento de Patologia, UFF, Niterói, RJ, Brasil[2] and Departamento de Bioquímica e Imunologia, UFMG, Belo Horizonte, MG, Brasil[3].

The chemokine CCL3/Macrophage inflammatory protein-1α (MIP-1α), a member of the CC-chemokine family, has been associated with macrophage recruitment to cardiac tissue and parasite control during the acute phase of *Trypanosoma cruzi* infection. The role played by CCL3 in chronic chagasic cardiomyopathy (CCC), the main clinical form of Chagas disease, remains to be approached. High levels of CCL3 are detected in the heart tissue during the acute and chronic phases of infection of C57BL/6 with the Colombian strain of *T. cruzi*. The infection of CCL3-deficient mice revealed that parasitemia and survival are not affected by CCL3 deficiency. In the chronic phase, cardiac parasitism is decreased in absence of CCL3. Further, heart inflammation due to $CD8^+$ cells and macrophages, but not $CD4^+$ cells, is reduced in CCL3-deficient mice, in comparison with the wild-type C57BL/6 mice. Stimulation of CCL3-deficient macrophages with interferon-gamma (IFNγ) improved parasite control, but significantly reduced nitric oxide (NO_x) and tumor necrosis factor (TNF) levels in the supernatant of cultures, without interfering with interleukin-10 (IL-10) levels. Crucially, in the heart tissue concentrations of TNF and IFNγ are decreased, whereas IL-10 levels are not affected by CCL3 deficiency. Chronically *T. cruzi*-infected CCL3-deficient mice showed reduction of prolongation of the QTc interval and CK-MB activity, markers of heart injury, in comparison with the CCL3-expressing mice. Thus, our data suggest that in chronic *T. cruzi* infection CCL3 may favor parasite persistence, the formation of a milieu of pro-inflammatory cytokines and the establishment of a macrophage- and CD8-enriched inflammation, features crucially linked to heart injury.

Support: PAPES-Fiocruz, PAEF-IOC, CNE-FAPERJ, CNPq.

Quimioterapia (drogas e esquemas de tratamento etiológico)
Chemotherapy (drugs and schemes of etiological treatment)

In silico studies and antitrypanosomal activity of ravenelin B, a new xanthone, as potential inhibitors of cruzain

João Victor Silva-Silva1*; Jeferson Rodrido S. Pina2; Jordano Ferreira Reis3; Celeste da Silva Freitas de Souza1; Juan Matheus Pereira Fernandes1; Flávia de Oliveira Cardoso1; Agnaldo da Silva Carneiro3; Fernando Almeida-Souza1,4; Kátia da Silva Calabrese1; Andrey Moacir do Rosario Marinho2; Patrícia Santana Barbosa Marinho2

1Laboratório de Imunomodulação e Protozoologia, Instituto Oswaldo Cruz, FIOCRUZ, 21040-360 Rio de Janeiro - RJ, Brasil 2Laboratório de Química e Pesquisa, ICEN, UFPA, 66075-110, Belém - PA, Brasil 3Laboratório Computacional de Sistemas Biológicos, Instituto de Ciências da Saúde, UFPA, 66075-110, Belém - PA, Brasil 4Mestrado em Ciência Animal, Universidade Estadual do Maranhão, 65055-310 São Luís - MA, Brasil

*e-mail: jvssilva89@gmail.com

Chagas disease is a potentially life-threatening illness caused by the protozoan parasite, *Trypanosoma cruzi*. It is estimated that over 10 000 people die every year from clinical manifestations of Chagas disease, and more than 25 million people risk acquiring the disease, and can only be treated with benznidazole or nifurtimox. However, frequent instances of treatment failure have been reported, making important the search for new molecules as alternatives *Trypanosoma cruzi* drugs. Plant endophytic microorganisms have been shown to be an important and novel source of natural bioactive products with antiparasitic properties. Therefore, this work aims to study the natural bioactive product, not yet described in the literature, isolated from fungus *Exserohilum rostratum*, acquired from the species *Bauhinia guianensis* as potential inhibitors of cruzain with trypanocidal activity. The compound ravenelin B (unpublished substance) was obtained from cultures of *E. rostratum* in rice by chromatographic procedures and identified through spectral methods 1D and 2D nuclear magnetic resonance and mass spectrometry. Initially, there was performed docking simulation of the interaction between cruzain (PDB ID: 1ME4) and trans-sialydase (PDB ID:1S0I) and the compounds ravenelin B;T10, known cruzain inhibitor; and sialyl-lactose, a sialidase substrate; using the SwissDock Portal, with normal parameters. Then, for this compound, the cytotoxicity was determined by Thiazolyl Blue Tetrazolium Bromide (MTT) method and the viability of parasites *T. cruzi* Y strain (epimastigote and trypomastigote) were evaluated after treatment by counting the total number of live parasites, taking into account the flagellar motility, using Neubauer's camera and optical light microscope. To evaluate the intracellular amastigote, the coverslips with infected cells with trypomastigote forms were treated with Ravenellin B and Bouin-fixed, stained with Giemsa and examined by light microscopy. IC 50 (µg/mL) was calculated with the GraphPad Prism 6.01 software. In the molecular docking simulations, ravenelin B exhibited a good binding to cruzain with an energy value of -7.10 kcal/mol while T10 presented -8.33kcal/moldue to the hydrogen bond between the compounds and Cys25, and van-der-Waals interactions with other residues shown after PoseView analysis. Renavelin B did not seem to interact with trans-sialidase active site while sialyl-lactose presented a highly similar binding mode to the *in vitro* experiments with a binding energy of -12.38 kcal/mol. The compound ravenelin B showed remarkable activity again epimastigote, trypomastigote and intracellular amastigote, with IC50 of 1.356 ± 1.126 µg/mL, 0.4272 ±1.073, 2.462 ± 1.539 respectively. Moreover, ravenelin B exhibited a selectivity index of 35.2, 111.7 and 19.4 µg/mL, respectively, showing to be a promising substance. Thus, studies to calculate free binding energy, molecular dynamics simulations and evaluation of the effects of ravenelin B *in vitro* against cruzain, as well as the investigations of their mechanisms of action, are currently underway. **Keywords**: *Trypanosoma cruzi; Exserohilum rostratum;* endophytic fungi; *in sílico*.

Acknowledgment

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001. Just as the authors thank the Fundação Amazônia de Amparo a Estudos e Pesquisa do Pará (FAPESPA) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

Quimioterapia (drogas e esquemas de tratamento etiológico)
Chemotherapy (drugs and schemes of etiological treatment)

Study of the *in vitro* activity of hybrid compounds of the pyridine prototypes with the 1,3,4-tiadiazolic subunit of megazole on *Trypanosoma cruzi*

Juliana Barbosa Magalhães Chaves[1], Solange Lisboa de Castro[1], Rosana Freitas[2], Carlos Alberto Manssour Fraga[2], Kelly Salomão[1].

[1]Fundação Oswaldo Cruz, Instituto Oswaldo Cruz, Laboratório de Biologia Celular.

[2]Universidade Federal do Rio de Janeiro, Laboratório de Avaliação e Síntese de Substâncias Bioativas

There is an intense effort to find new drugs of Chagas disease, since the available ones, benznidazole (**Bz**) and Nifurtimox (**Nif**) are not satisfatory, showing poor activity in the late chronic phase, severe collateral effects and limited efficacy against different parasitic isolates. In this study we determined the *in vitro* effect of hybrid compounds of a prototype pyridine, which is a sterol biosynthesis inhibitors (SBIs), with **megazol**. The effect of these compounds was evaluated on Y and Tulahuen strains. Among the drugs tested on trypomastigotes, of the Y strain, 8 were most active than SBIs of reference: **ketoconazole** and **posaconazole**. Besides, the compounds **2033** and **2035** tested on intracellular amastigotes, of the Tulahuen strain, also were most active than IBEs of reference. The compounds **2035** and **2035HCl** were the most effective against trypomastigotes of strain Y, but the most selective was **1947HCl**, presenting low toxicity on macrophages and cardiomyocytes. For this reason, it was selected for the activity assays on intracellular amastigote forms and for evaluation of the mechanism of action on trypomastigotes (Y strain). Results of intracellular amastigote suggest that in 24 and 48 hs of treatment with **1947HCl** there is a decrease in the endocytic index. For the investigation of its mode of action, we analyzed by cytometry: the generation of reactive species of oxygen (ROS), the integrity of the plasma membrane and mitochondrial membrane potential. Interestingly, no changes were observed in the parameters tested by cytometry in parasites treated with **1947HCl**, suggesting that the mode of action should not be related to inhibition of sterol biosynthesis or generation of ROS. We also analyzed the ultrastructure of trypomastigotes treated with **1947HCl** by electron microscopy. The electron microscopy showed the formation of blebs, changes in kinetoplast and retraction of the parasite body in trypomastigostes treated with **1947HCl.**

Keywords: T*rypanosoma cruzi,* inhibitors of ergosterol biosynthesis and nitroimidazoles.

Terapias (imunoterapia, terapia celular e outras)
Therapies (immunotherapy, cellular therapy and others)

TGF-β neutralization improves cardiac function during the chronic phase of Chagas' disease in a murine experimental model

João Vitor Geisteira Oliveira da Silva[1], Roberto Rodrigues Ferreira[1], Rayane da Silva Abre[1], Glaucia Vilar-Pereir[1], Wim Degrave[1], Marcelo Meuser-Batist[1], Nilma Valéria Caldeira Ferreira[1], Ellen Mello de Souza[1], Jean Jacques-Feige[2], Joseli Lannes-Vieira [1], Tania Araujo Jorge[1], Mariana Caldas Waghabi[1]
[1] IOC - FIOCRUZ - Instituto Oswaldo Cruz - Fundação Oswaldo Cruz (Rio de Janeiro, RJ, Brasil), [2] INSERM - Institut National de la Santé et de la Recherche Médicale (U1036, 38000 Grenoble, França

Cardiac commitment is the most severe and frequent manifestation of chronic Chagas' disease. TGF-β is involved in the development of chronic chagasic cardiopathy with increased serum levels of this cytokine and activation of its signaling pathway in the cardiac tissue, thus resulting in increased expression of extracellular matrix proteins, which characterizes fibrosis. Inhibition of TGF-β signaling pathway significantly attenuates *T. cruzi* infection, preventing the development of cardiac damage during the acute phase of Chagas disease in an experimental model. Thus, the main goal of this study is to evaluate the effect of a neutralizing antibody anti TGF-β (1D11) during the chronic phase of Chagas' disease in a murine experimental model. Female mice were infected with trypomastigotes of the Colombian strain of *T. cruzi* and were monitored electrocardiographically to observe the evolution of myocarditis. After 120 dpi, treatment with anti TGF-β (10mg / kg) was initiated in two different schemes: single dose and once a week up to 150 dpi. The heart of the animals was collected for observation of the fibrotic process. In addition, the blood of the animals was collected to obtain the serum and to quantify the circulating levels of inflammatory cytokines: TNF-α and INF-γ. In this study, we observed that the infection altered the cardiac electrical conduction: decreasing the heart rate, increasing the PR interval and the duration of the P wave. The treatment with anti TGF-β reversed this process. We also observed that the circulating levels of TNF-α and INF-γ were significantly higher during chronic infection and that the treatment with 1D11 did not alter these levels. In addition, TGF-β neutralization was effective for the recovery of Conexinas-43 plaques, which are fundamental for the conduction of the electric impulse, and which are structurally disorganized with *T. cruzi* infection. Moreover, the treatment with anti- TGF-β reversed collagen deposition and reduced the expression of TGF-β receptors (TβRI / TβRII) in the heart of infected animals. Thus, TGF-β signaling pathway is a possibility for the treatment of fibrosis during the chronic phase of Chagas' disease.

Financial support: CNPq, DECIT, Inserm, FAPERJ

CICLO CARLOS CHAGAS DE PALESTRAS 2019
7ª EDIÇÃO
110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

Terapias (imunoterapia, terapia celular e outras)
Therapies (immunotherapy, cellular therapy and others)

Cardiac regeneration after TGF-β inhibitor therapy in a pre-clinical study of chronic Chagas' heart disease

Roberto Rodrigues Ferreira[1], Rayane da Silva Abreu[1], Glaucia Vilar-Pereira[2], Wim Degrave[1], Marcelo Meuser-Batista[3,4], Nilma Valéria Caldeira Ferreira[4], Otacílio da Cruz Moreira[5], Natália Lins da Silva Gomes[5], Elen Mello de Souza[6], Isalira Ramos[7], Sabine Bailly[8], Jean-Jacques Feige[8], Joseli Lannes- Vieira[2], Tania C. de Araújo-Jorge[3], and Mariana Caldas Waghabi[1]

[1]Laboratório de Genômica Funcional e Bioinformática - Instituto Oswaldo Cruz, Fundação Oswaldo Cruz (Fiocruz), Rio de Janeiro RJ, Brasil, [2]Laboratório de Biologia das Interações - Instituto Oswaldo Cruz, Fundação Oswaldo Cruz (Fiocruz), Rio de Janeiro RJ, Brasil, [3]Laboratório de Inovações em Terapias, Ensino e Bioprodutos - Instituto Oswaldo Cruz, Fundação Oswaldo Cruz (Fiocruz), Rio de Janeiro RJ, Brasil, [4]Departamento de Anatomia Patológica e Citopatologia, Instituto Nacional de Saúde da Mulher, da Criança e do Adolescente Fernandes Figueira, Fundação Oswaldo Cruz (Fiocruz), Rio de Janeiro, RJ, Brasil, [5]Laboratório de Biologia Molecular e Doenças Endêmicas, Instituto Oswaldo Cruz (FIOCRUZ/RJ), Rio de Janeiro, Brazil, [6]Laboratório de Virologia Molecular - Instituto Oswaldo Cruz, Fundação Oswaldo Cruz (Fiocruz), Rio de Janeiro RJ, Brasil, [7]UFRJ, Centro Nacional de Biologia Estrutural e Bioimagem, Rio de Janeiro, RJ, Brazil, [8]Université Grenoble-Alpes, Inserm, CEA, Biology of Cancer and Infection Laboratory, Grenoble, France

Chronic chagasic cardiomyopathy (CCC) is the most important and frequent clinical manifestation of chronic Chagas' disease. During CCC, the parasite remains inside the cardiac cells, leading tissue damage, involving extensive inflammatory processes and irregular fibrosis. Some molecules act in the fibrosis formation, but one in particular plays a key role in the fibrogenic process inducing extracellular matrix synthesis: TGF- β. The aim of this study is to investigate the effect of 1D11 and GW788388 treatment during the chronic experimental model of Chagas disease. To this end, animals C57Bl/6 were infected with *T. cruzi* Colombian strain and treated after 120 days post–infection (dpi) with: 1D11 in two different schemes: single dose or once a week and; GW788388 in three different schemes: single dose; once a week or three times a week during 30 days. Functional analysis (electrocardiogram and echocardiogram), molecular (ELISA, RT-qPCR and Western blot) and histopathological analyses (immunofluorescence and immunohistochemistry) were performed before and after 1D11 and GW788388 treatment in control and infected animals. Our data suggested that the chronic model has 100% cardiac damage after 120 dpi and that GW1x and GW3x treatment schemes are more efficient than 1D11 treatment. GW788388 treatment: reestablished the electrocardiographic profile of the infected animals: reduced bradycardia, PR interval and P wave duration; restored the left ventricular ejection fraction, decreased during infection; reversed the higher levels of circulating TGF-β1; SMAD2/3 proteins, fibronectin and collagen type I and collagen deposition in the heart of infected animals; increased MMP-9 and Sca-1, reduced TIMP-1/TIMP-2/TIMP-4, and partially restored GATA-6 and Tbox-5 transcription, supporting cardiac regeneration. The therapeutic effects of GW788388 are promising and suggest a new possibility to treat cardiac fibrosis in the chronic phase of Chagas' heart disease by TGF-β inhibitors.

Supported by: INSERM / FIOCRUZ / CNPq / FAPERJ / DECIT

Vetor, ciclos de transmissão, ecologia e biodiversidade
Vector, transmission cycle, ecology and biodiversity

Panstrongylus lutzi (Hemiptera: Triatominae) an important vector of Chagas disease transmission cycle in the Jaguaribe Valley region - CE, Brazil

Jéssica Gomes Pereira*, Tânia Maria Rodrigues dos Santos[1], Otília Maria Fonseca Sarquis[1] & Marli Maria Lima[1]

*Bolsista do Programa de Estágio Curricular (PEC – Fiocruz/Ciee). E-mail: pereira.jessicagomes@oi.com.br
[1]Laboratório de Ecoepidemiologia da Doença de Chagas, Instituto Oswaldo Cruz, Fiocruz, Rio de Janeiro, RJ, Brasil.

Triatomines are important insects in public health, since they are vectors of the parasite *Trypanosoma cruzi*, the Chagas disease agent in Latin America. The main way to control the disease transmission is monitoring and controlling the vector species populations. For a long time, several programs have obtained success in the control of the domiciled species. However, native species with capacity to transmit *T. cruzi* and potential for household colonization are difficult to be controlled. In this context, the Northeast of Brazil has considerable epidemiological importance, because it is an endemic region of the disease, where 21 species of native triatomines can infest domiciles. Among these, *Panstrongylus lutzi* Neiva & Pinto 1923 that is a species of the northeastern semi-arid region, whose natural habitat are armadillos and wild rodents, it has been found invading peridomiciliar annexes - in chicken coop – and even intradomiciles. Until now, there are no evidences of intra-household colonization. Investigations carried out by the Laboratory of Ecoepidemiology of Chagas Disease (LEDOC, IOC/Fiocruz) in rural areas of the Jaguaribe Valley region, Ceará have detected the presence of *P. lutzi* adults in peridomiciliar and intradomiciliar environments, with high rates of *T. cruzi* infection, supporting the possibility of occurrence of the vector transmission cycle in these regions. *P. lutzi* is a wild species; however, in these endemic areas, the households are located close to its natural environment as well as those of the *T. cruzi* reservoirs, which are primary sources of this vector feeding, contributing to the maintenance of the disease cycle. Thus, studies related to the bionomics and ecology of *P. lutzi*, as well as the food source of the specimens captured in home environments, become relevant, and may help in the development of control programs for native triatomine species in adaptation process to the households, such as *P. lutzi*.

Keywords: Chagas Disease, vector transmission, triatomines, *Panstrongylus lutzi*.

Vetor, ciclos de transmissão, ecologia e biodiversidade
Vector, transmission cycle, ecology and biodiversity

Spatio-temporal distribution analysis and *Trypanosoma cruzi* natural infection rate in triatomines in Espírito Santo state, Brazil

Gabriel Magro dos Santos[1*], Maria Augusta Dario[1], Mauro César Louzada [2], Luiz Felipe Ferreira[3], Ana Maria Jansen[1], Samanta Cristina das Chagas Xavier[1]
1Laboratório de Biologia de Tripanosomatídeos, IOC/Fiocruz;
2Núcleo de Entomologia e Malacologia, Sesa/ES;
3Instituto Militar de Engenharia, IME

Triatomines are insect vectors capable to transmit *Trypanosoma cruzi*, the etiologic agent of Chagas disease. Due to ecosystems destruction, these vectors are losing their natural habitat and may come in contact with domestic animals and humans. In Espírito Santo (ES) state, little is known about triatomines species distribution. *Trypanosoma cruzi* infection in vectors is high and it necessary to know if this high infection still remains. The aim of this study was to analyze triatomine species spatio-temporal distribution and its *T. cruzi* infection in different regions of ES state. For this, a data survey was carried out, in collaboration with the Núcleo de Entomologia e Malacologia (Nemes SESA/ES), of triatomine species occurrence and *T. cruzi* natural infection from 2010 to 2018, in three different ES regions (Central, Metropolitana and Sul). Quantification of triatomines specimens and *T. cruzi* natural infection rate were performed by region and studied periods. A total of 2527 triatomines specimens were observed, in which 2432 were adult and 95 were nymphs. Adult specimens identified were: *Triatoma vitticeps* (n=2252), *Triatoma* spp. (n=19), *T. tibiamaculata* (n=1), *Panstrongylus geniculatus* (n=122), *P. megistus*(n=23) and *P. diasi* (n=15). In relation to *T. cruzi* natural infection rate, 1421 adults (n=2432) and nine nymphs (n=95) were infected. The infection rate was higher in *Triatoma* (1380/2272) than in *Pasntrongylus* genus (41/160). *Trypanosoma cruzi* infection rates per species were: *T. vitticeps* (1369/2252), *Triatoma* spp. (10/19), *T. tibiamaculata* (1/1), *P. geniculatus* (34/122), *P. megistus* (6/23) and *P. diasi* (1/15). In spatial distribution analysis by region, triatomines' greater abundance (n = 1519) and species richness (n= 6) were observed in Metropolitana region, followed by Sul (n = 961) and Central (n= 47) regions. The Metropolitana region also presented the highest infected triatomines number (875/1519), followed by Sul (542/961) and Central (13/47) regions. The temporal analysis demonstrated that between 2013 to 2015 there were a greater number of triatomine specimens collected (ranged from 445 to 492) and *T. cruzi* infecion rate was higher in 2011 (73%) and 2012 (76%). There is a prediminance of *Triatoma* genus in ES state, wherein *Triatoma vitticeps* is the main species. Also, *T. vitticeps* still remains with *T. cruzi* high natural infection rates. Triatomines distribuition occurred in the three regions, with predominance in Metropolitana region, possibly influenced by dynamics and environmental factors. This scenario could help explain the acute Chagas' disease case occurrence in Guarapari municipality, located in metropolitan region, in 2012.

Key-words: Triatominae, *Trypanosoma cruzi*, distribution, infection, Espiríto Santo state
Financial support: CNPq, Capes, Faperj

Vetor, ciclos de transmissão, ecologia e biodiversidade
Vector, transmission cycle, ecology and biodiversity

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

Thaiane Verly[1], Stephanie Costa[1], Jasiel Santos Junior[1], Nathanielly Lima[2], Jacenir Mallet[2], Francisco Odêncio[3], Mirian Pereira[3], Carlos Moreira[4], Cleber Galvão[5], Márcio Pavan[6], Constança Britto[1]

[1]Laboratório de Biologia Molecular e Doenças Endêmicas, [2]Labotatório Interdisciplinar de Vigilância Epidemiológica de Diptera e Hemiptera, [3]Laboratório de Ultraestrutura Celular, [4]Laboratório de Doenças Parasitárias, [5]Laboratório Nacional e Internacional de Referência em Taxonomia de Triatomíneos, [6]Laboratório de Transmissores de Hematozoários.
Fundação Oswaldo Cruz/RJ

Chagas disease (CD) is caused by *Trypanosoma cruzi*, and the control method focuses on the eradication of triatomine vectors, which have been proven to be adapted to human households. The risk of *T. cruzi* transmission persists due to environmental devastation, low living conditions of the population, presence of infected reservoirs, and re-infestation of previously treated houses by native wild triatomines. Investigations about the biology and behavior of vectors are important for a better understanding of the host-vector interaction and the epidemiological risk of a given species. Although the species of the *Triatoma rubrovaria* subcomplex are sylvatic, invasion of *T. rubrovaria* in human habitations has been observed. In this way, our study proposes to identify the species of the *T. rubrovaria* subcomplex by molecular taxonomy and to analyze its vectorial potential in the transmission dynamics of *T. cruzi* in the Pampa biome. Distinct aspects related to vector capacity were evaluated, such as food source, infection rate and parasite genotyping of triatomines collected in the field. In parallel, *T. rubrovaria* bionomic parameters after infection with *T. cruzi* TcVI were experimentally analyzed. For this, insects were fed in mice infected with TcVI at the peak of parasitemia. Feeding and dejection behaviors were observed. The observation (counting) of parasites in the feces was performed at 30, 60 and 90 days post-infection (dpi). In 30 dpi, it was possible to detect the presence of epimastigote, intermediate and metacyclic trypomastigote forms in the feces of *T. rubrovaria*; the infecting forms were observed, mainly, in 60 dpi. Most infected insects presented short periods of feeding, dejection, and short distance between the feces and the site of the bite. A total of 1,724 triatomines were collected in Rio Grande do Sul, 936 of which were used for the molecular analysis. It was observed an infection rate of 2.8% (26/936), a parasitic load variation of 1.5×10^1 to 2.3×10^7 parasite equivalents, and the presence of TcI, TcV and TcI + TcIV coinfection. The food sources found were: man, chicken, mouse, opossum and sheep. Based on the data obtained, we intend to contribute to a better understanding of the transmission dynamics of *T. cruzi* in the studied areas, seeking to help in the elaboration of strategic plans for more adequate and effective control of CD in the country.

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

Vetor, ciclos de transmissão, ecologia e biodiversidade
Vector, transmission cycle, ecology and biodiversity

BEHAVIORAL AND MORPHOMETRIC CHARACTERIZATION OF SEXUAL SELECTION IN MALES OF THE *TRIATOMA BRASILIENSIS* COMPLEX

Letícia Paschoaletto[1], Cauan Antunes[1], Gabriel A. G. Passos[2], Jader de Oliveira[3], João A. da Rosa[3], Catarina M. Lopes[4], Teresa C. M. Gonçalves[4], Jane Costa[1].
[1] Laboratório de Biodiversidade Entomológica, IOC/ Fiocruz, RJ.
[2] Programa de Pós-Graduação em Educação, Univ. Federal do Est. do Rio de Janeiro, RJ.
[3] Laboratório de Parasitologia, Fac. de Ciências Farmacêuticas, UNESP-Araraquara, SP.
[4] Lababoratório Interdisciplinar de Vigilância Entomológica em Diptera e Hemiptera, IOC/ Fiocruz, RJ.

In triatomines, the study of experimental hybrids was applied to the understanding of insect biology and phylogenetic relationships among species. Some studies on experimental crosses in the laboratory were carried out using all the possible combinations between the different species of the *Triatoma brasiliensis* complex, which evidenced a gradation of reproductive affinities among them. Later, based on the reproductive affinities and the analysis of the morphological characteristics of the complex *T. brasiliensis*, a hypothesis was raised on the possible homoploidal hybrid speciation that could have originated *Triatoma brasiliensis macromelasoma* in the State of Pernambuco. However, little is known about the reproductive behavior of the species of the aforementioned complex, especially with respect to males in face of multiple choices. In this way, the main objective of this study was to record for the very first time, the male copulation behavior of the *T. brasiliensis* complex, as well as geometric morphometry of the wings of the specimens that were successful in sexual selection, in order to analyze the existence of possible morphological characteristics correlated with reproductive behaviors. The following species of the *T. brasiliensis* complex were observed: *Triatoma brasiliensis brasiliensis, Triatoma sherlocki* and *Triatoma juazeirensis; Triatoma infestans* specimens were included as external group. Parameters of copula behavior previously defined were recorded: the choice of the female, the time of displacement to the female for the purpose of copulation, and the copula itself (number of attempts, number and type of rejection, and occurrence). For the experiment, a mating arena was developed, where a male was observed and filmed, for 15 minutes, having mating options with one coespecific female and two noncoespecific ones. After the records, females and males were maintained in 70% ethanol for later analysis by means of geometric morphometry. Males were not restricted to attempts at co-specific copulation and their success was determined by the rejection behaviors of females. The results showed that males of *T. sherlocki* and *T. infestans* are more eager to copulation, being accepted by females of all species tested. Regarding the geometric morphometry, no correlation was observed between wing size and conformation and the most effective behavioral copulation characteristics. Therefore, in the areas of sympatry of the species studied, if there are no ecological barriers, a natural hybridization process might be possible, which may reflect in the epidemiological aspects of the Chagas' disease transmission.
Keywords: vectors, copula behavior, selective copula, morphology.

Support: CNPq e Capes.

CICLO CARLOS CHAGAS DE PALESTRAS

7ª EDIÇÃO

2019

110 ANOS DA PUBLICAÇÃO DO CICLO DA DOENÇA DE CHAGAS

IOC Instituto Oswaldo Cruz

Ministério da Saúde FIOCRUZ Fundação Oswaldo Cruz

MINISTÉRIO DA SAÚDE

PÁTRIA AMADA BRASIL GOVERNO FEDERAL