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IMPORTÂNCIA DO EVENTO

O Programa de Pós-graduação em Imunologia (PPGI_m) há mais de 30 anos, vem formando recursos humanos de excelência, capacitados para as atividades de ensino e pesquisa em Imunologia e áreas correlatas, muitos já absorvidos por instituições da Bahia e de outros estados. O PPGI_m tem realizado reuniões científicas visando difusão do conhecimento científico e integração acadêmica com a graduação e a pós-graduação da própria UFBA e outras IES. A ExpoPPGI_m, Reunião Anual do Programa, já se tornou um evento tradicional, que acontece a cada ano, com a primeira edição no ano 2000, constituindo um fórum de integração de profissionais, pesquisadores e jovens cientistas, alunos de graduação e pós-graduação da UFBA e outras IES do Estado da Bahia, do Brasil e de outros Países com interesse no amplo domínio da Imunologia. O objetivo da ExpoPPGI_m é divulgar conhecimento científico em Imunologia e áreas correlatas, gerado localmente, na Bahia, no Brasil, e outros países, tendo como público-alvo estudantes de graduação e pós-graduação, pesquisadores da UFBA e outras IES e profissionais da área. Esta XX Edição da ExpoPPGI_m foi realizada inteiramente de forma virtual e contou com a participação como palestrantes além de pesquisadores da própria UFBA, pesquisadores vinculados a outras instituições de ensino e pesquisa da Bahia, do Brasil e do exterior, que apresentaram palestras em 6 sessões temáticas, relacionadas às linhas de pesquisa do Programa. Ainda, durante os 5 dias do evento, discentes do Programa apresentaram e discutiram sobre seus projetos de pesquisa em desenvolvimento através de vídeo-pôsteres, distribuídos em 8 sessões, e assim também contribuindo para a integração acadêmica e a difusão do conhecimento científico em Imunologia e seus correlatos.

XX ExpoPPGIm
Reunião Anual do Programa de Pós-graduação em Imunologia
1 a 5 de setembro de 2020
<http://www.ppgim.ics.ufba.br/>
<https://zoom.us/>

PROGRAMAÇÃO

01/09	ABERTURA DO EVENTO 09: 00 – 09: 15 h	
	APRESENTAÇÃO DO PROGRAMA DE PÓS-GRADUAÇÃO EM IMUNOLOGIA DA UFBA Sílvia Lima Costa – Coordenadora do PPGIm	
	CONFERÊNCIA PLENÁRIA 09: 15 – 11: 00 h Moderador: Vitor Antônio Fortuna – Vice-coordenador do PPGIm	
	TESTES SOROLÓGICOS E RESPOSTA IMUNE A SARS-COV2 Roberto José Meyer Nascimento Laboratório de Imunologia e Biologia Molecular (LabImuno) – UFBA	
01/09	SESSÃO TEMÁTICA – IMUNOLOGIA APLICADA 13: 00 – 15: 00 h Moderadores: Songelí M. Freire, Alex Torres e Rosimére Torres	
	Challenges in schistosomiasis control – point-of-care circulating cathodic antigen (POC-CCA).	Ricardo Riccio Oliveira Fundação Oswaldo Cruz-CPqGM
	Recombinant proteins for HCV diagnostic evaluation and / or monitoring	Paulo Inácio da Costa Faculdade de Medicina de Ribeirão Preto Universidade do estado de São Paulo
	Diagnosis of malignant hemopathies by flow cytometry immunophenotyping.	Herbert Henrique Santos Melo Serviço de hematologista do HUPES LabImuno – UFBA

01/09	SESSÃO – APRESENTAÇÃO DISCENTES 1 16: 00 – 18: 00 h Moderadores: Victor Diógenes Silva e Jéssika Amparo	
	Proposition of natural compounds and chimeric proteins for novel prophylactic methods against <i>Streptococcus equi</i> .	<u>Bernardo Mirabal Santos</u> , Sarah Pereira Andrade de Souza, Igor Batista dos Santos Oliveira, Letícia Vivas Carvalho, Nubia Seyffert, Thiago Luiz de Paula Castro.
	Evaluation of microbiological and immunological markers in the association between chronic periodontitis and metabolic syndrome.	Patricia Mares de Miranda, <u>Rebeca Pereira Bulhosa Santos</u> , Michelle Miranda Lopes Falcão, Johelle De Santana Passos Soares, Soraya Castro Trindade.
	Antigenic reactivity of RPKNG, RSPAC, RSODC and RNANH in a goat and sheep serum.	<u>Ramon Mendes dos Santos</u> , Silvana Beutinger Marchioro, Caio Lopes Borges Andrade, Rogerio Reis Conceição, Maria Isabel Cerqueira, Hévllyn Ribeiro de Araújo, Marcos Borges Ribeiro, Roberto Jose Meyer Nascimento, Songelí Meneses Freire.
	Nanovaccine development using recombinant proteins of <i>Corynebacterium pseudotuberculosis</i> linked to polymeric nanoparticle	<u>Vítor Cordeiro Pereira</u> , Vagner de Oliveira Machado, Marcos Borges Ribeiro, Roberto Jose Meyer Nascimento, Luan Santana Moreira, Silvana Beutinger Marchioro
	Peripheral blood CD4+ t cells profile in sickle cell disease patients with osteonecrosis	<u>Paula Braga Daltro</u> , Vitor Antônio fortuna, Roberto José Meyer Nascimento
	Effects of ASC conditioned media in tissue regeneration.	<u>Brysa Mariana Dias Silveira</u> , Songelí Meneses Freire, Vitor Antônio fortuna
	Quantification and comprehensive analysis of mesenchymal stromal cells in bone marrow samples from sickle cell disease patients with osteonecrosis.	<u>Tiago Oliveira Ribeiro</u> , Songelí Meneses Freire, Vitor Antônio fortuna

02/09	SESSÃO – APRESENTAÇÃO DISCENTES 2 09: 00 -11: 00 h Moderadores: Clarissa Schitine e Janaína Ribeiro Soares	
	Combined adjuvant therapy involving BCG and imiquimod increases the survival of C57BL/6 mice during experimental melanoma.	<u>Maiara Nelma Bonfim Costa</u> , Amanda Catariny de Oliveira Silva, Davi Salles Xavier, Rosa Pinho, José Mengel, Fabiola Cardillo.
	Dynamics of seroconversion and immune cell response as markers for diagnosis and predictors of prognosis in SARS-CoV 2 infection.	<u>Isa Rita Brito de Morais</u> , Alex José Leite Torres.
	Immunological characterization of patients with diagnosis of COVID-19 and relationship with markers of vascular inflammation and neuroinflammation.	<u>Nívia Nonato Silva</u> , Maria de Fátima Dias Costa, Victor Diógenes Amaral da Silva, Clarissa Schitine, Balbino Lino dos Santos, Ravena Pereira Nascimento, Vitor Antônio Fortuna, Sílvia Lima Costa.
	Identification of natural polyphenol and synthetic derivatives as new candidates for the treatment of sars-cov2 infections based on their neuroprotective in preclinical models of neuroinflammation.	<u>William Douglas Lacerda Novais</u> , Clarissa Schitine, Juciele Valéria Oliveira, Maria de Fátima Dias Costa, Balbino Lino dos Santos, Ravena Pereira Nascimento, Victor Diógenes Amaral da Silva, Sílvia Lima Costa.
	Influence of temperature and antipyretic use on cell viability in primary CNS crops of neonate rats.	<u>Itamara Raquel dos Anjos</u> , Sílvia Lima Costa, Denis de Melo Soares, Clarissa Schitine.
02/09	SESSÃO TEMÁTICA – IMUNOLOGIA DA ASMA 13: 00-15: 00 h Moderadores: Ryan Costa, Valdirene Carneiro e Washington Antunes	
	Genetic analysis technologies helping to study asthma immunology.	Rafael Valente Veiga Laboratório de Alergia e Acarologia – UFBA
	New immunological and molecular biomarkers in severe asthma.	Emília Maria Medeiros de Andrade Belitardo Laboratório de Alergia e Acarologia – UFBA
	Asthma epigenetics – How environmental factors can affect the regulation of gene expression in asthma.	Cinthia Vila Nova Santana Escola Bahia de Medicina e Saúde Pública
	Monocytes with pro-fibrotic phenotype in the pathogenesis of severe asthma.	Jamille Souza Fernandes Universidade Federal do Oeste da Bahia

02/09	SESSÃO APRESENTAÇÃO DISCENTES 3 16: 00-18: 00 h Moderadores: Maria de Fátima Dias Costa e Karina Costa da Silva	
	Polymorphisms in IFI16 gene are associated with periodontal disease in a population in Salvador/BA–Brazil	<u>Marcia Otto Barrientos</u> , Tatiane de Oliveira Teixeira Muniz Carletto, Helena Teixeira, Soraya Castro Trindade, Álvaro A. S. Cruz, Camila Alexandrina Viana Figueiredo, Ryan dos Santos Costa
	A missense-type variant, RS41347648, decreases risk of atopy in Brazilians but not asthma	Talita dos Santos de Jesus, Helena Teixeira, Gabriela P. Pinheiro, Álvaro A. S. Cruz, Ryan dos Santos Costa, Camila Alexandrina Viana Figueiredo
	Characterization of the immunological mechanisms induced in vitro by the SM29 antigen in macrophages of asthmatic individuals	<u>Luís Eduardo Viana Silva Ribeiro</u> , Tarciano Nascimento Pereira, Dário Jesus de Pascali, Gabriela P. Pinheiro, Jordana Batista Santana, Diego Mota Lopes, Sergio Costa Oliveira, Edgar Marcelino De Carvalho Filho, Álvaro A. S. Cruz, Luciana Santos Cardoso
	Association of RETN gene polymorphism with asthma – effect modification by abdominal obesity.	<u>Raísa Santos Coelho</u> , Ana Paula Castro Melo, Hatilla Santos, Helena Teixeira, Jamile S Fernandes, Gabriela P. Pinheiro, Adelmir S Machado, Álvaro A. S. Cruz, Camila Alexandrina Viana Figueiredo, Ryan dos Santos Costa.
	Association of variants in the PPARY gene with obesity in a Brazilian population.	<u>Ana Paula C. Melo</u> , Helena Mariana Pitangueira Teixeira; Raísa Santos Coelho, Neuza Maria Alcântara-Neves, Maurício Lima Barreto, Ryan Dos Santos Costa, Laise C.Pinto, Camila A. Figueiredo.
	Cytokine profile induced by <i>Dermatophagoides pteronyssinus</i> in whole blood cell culture from teenagers in SCAALA 2013.	<u>Flávia de Araújo Sena</u> , Emília Maria Medeiros de Andrade Belitardo, Alana Alcântara Galvão, Laure Laiane dos Santos de Jesus, Daniel dos Santos Rocha, Anaque de Oliveira Pires, Gerson de Almeida Queiroz, Álvaro A. S. Cruz, Maurício Lima Barreto, Camila Alexandrina Viana Figueiredo, Neuza Maria Alcântara Neves.
02/09	SESSÃO – APRESENTAÇÃO ORAL DISCENTES 4 19: 00-21: 00 h Moderadores: Juciele Valéria Oliveira e Andressa Souza Marques	
	HOMER2 gene variants are associated with BDR in asthmatics.	<u>Helena Teixeira</u> , Hatilla Santos, Ana Paula Castro Melo, Talita dos Santos de Jesus, Maria Borges Rabêlo de Santana, Ryan dos Santos Costa, Camila Alexandrina Viana Figueiredo.
	Association of variants in genes of the glucocorticoid pathway with lack of control in patients with severe asthma.	<u>Maria Borges Rabêlo de Santana</u> , Helena Teixeira, Hatilla Santos, Álvaro A. S. Cruz, Camila Alexandrina Viana Figueiredo, Ryan dos Santos Costa.
	Screening of machine learning algorithms for the prediction of asthma using genetic markers.	<u>Luciano Gama da Silva Gomes</u> , Camila Alexandrina Viana de Figueiredo, Álvaro Augusto Souza da Cruz Filho, Ryan dos Santos Costa.
	Genetic variant in mirna4500 are association with asthma and bronchodilator response	<u>Jéssica F de Araújo</u> , Hatilla S. Silva, Raísa S. Coelho, Helena M. P. Teixeira, Álvaro A. Cruz, Camila A. Figueiredo, Ryan dos S. Costa

03/09 03/09	SESSÃO TEMÁTICA – SARS-COV2 09: 00-11: 00 h Moderadores: Ricardo Wagner Portela, Vitor Antônio Fortuna e Rodrigo Carreira	
	A Brazilian experience in the diagnosis of Covid19.	Abelardo Silva Junior Universidade Federal de Viçosa
	Development of new methodologies for the diagnosis of SARS-COV2 infection.	Jussi Hepojoki Universidade de Helsinki
	SARS-VOC-2 infection in animals and its diagnosis.	Luiz Eduardo Ristow Laboratório TECSA
	SESSÃO TEMÁTICA – NEUROIMUNOENDOCRINOLOGIA E IMUNOFARMACOLOGIA 13: 00-15: 00 h Moderadores: Sílvia Lima Costa, Clarissa Schitine e Karina Costa	
	MicroRNAs in neuroinflammation: implications for neurodegenerative diseases.	Dora Brites Universidade de Lisboa
	Aspects of neuroinflammation associated with Parkinson's disease.	Maria Trinidad Herrero Ezquerro Universidade de Murcia
Neuroimmunological consequences of corticosterone depression.	Cecilia Hedin Pereira Universidade Federal do Rio de Janeiro	
The anti-inflammatory properties shown by a new biflavonoid represent a promising modifying therapy for demyelinating diseases.	Monique Marylin Alves de Almeida Laboratório de Neuroquímica e Biologia Celular – UFBA	
03/09	SESSÃO – APRESENTAÇÃO ORAL DISCENTE 5 16: 00-18: 00 h Moderadores: Simone Garcia Macambira e Cleonice Creusa dos Santos	
	Rutin inhibits glial activation and protects dopaminergic neurons against 6 – OHDA and aminochrome cytotoxicity in animal model.	<u>Fillipe Mendes De Araujo</u> , Annyta Fernandes Frota, Livia Bacelar De Jesus, Sílvia Lima Costa, Maria Trinidad-Herrero, Víctor Diógenes Amaral Da Silva.
	Effects of flavonoid rutin on gastrointestinal function and integrity in an experimental model of Parkinson's Disease.	<u>Livia Bacelar de Jesus</u> , Annyta Fernandes Frota, Fillipe Mendes De Araujo, Rafael Leonne Cruz de Jesus, Víctor Diógenes Amaral da Silva, Darizy Flavia Silva, Marcelo Biondaro Gois, Gyselle Chrystina Bacchan, Sílvia Lima Costa.
	The flavonoid agathisflavone modulates microglial activation and presents neuroprotective effects in vitro model of neuroinflammation.	<u>Balbino Lino dos Santos</u> , Cleonice Cleuza dos Santos, Víctor Diógenes Amaral da Silva, Sílvia Lima Costa.
	Agathisflavone increases the astrocytic population in the subventricular zone and modulates reactive gliosis in vivo.	<u>Juliana Helena Castro e Silva</u> , Francesca Pieropan, Andrea Rivera, Arthur Morgan Butt, Víctor Diógenes Amaral da Silva, Sílvia Lima Costa.
	The glucocorticoid receptor contributes to reduction of Ips-induced glial reactivity in vitro by agathisflavone.	<u>Áurea Maria Almeida</u> , Cleonice Cleuza dos Santos, Gloriene Carvalho De Jesus, Víctor Diógenes Amaral da Silva, Suzana Braga de Souza, Sílvia Lima Costa.
	Evaluation of the neuroprotector potential of flavonoids bis-apigenin and apigenin on amyotrophic lateral sclerosis models.	<u>Rodrigo Barreto Carreira</u> , Víctor Diógenes Amaral da Silva, Ravena Pereira Nascimento, Lucas Matheus Gonçalves de Oliveira, Luis Barbeito, Sílvia Lima Costa.

03/09	SESSÃO – APRESENTAÇÃO ORAL DISCENTE 6 19: 00-21: 00 h Moderadores: Luciana Cardoso e Luciano Gama	
	Nicotine inhibits aminochrome-induced in vitro cytotoxicity: perspectives for application in Parkinson's disease.	Érica Novaes Soares, Cleonice Cleuza dos Santos, Ana Carla dos Santos Costa, Maria de Fátima Dias Costa, Sílvia Lima Costa, Victor Diógenes Amaral da Silva.
	Evaluation of antioxidant mechanisms of the flavonoid agathisflavone against neuroinflammatory damage	Janaina Ribeiro Pereira Soares, Sílvia Lima Costa, Juçiele Valéria Ribeiro de Oliveira
	Prospecting for n-heterocyclic compounds to characterization of anti-glioma action mechanisms in glioblastoma cells and in interaction with microglia.	Jéssika Alves Oliveira Amparo, Raimundo Francisco dos Santos Filho, Victor Diógenes Amaral da Silva, Prof. Dr. Sílvio Desterro Cunha, Ravena Pereira do Nascimento, Sílvia Lima Costa.
	Study of the molecular mechanisms associated with anti-glioma and immunomodulatory effects of flavonoids.	Monique Reis de Santana, Ravena Pereira do Nascimento, David Gilot, Sílvia Lima Costa.
	Characterization of mi-RNAs in the phenotypic dysregulation of glioblastoma and microglial cells and as targets of antitumoral flavonoids.	Karina Costa da Silva, Balbino Lino dos Santos, Dora Brites, Sílvia Lima Costa.
04/09	SESSÃO – APRESENTAÇÃO ORAL DISCENTE 7 09: 00-11: 00 h Moderadores: Alexandre Moraes Pinheiro e Balbino Lino dos Santos	
	Immunomodulation of the ethanolic extract of <i>Phyllis angulata</i> on microglia cell crops infected by <i>Neospora caninum</i> .	Washington Santos Antunes, Sílvia Lima Costa, Alexandre Moraes Pinheiro.
	Evaluation of immunomodulatory effects of selenium dioxide in microglial rat cell cultures infected with <i>Neospora caninum</i> .	Brenda Valerio Souza, Ana Elisa Del'Arco Vinhas Costa, Maria de Fátima Dias Costa, Sílvia Lima Costa, Alexandre Moraes Pinheiro.
	Reverse vaccinology in murine model and canine for the control of <i>Toxocara canis</i> infection.	Dumar Alexander Jaramillo Hernández, Carina da Silva Pinheiro, Luis Fabián Salazar Garcés, Neuza Maria Alcântara Neves.
	Influence of <i>Trypanosoma cruzi</i> coinfection on the immune response and clinical outcome of patients with cutaneous leishmaniasis from the endemic area of Corte de Pedra-Bahia, Brazil.	Mônica Sousa Pita, Andréa Santos Magalhães, Lucas Pedreira de Carvalho.
	Heterologous production of recombinant <i>Schistosoma</i> elastase.	Carolina Orrico Melo Ferreira de Jesus, Barbara de Castro Pimentel Figueiredo, Carina da Silva Pinheiro, Beatriz de Souza Santos.
	Protective and profibrotic cytokines mediated by CD4+ T lymphocytes in periportal fibrosis secondary to schistosomiasis.	Jordana Batista Santana, Tarcísio Vila Verde S. de Almeida, Diego Mota Lopes, Luís Eduardo Viana Silva Ribeiro, Néstor A. Guerrero Gutierrez, Edgar Marcelino de Carvalho Filho, Luciana Santos Cardoso.
	The use of tumor antigens in the immunization of animals chronically infected with <i>Trypanosoma cruzi</i> previously treated with adjuvants	Amanda Silva, Davi Salles, Maiara Bonfim, Jose Mengel, Fabiola Cardillo

04/09	SESSÃO TEMÁTICA – IMUNOLOGIA DAS DOENÇAS INFECCIOSAS E PARASITÁRIAS 13: 00-15: 00 h Moderadores: Barbara de Castro Figueiredo, Carina da Silva Pinheiro e Rosimére Torres	
	<i>Schistosoma mansoni</i> surface proteins: their anti-inflammatory properties and role as potential molecules for therapeutics.	Sergio Costa Oliveira Universidade Federal de Minas Gerais
	How the development of a Recombinant BCG vaccine against <i>Bordetella pertussis</i> lead to an improved Tuberculosis vaccine.	Luciana Cezar de Cerqueira Leite Instituto Butantan
	Platforms for COVID-19 diagnosis and monitoring.	Luiz Ricardo Goulart Filho Universidade Federal de Uberlândia
	Inflammasome activation by CD8+ T cells from Patients with Cutaneous Leishmaniasis caused by <i>Leishmania braziliensis</i> in the immunopathogenesis of the disease.	Cláudia Ida Brodskyn Fundação Oswaldo Cruz-CPqGM
04/09	SESSÃO – APRESENTAÇÃO ORAL DISCENTES 8 16: 00-18: 00 h Moderadores: Alex José Leite Torres e Natália da Rocha Lopes	
	Study of glial response in a new in vitro model of cerebellar cell culture.	<u>Lucia Fonseca Santana</u> , Cleonice Creuza dos Santos, Rafael Short Ferreira, Maria Victoria Lima de Castro, Sílvia Lima Costa, Victor Diogenes Amaral da Silva.
	Evaluation of the therapeutic potential of mesenchymal cells that overexpress IGF1 on skeletal muscle injury induced by inoculation of <i>Bothrops snake</i> venom.	<u>Kaenna Baraúna Campos</u> , Luciana Lyra Casais E. Silva, Clara Macêdo Mimoso, Simone Garcia Macambira.
	Skeletal muscle injury induced by <i>Bothrops leucurus</i> venom and tissue repair: inflammatory profile and mechanisms involved.	<u>Clara Macêdo Mimoso</u> , Kaenna Baraúna Campos, Simone Garcia Macambira, Luciana Lyra Casais E. Silva.
	Pretreatment neutrophil-to-lymphocyte ratio as prognostic parameter for surgical resection in advanced oral squamous cell carcinoma patients.	<u>Renata Freitas Araujo-Calumby</u> , André Leonardo de Castro Costa, Deyse Souza Carvalho Da Silva, Daniel Nascimento, Anna Beatriz Pereira Simões Alves, Miguel de Jesus Oliveira Santos, Lucianna Stutz Souza Carneiro de Campos, Gessualdo Seixas Oliveira Junior, Matheus Antonio da Hora Borges, Camila da Silva Souza, Marcus Antonio de Mello Borba, Lucas Gomes Da Silva, Iguaracyra Barreto de Oliveira Araujo, Rodrigo Tripodi Calumby, Sílvia Lima Costa, Deise Souza Vilas Bôas.
Evaluation of mapkp38, JNK and ERK1 / 2 signaling pathways in chronic periodontitis	<u>Rebeca Pereira Bulhosa Santos</u> , Patricia Mares de Miranda, Michelle Miranda Lopes Falcão, Soraya Castro Trindade	

05/09	SESSÃO TEMÁTICA – IMUNOGENÉTICA, GENÔMICA E PROTEÔMICA 9: 00-11: 00 h Moderadores: Thiago Luiz Castro, Silvana Marchioro e Clara Macêdo	
	Omics as a tool for control of infection by <i>Aeromonas hydrophila</i> in aquatic organisms.	Mateus Matiuzzi da Costa Universidade do Vale do São Francisco
	Omics applied to the study of pathogenic microorganisms.	Pablo Ivan Pereira Ramos Fundação Oswaldo Cruz-CPqGM
	Proteomic analysis of macrophages infected with <i>Mycobacterium smegmatis</i> after consumption of cholesterol.	Agenor Valadares Santos Universidade Federal de Pará
	Adding new allergens in the World Health Organization official list for <i>Blomia tropicalis</i> IgE-binding proteins by proteomic analysis	Eduardo Santos da Silva Laboratório de Alergia e Acarologia – UFBA
05/09	SESSÃO TEMÁTICA – IMUNODEFICIÊNCIA E IMUNOPATOLOGIA 13: 00-15: 00 h Moderadores: Simone Garcia Macambira, Vitor Antônio Fortuna e Nívia Nonato	
	Research of new drugs in experimental models of inflammation.	Jaime Ribeiro Filho Fundação Oswaldo Cruz-CPqGM
	Immunomodulation of Chagas Disease.	Juliana Fraga Vasconcelos Escola Bahiana de Medicina e Saúde Pública
	Lipid mediators in diabetes and increased susceptibility to infections.	Natália Machado Tavares Fundação Oswaldo Cruz-CPqGM
	Physalins and their pharmacological potential as an immunomodulator.	Vinícius Pinto Costa Rocha Fundação Oswaldo Cruz-CPqGM
05/09	SESSÃO PLENÁRIA – PREMIAÇÕES E ENCERRAMENTO 15: 00 – 16: 00 h Moderadores: Sílvia Lima Costa e Vitor Antônio Fortuna	

OBS. O acesso às Sessões do evento será através da plataforma <https://zoom.us/>
O Meeting ID e o Passcode para cada Sessão será disponibilizado 30 minutos antes do início de cada Sessão em <http://www.ppgim.ics.ufba.br/>

PESQUISADORES

PROTEOMIC ANALYSIS OF MACROPHAGES INFECTED WITH MYCOBACTERIUM SMEGMATIS AFTER CHOLESTEROL CONSUMPTION

Jaqueline Batista De Lima ¹, Juliana Silva Cassoli ¹, Rafael Valadares Borges², Chubert Bernardo Castro De Sena ¹,
Agenor Valadares Santos¹

1-Universidade Federal do Pará, 2- Instituto Tecnológico Vale

ABSTRACT: Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* and mainly affects lungs. Alveolar macrophages are main host that form granulomas in order to contain bacterial dissemination compromising lung integrity. This work aims to study interactions between macrophages and *Mycobacterium smegmatis* after it was induced to consume cholesterol through minimal medium cultivation and evaluate changes caused in the host through expression profile of proteins involved in the infection. This kind of bacterium is used as an in vitro study model for tuberculosis due to its accelerated metabolism allowing rapid growth and, not pathogenicity, and per sharing cell wall structure similar to *Mycobacterium tuberculosis*. Cholesterol is used to mimic the conditions that bacillus undergoes in the pulmonary granulomas of tuberculosis patients. On this environment, it causes a large accumulation of host cholesterol and uses it as a source of energy and carbon for its survival, as well as to modulate changes in bioactive molecules in its cell wall, which play an important role in its pathogenicity and interaction with the cells phagocytic cells. To relate bacillus cholesterol consumption to response to macrophage infection, *Mycobacterium smegmatis* was cultivated in 7H9 complete medium supplemented with glycerol, minimal medium supplemented with cholesterol and in minimal medium without supplementation and after macrophages line J774A.1 was infected with these bacilli. Our results demonstrated that *Mycobacterium smegmatis* after consuming cholesterol is able to induce macrophages to form granuloma-like structures in vitro. Through proteomic analyzes we suggest that the consumption of cholesterol by *M. smegmatis* modifies the bacillus to the point where it interacts with the host cell the same way as the pathogenic strain of *M. tuberculosis*. Differential expression of some proteins may be causing inhibition of phagosome acidification, blocking phagolysosome fusion and production of inflammatory mediators. In addition, it may be suppressing important host metabolic pathways to modulate the immune response and favor survival and formation of granuloma-like structures.

Keywords: *Mycobacterium*, proteomics, cholesterol, infection, macrophages.

Support: CAPES

NEUROIMMUNOLOGICAL CONSEQUENCES OF CORTICOSTERONE IN A DEPRESSION MODEL

Caio Oliveira de Sá-Ferreira, Cecilia Hedin-Pereira

VPPCB, Fiocruz and Laboratory for Cellular NeuroAnatomy, ICB, UFRJ

ABSTRACT: Major depression is the most common neuropsychiatric disorder leading even to suicide. Along with the mood changes biochemical and structural modifications occur in the brain. The etiology of depression is multifactorial, however, unbalance of the HPA axis appears to be an important factor. Since the chronic activation of the HPA axis commonly underlies depression we have developed a mouse model of high corticosterone by administration in drinking water to mimic chronic stress conditions. Mice submitted to this paradigm developed depression in 28 days of corticosterone with decrease in serotonin and dopamine levels and depressive-like behavior. Previous studies have shown alterations in hippocampal neurogenesis and myelin damage in humans. We therefore investigated whether myelin disturbances occur and the regenerative capacity of oligodendrocyte progenitors. Furthermore, we analyzed the neuro-inflammatory response by measuring cytokines (pro-inflammatory and anti-inflammatory) and the microglial population at the subventricular zone (SVZ) corpus callosum (cc) and frontal cortex. Analyzing cytokines IL-1, 6, TNF and IL-10. We showed they were not increased in the SVZ. The cellular analysis of SVZ and cc were carried

out by immunohistochemistry. Our data revealed an increase in oligodendrocyte lineage cells (Olig2+) in the SVZ concomitant to a reduction of Olig2+ cells in corpus callosum of CORTICO/ISO group. Also, electron microscopy analysis showed both reduced fiber and axon areas in the corpus callosum of CORTICO/ISO group compared to control and a myelin area reduction as well, suggesting that myelination may be compromised in the pathophysiology of major depression. Finally, we showed an increased population of microglia (Iba1+ cells) in the CORTICO/ISO group in SVZ and peri SVZ when compared with control, which reveals a possible role of microglial cells in the disorder. Hence, we show that this model promotes consistent behavioral depressive-like symptoms. Also, we described for the first time an increase in oligodendrocyte committed cells in SVZ accompanied by a decrease within the corpus callosum with cellular and myelin disturbances. Therefore, our study unveils profound cellular changes in neuronal and nonneuronal populations in a corticosterone induced depression model which are promising therapeutic targets for the disorder.

Keywords: immunohistochemistry; corticosterone; depression

Support: CAPES

INFLAMMASOME ACTIVATION BY CD8⁺T CELLS FROM PATIENTS WITH CUTANEOUS LEISHMANIASIS CAUSED BY *LEISHMANIA BRAZILIENSIS* IN THE IMMUNOPATHOGENESIS OF THE DISEASE.

Thiago Marconi Cardoso^{1,2,3}; Jonilson B. Lima⁶; Ícaro Bonyek-Silva,^{1,5} Sara Nunes,^{1,5} Daniel Feijó¹; Hugo Almeida¹ Juliana Silva.²; Aldina Barral^{1,4}; Viviane Boaventura,^{1,5} Valéria M. Borges¹; Dario S. Zamboni⁷; Lucas Pedreira de Carvalho,^{1,2,3}; Edgar M. Carvalho^{1,2,3}; Natalia M. Tavares,^{1,4,5}; Cláudia Brodskyn^{1,4,5}

1.Fiocruz-BA, Instituto Gonçalo Moniz, Salvador, Bahia, Brazil. 2.Serviço de Imunologia, Hospital Universitário Prof. Edgar Santos, Universidade Federal da Bahia, Salvador, BA, Brazil. 3.Instituto Nacional de Ciência e Tecnologia de Doenças Tropicais - INCT-DT (CNPq/MCT), Salvador, BA, Brazil. 4.Instituto Nacional de Ciência e Tecnologia de Instituto de Investigação de Imunologia (CNPq/MCT), São Paulo, SP, Brazil. 5.Faculdade de Medicina da Universidade Federal da Bahia, Salvador, Bahia, Brazil. 6.Centro de Ciências Biológicas e da Saúde, Universidade Federal do Oeste da Bahia (UFOB). 7.Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo.

ABSTRACT: Our group previously showed that CD8⁺T cells contribute to the immunopathogenesis of Cutaneous Leishmaniasis (CL) through the mediation of tissue injury and inflammation. Here we investigate the role of CD8T cells in the activation of the inflammasome and IL-1 β , which drives inflammation in skin lesions caused by *Leishmania braziliensis*. The investigation of fresh CL skin biopsies revealed increased expression of caspases-1 and -5, as well as NLRP3 and AIM2. Similar increases in expression were observed in PBMCs from CL patients stimulated with *L. braziliensis*, and in co-cultures of CD8⁺T cells and infected macrophages. Skin biopsies of lesions, as well as co-cultures of infected macrophages and CD8⁺T cells, showed increased active caspase-1 expression, as evidenced by ELISA, FLICA and IL-1 β protein, in contrast to decreased expression observed through the inhibition of the CD8 cytolytic enzymes. In contrast caspase-1 or IL-1 β production were not increased in infected macrophages or in co-cultures of infected macrophages and CD4⁺T cells. These results suggest that cytolytic process in *Leishmania*-infected macrophages induced by perforin and granzyme can lead to an osmotic imbalance in the cellular membrane. The consequent release of potassium triggers inflammasome activation and IL-1 β production, contributing to the persistent inflammation seen in CL lesions.

Keywords: leishmania braziliensis, cytotoxicity, inflammasomes

Support: Fapesb and CNPq

MICRORNAS IN NEUROINFLAMMATION: IMPLICATIONS IN NEURODEGENERATIVE DISORDERS

Dora Brites^{1,2}

¹*Neuron-Glia Biology in Health and Disease, Research Institute for Medicines (iMed.Ulisboa), Faculty of Pharmacy, Universidade de Lisboa, Lisbon, Portugal*

²*Department of Biochemistry and Human Biology, Faculty of Pharmacy, Universidade de Lisboa, Lisbon, Portugal*

ABSTRACT: Neurodegenerative disorders, such as amyotrophic lateral sclerosis (ALS), Alzheimer's disease (AD) or Parkinson's disease, occur by neuronal degeneration (Neurocentric view) and neuroinflammation associated to astrocyte reactivity and microglia activation (Gliocentric view). Though not yet clarified what comes first, the deregulated communication between these cells at the central nervous system (CNS) are without doubt involved in disease progression. In addition, besides similarities between such disorders, there are as well pathological differences that associate to each cell response to a stimulus, its heterogeneity and regional diversity. Microglia comprise 5-10% of the total CNS in humans and mice. They colonize the CNS early in embryonic development and are the innate immune cells of the brain. Astrocytes are at least 50% of the cells at the brain and spinal cord and provide trophic **Support** to neurons. Both are key players in sustaining CNS homeostasis and synapse dynamics. Changes in microglia and astrocyte transcriptomes in response to a variety of CNS pathologies were recently identified. However, due to the complexity of cell subtypes, as well as a kaleidoscope of autocrine and paracrine signaling, and their dependence of disease progression stages, it has been difficult to identify cell specific pathological effectors and their targets. Intercellular communication involves in addition to cell-to-cell contacts, signaling pathways by soluble factors and extracellular vesicles (EVs), which are released from most cells, including neurons, astrocytes, and microglia [1]. Among the molecules that are transmitted between cells, noncoding RNAs [microRNAs (miRNAs)] that circulate in the soluble form or encapsulated in EVs have a crucial role in intercellular communication at short and long distances, respectively. In this talk we will address the miRNAs more associated to the neuroinflammatory processes subsequent to astrocyte and microglia activated polarization and we will give examples of their signature in ALS and AD when using mice and human models [2, 3], as well as their potential applications for diagnosis and therapeutics.

Keywords: Neurodegenerative disorders; neuroinflammation; miRNAs.

Support: EU Joint Programme-Neurodegenerative Disease Research (JPND) and Fundação para a Ciência e a Tecnologia (FCT-JPco-fuND/0003/2015 to DB), Santa casa da Misericórdia de Lisboa (SCML - ALS Research Grant ELA-2015-002 to DB), FCT (PTDC/MED-NEU/31395/2017 and LISBOA-01-0145-FEDER-031395 to DB), and in part by UID/DTP/04138/2019 to iMed.Ulisboa. [1] *Brites D Glia 2020*; [2] *Fernandes et al Biochimie 2018*; *Gomes et al Exp Cell Res 2020*.

ADDING NEW IGE-BINDING PROTEINS OF *BLOMIATROPICALIS* IN THE WORLD HEALTH ORGANIZATION OFFICIAL LIST OF ALLERGENS THROUGH PROTEOMIC ANALYSIS

EDUARDO SILVA¹; JOÃO PONTE¹; MÁRCIA SILVA¹; CARINAPINHEIRO¹; LUIS PACHECO¹; FÁTIMA FERREIRA²; PETER BRIZA¹; NEUZA ALCÂNTARA-NEVES¹

¹*Laboratório de Alergia e Acarologia, Departamento de Ciências da Biointeração, Instituto de Ciências da Saúde, Universidade Federal da Bahia, Salvador, Brazil*; ²*Department of Biosciences, University of Salzburg, Salzburg, Austria*;

ABSTRACT: House dust mites (HDM) represent one of the main sources of IgE-binding proteins and risk factors for different allergic illnesses. Initially identified as a storage mite, *Blomia tropicalis* also constitutes a very important HDM species, whose allergens have been partially recognized by the World Health Organization and International Union of Immunological Societies (WHO/IUIS) Allergen Nomenclature Sub-committee. Other HDM species had a larger list of acknowledged allergens in comparison to *B. tropicalis*, mainly due to the advent of the "omics" studies, which have largely been restricted to *Dermatophagoides* spp. **Aim:** To increase the knowledge and number of *B. tropicalis* allergens in WHO/IUIS official list through proteomic analysis. **Methods:** Eleven in-bred lineages of *B. tropicalis* were generated from 11 unique different pregnant females. Their somatic extracts were analyzed and compared with a commercially

available extract by liquid chromatography tandem mass spectrometry (LC-MS/MS). After this *in solution* analysis, one of the extracts were analyzed by two-dimensional gel electrophoresis as well as IgE immunoblotting using a pool of sera from *B. tropicalis*-sensitized patients. Spots of interest were excised and the proteins were digested with trypsin before subjecting the peptides to LC-MS/MS and database search. All non-acknowledged isoallergens with sufficient data for WHO/IUIS recognition were sent to the subcommittee. **Results:** The generated breeds displayed considerable differences in the protein expression profiles, and most of them exhibited higher content of major allergens than the commercially available extract. The most prominent allergenic protein was Blot 2. Fourteen new isoforms and six WHO/IUIS non-recognized allergens were identified by *in solution* analysis. In-gel digestion analysis allowed us to confirm the presence of two new allergens, and two new isoforms, among other allergens already acknowledged by WHO/IUIS. Contrarywise, three previously recognized *B. tropicalis* allergens were not found in our analyses. From the ten files sent to WHO/IUIS, four have been analyzed so far and three allergens were added to *B. tropicalis* official list. **Conclusions:** Inbreeding impacts allergen content and LC-MS/MS may be a useful method not only as a quality control tool for allergen extracts, but also to increase the knowledge on allergens from HDM species.

Keywords: proteome, house dust mite, immunoblotting.

Support: CAPES, project No.077/2012

DIAGNOSIS OF MALIGNANT HEMOPATHIES BY FLOW CYTOMETRY IMMUNOPHENOTYPING

Herbert Henrique Santos Melo

Serviço de hematologista do HUPES LabImuno - UFBA

ABSTRACT: Flow cytometry is a technique used as a mean of obtaining basic parameters such as size and shape. However, technological improvements and scientific breakthroughs, for example, the production of monoclonal antibodies initiated a series of changes in the laboratorial routine, that now can be used by biomedical professionals, as an example, hematological, molecular biology and others. Flow cytometry is a technique that makes possible a multi-parametric analysis of blood cells, something that is possible because of the development of monoclonal antibodies and combination of them to fluorochromes, something that contributed to the process of understanding physiological changes that occur during the maturation and differentiation of all the normal elements of the hematopoietic system, similar to those that may occur during the development of pathological process. Immunophenotyping of neoplastic of hematopoietic cells not only helps the differential diagnosis and leads to the appropriate therapy but also contributes to the classification of leukemias.

Keywords: Leukemias, Flow Cytometry, Blood cells

Support: Fundação de Apoio à Pesquisa e Extensão - FAPEX

Investigation of new drug candidates for the treatment of inflammatory diseases

Gustavo Marinho Miranda, Vitória Ohana Ramos e Santos, Tiago Santos Carvalho Da Rocha, Sânzio Silva Santana, Jamile de Jesus Vieira, Sètonджи Cocou Modeste Alexandre Yahouédéhou, Marilda Souza Goncalves and Jaime Ribeiro-Filho*

INSTITUTION: *Instituto Gonçalo Moniz, Fundação Oswaldo Cruz, Salvador 40296-710, Brasil*

*Correspondence: jaime.ribeiro@fiocruz.br

ABSTRACT: The inflammatory response to tissue damage can occur through different mechanisms of induction, regulation, and resolution. While inflammation is an essential process for the host defense against pathogens, failures in the resolution of this process have been associated with the development of chronic diseases that require long-term therapy. As the currently available anti-inflammatory drugs present significant therapeutic limitations, the development of novel drugs remains an extremely relevant topic. We have used both *in vivo* and *in vitro* models to investigate the anti-inflammatory potential of new compounds, with an emphasis on natural products such as curine, an alkaloid that has demonstrated antiallergic, analgesic, and immunomodulating properties in different models of inflammation. Curine was found to inhibit leukocyte recruitment activation, which was associated with inhibition of inflammatory mediator production both *in vivo* and *in vitro*. Curine also inhibited allergic symptoms in murine models of asthma, anaphylaxis, and skin allergy. This alkaloid also presented analgesic effects that were associated with anti-inflammatory mechanisms (in particular, inhibition of PGE₂ production), and evidence has demonstrated that the mechanism of action by curine depends, at least partially, on inhibition of a calcium-dependent response. Our research has also evaluated the use of carrier nanoparticles such as cyclodextrins to improve the physicochemical and biopharmaceutical properties of natural products such as essential oils and their isolated components. In **Conclusion**, natural products represent promising sources of bioactive compounds with the potential to be used in anti-inflammatory drug development.

Keywords (3): Inflammation. Drug development. Natural products

Support: Instituto Gonçalo Moniz, Fundação Oswaldo Cruz

IMMUNOMODULATION IN CHAGAS DISEASE

Juliana Fraga Vasconcelos

Escola Bahiana de Medicina e Saúde pública

ABSTRACT: Chronic chagasic cardiomyopathy is a leading cause of heart failure in Latin American countries, being associated with intense inflammatory response and fibrosis. Currently, there is no drug capable of improving the established CCC, being the inflammatory response an important target. Here we are going to discuss the main immunomodulation strategies for chagasic myocarditis that occur in the chronic phase of the disease, with emphasis on the role of pro and anti-inflammatory mediators.

Keywords: CCC. Inflammation. Fibrosis.

Support: Escola Bahiana de Medicina.

HOW THE DEVELOPMENT OF A RECOMBINANT BCG VACCINE AGAINST BORDETELLA PERTUSSIS LEAD TO AN IMPROVED TUBERCULOSIS VACCINE.

Luciana Cezar de Cerqueira Leite

Instituto Butantan

ABSTRACT: New strategies against *Mycobacterium tuberculosis* (*Mtb*) have become a global priority, since *Mycobacterium bovis* Bacille Calmette-Guérin (BCG), has shown variable results of protective efficacy and there is a rising frequency of multi-drug resistant (MDR) *Mtb* strains. We have previously developed a recombinant BCG expressing the S1 subunit of pertussis toxin as a neonatal vaccine against Whooping cough. These studies revealed the immunomodulatory properties of toxin derivatives, leading to the development of arBCG strain expressing the adjuvant LTAK63 (rBCG-LTAK63). This strain has been shown to be more protective than BCG against tuberculosis (TB) using an intratracheal challenge animal model. Our results show that the rBCG-LTAK63 induces enhanced innate immunity, increased Th1 responses in the lungs and Th17 long-term immune responses as compared to BCG wild type.

Keywords: Recombinant BCG, Pertussis, Tuberculosis

Support: FAPESP, BNDES.

PLATFORMS FOR COVID-19 DIAGNOSIS AND MONITORING.

Luiz R. Goulart, Thulio M. Cunha, Mário M. Martins, Anderson R. Santos, Murillo. G. Carneiro e Robinson Sabino-Silva.

Federal University of Uberlandia

ABSTRACT: Novel alternatives for disease diagnostics and monitoring have been developed based on biophotonics and mass spectrometry platforms. We will present two technologies that are reagent-less, used specifically in the COVID-19 pandemic, that not only integrate artificial intelligence tools, but also Big Data applications. Spectroscopic and spectrometric signatures can define new strategies for approaching personalized medicine as well as public policies, providing simplified diagnosis and monitoring of complex and chronic-degenerative diseases. The new disruptive platforms will be discussed regarding their impact on the diagnostic market.

Keywords: Covid-19, Reagent-less diagnostics, Biophotonics.

Support: Imunoscan Engenharia Molecular Ltda, Federal University of Uberlandia, and Ministry of Science and Technology - FINEP.

“OMICS” AS A TOOL FOR CONTROL OF INFECTION BY *AEROMONAS HYDROPHILA* IN AQUATIC ORGANISMS

Mateus Matiuzzi da Costa¹, Ruan Emmanuell Franco de Abreu²

1-Federal University of São Francisco River Valley; Federal Rural University of Pernambuco

ABSTRACT: Fish farming represents one of the fastest growing agricultural activities in Brazil. Super intensive production systems provide stressful situations to animals, causing advantage to opportunistic pathogens to explore immunosuppression to institute the disease process. *Aeromonas hydrophila* are distributed naturally in diverse aquatic ecosystems, where they are easily isolated from disease cases in aquatic organisms. In these animals the infections by these opportunistic pathogens are associated to hemorrhagic lesions and septicemia. Metagenomic, transcriptomic, and metabolomic methods, colloquially called “omics,” are approaches that can better inform the relationship among pathogens and its host defenses. The integration of multiple omic data using bioinformatic and statistical tools and *in*

silico models are important to allow the development of prophylaxis strategies. As result of *in vitro* study identified that signals from environmental (ammonia concentration) has effects in *A. hydrophilavirulence* gene expression, as *fla* linked to motility and biofilm formation. *In vivo* study involving *A. hydrophila* infection in Nile Tilapia by skin transcriptome analysis demonstrated the role of innate immunity on the initial infection of *A. hydrophila* and the contribution of iron regulation in the disease and mortality process.

Keywords: Fish, RNA-Seq, Vaccine.

Support: CAPES, FACEPE

ANTI-INFLAMMATORY PROPERTIES DISPLAYED BY A NOVEL BIFLAVONOID REPRESENT A PROMISING DISEASE-MODIFYING THERAPY FOR DEMYELINATING DISEASES

Monique Marylin Alves de Almeida

Universidade Federal da Bahia/University of Portsmouth-UK

ABSTRACT: Inflammation and myelin dysfunction play a significant role in the pathogenesis of various neurodegenerative diseases. Therefore, there is a critical need to develop more effective therapies for the treatment of these disorders. In this study, we examined the effect of the flavonoid agathisflavone on neuroinflammation and demyelination, which are hallmarks of demyelinating diseases, such as multiple sclerosis. Agathisflavone showed an important anti-inflammatory response in the different models approached, and, consequently, it accelerated remyelination, an effect that seems to be attributed to its affinity for binding to estrogen receptors.

Keywords: Flavonoids; Demyelination; Inflammation.

Support: This work was Supported by the Multiple Sclerosis Society (AB, FP-Award Reference: 40) and the Biological Sciences Research Council (AB, Grant number: BB/M029379/1). This work was also Supported by the Coordination of Personnel Improvement of Higher Level (CAPES, Process Nº 88881.117666/2016-01, and PDSE Scholarship Nº 88881.133939/2016-01), Foundation for Research Support of the State of Bahia (Process Nº INT 0016/2016) and the National Council for Scientific and Technological Development (CNPq, Scholarship Nº 140333/2016-9, Post-Graduation Program in Immunology- Federal University of Bahia-Brazil).

MEDIADORES LIPÍDICOS NO DIABETES E AUMENTO DA SUSCEPTIBILIDADE À INFECÇÕES.

Bonyek-Silva, Icaro; Nunes, Sara; Santos, Reinan; Lima, Filipe; Lago, Alexandro; Silva, Juliana; Carvalho, Lucas; Arruda, Sergio; Serezani, Henrique; Carvalho, Edgar; Brodskyn, Claudia ; Tavares, Natalia

Instituto Gonçalo Moniz (IGM) - Fiocruz/BA

ABSTRACT: Poorly controlled diabetes mellitus leads to several comorbidities, including susceptibility to infections. Hyperglycemia increases phagocyte responsiveness, however immune cells from people with diabetes show inadequate antimicrobial functions. We and others have shown that aberrant production of leukotriene B4 (LTB4) is detrimental to host defense in models of bacterial infection. Here, we will unveil the consequences of high glucose in the outcome of *Leishmaniabraziliensis* skin infection in people with diabetes and determine the role of LTB4 in human phagocytes. We show that diabetes leads to higher systemic levels of LTB4, IL-6 and TNF- α in cutaneous leishmaniasis. Only LTB4 correlated with blood glucose levels and healing time in diabetes comorbidity. Skin lesions of people with leishmaniasis and diabetes exhibit increased neutrophil and amastigote numbers. Monocyte-derived macrophages from these individuals showed higher *L. braziliensis* loads, reduced production of Reactive Oxygen Species and unbalanced LTB4/PGE2 ratio. Our data reveal a systemic inflammation driven by diabetes comorbidity in opposition to a local reduced capacity to resolve *L. braziliensis* infection and a worse disease outcome.

Keywords: Diabetes, human leishmaniasis, lipid mediators.

Support: FAPESB, CNPq, CAPES.

OMICS APPLIED TO THE STUDY OF PATHOGENIC MICROORGANISMS

Pablo I. P. Ramos

Instituto Gonçalo Moniz, FIOCRUZ-Bahia

In this talk, I will explore the tremendous impacts of high-throughput sequencing efforts to the understanding of the biology of pathogenic organisms, particularly multidrug-resistant bacteria. Some examples of bacterial isolates whose genomes were determined in Brazil will be given, and how this integrated understanding may lead to novel ways to counter these pathogenic organisms will be briefly presented.

Keywords: genomics; bioinformatics; bacteria; pathogens

Support: Instituto Gonçalo Moniz, FIOCRUZ-Bahia

RECOMBINANT PROTEINS FOR HCV DIAGNOSTIC EVALUATION AND / OR MONITORING

Costa, Paulo Inácio da; Kenfe, Flávia Regina

Faculdade de Medicina de Ribeirão Preto Universidade do estado de São Paulo

ABSTRACT: The hepatitis C virus (HCV) is an enveloped virus of about 50 to 70 nm in diameter, positive strand RNA, and belongs to the genus Hepacivirus and the family Flaviridae. The detection and quantification of the core antigen, HCV nucleocapsid protein, has been successful in many trials and is considered a marker of viral replication, since it presents a sequence of highly conserved amino acids, giving it high sensitivity and specificity. The E2 protein is an envelope glycoprotein of HCV with 11 glycosylation sites, most of these well-conserved, making it a target antigen. The aim of this study was to develop high sensitivity, low cost diagnostic methods for HCV which could be used for serological screening. The genomic regions encoding the core (part 136 aa) and E2 proteins of HCV were expressed in *E. coli* Rosetta strain, cloned in expression vector pET-42a, and induced with 0.4 mM IPTG, producing recombinant proteins fused to GST protein (glutathione S-transferase), which were then purified by affinity chromatography. The immunoreactivity was assessed by Western blot, Slot Blot and the developed and improved diagnostic methods (enzyme-linked immunosorbent assay (ELISA) capture and indirect, immunoblotting and immunochromatographic). The methods developed were more sensitive and specific using the mixture of the recombinant proteins fused to GST (core + E2).

Keywords: Hepatite C; Proteínas ;Teste imunoenzimático

Support: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP)

CHALLENGES IN SCHISTOSOMIASIS CONTROL

SANTOS RA; DE JESUS KEM; TABAJARA Y; SILVA TM; MACEDO MN; FIALHO TRS; OLIVEIRA BSS; CASAES AC; PINHEIRO E; GRATIVAL B; FRANCISCO MVLO; CARDOSO LS; PITANGA TN; GONÇALVES MS; SIQUEIRA IC; OLIVEIRA RR

GONÇALO MONIZ INSTITUTION – FIOCRUZ-BA

ABSTRACT: Schistosomiasis is a parasitic disease of great relevance to public health. In Brazil, the disease is caused by *Schistosomamansonii*. The Point-Of-Care Circulating Cathodic Antigen (POC-CCA), is a rapid test for the diagnosis of schistosomiasis in urine. Since the POC-CCA is still being studied in Brazil, it is necessary to evaluate factors that may interfere with the test performance. Our goal is to investigate whether physicochemical factors in urine may interfere with the result of POC-CCA. Residents of rural areas in the municipality of Conde-BA were included, who provided samples of feces and urine, for making two Kato-Katz slides and performing POC-CCA and urine tape. Of the 189 individuals included in the study, 116 (61.4%) were positive for Kato-Katz schistosomiasis. A total of 89 (76.7%); 22 (19.0%) and 5 (4.3%) individuals had low, medium and high parasitic loads, respectively. POC-CCA positivity was observed in 102 (54.0%) urine samples, with a kappa agreement of 0.267 between Kato-Katz and POC-CCA. As Kato-

Katz has low sensitivity, but specificity close to 100%, we decided to evaluate the urine characteristics of the 41 individuals (21.7%) who presented false-negative results for POC-CCA. It was observed that almost all individuals who present false-negative results for POC-CCA have low parasitic load (87.8%, $p < 0.01$). Likewise, 79.2% of the false-negative results were obtained from urines that showed high density ($> 1025 \text{ Kg / m}^3$; $p < 0.0001$). All individuals who had blood in the urine ($n = 2$) had a false negative result. While of the individuals who had leukocytes in the urine ($n = 4$), 75% were false-negative for POC-CCA. We conclude that the low parasitic load and physico-chemical changes in the urine may interfere with the result of the POC-CCA. This fact allows us to evaluate potential limitations in the performance of the method that can lead to failure to eradicate the disease, by covering up individuals who are truly positive.

Keywords: Schistosomiasis; POC-CCA; diagnosis

Support: FAPESB, CNPq, PGPAT, IGM-FIOCRUZ/BA

SCHISTOSOMAMANSONI SURFACE PROTEINS: THEIR ANTI-INFLAMMATORY PROPERTIES AND ROLE AS POTENTIAL MOLECULES FOR THERAPEUTICS

Sergio C. Oliveira^{1,2,*}, Luciana S. Cardoso^{2,3}, Edgar M. Carvalho^{2,4}, Fabio S. Mambelli¹, Suellen B. Morais¹, Mariana T.Q. de Magalhães¹, Barbara C. Figueiredo⁵

¹Departamento de Bioquímica e Imunologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

²Instituto Nacional de Ciência e Tecnologia em Doenças Tropicais (INCT-DT), Salvador, Bahia, Brazil. ³Departamento de Análises Clínicas e Toxicológicas, Faculdade de Farmácia, Universidade Federal da Bahia, Salvador, Bahia, Brazil.

⁴Instituto Gonçalo Moniz, FIOCRUZ, Salvador, Bahia, Brazil. ⁵Departamento de Bioquímica e Biofísica, Universidade Federal da Bahia, Salvador, BA, Brazil.

ABSTRACT: *Schistosomamansonii* is one of the main agents of schistosomiasis, which is the most important human helminthic infection in terms of global morbidity and mortality. Although schistosomiasis represents a major public health problem in endemic countries, evidences show that *S. mansoni* downregulates inflammatory responses in many diseases. Fortunately, the control of inflammatory responses is extended to pathogen-derived antigens, leading us to study two important molecules *S. mansoni* Sm29 and the Kunitz type protease inhibitor (*SmKI-1*). We have previously demonstrated that rSm29 reduces TNF- α and IFN- γ production and increases regulatory T cells in cutaneous leishmaniasis (CL) patients. Sm29 also acts in dendritic cells (DC) increasing IL-10 and IL-10 receptors expression in CL patients. We recently developed a gel formulation containing rSm29 and gold nanoparticles. In preliminary experiments in patients, we showed that rSm29 had no clinic or laboratory adverse reactions. We showed that the combination of glucantime (Sanofi-Aventis) plus topical Sm29 cured 87.5% of patients by day 90 while 57.1% of patients who use glucantime plus placebo cured their lesions. Our hypothesis is that the exaggerated inflammatory response induced by *L. braziliensis* limit and delays the response to glucantime therapy and that rSm29 combined with glucantime will accelerate the cure of CL patients. Regarding *SmKI*, our study has demonstrated this molecule plays an essential role in neutrophil elastase (NE) binding blockage, in neutrophil influx and as a potential anti-inflammatory molecule. Further, we demonstrate that *SmKI-1* possesses an anti-inflammatory potential in three different murine models of inflammatory diseases: acetaminophen (APAP)-mediated liver damage, gout arthritis, and pleural inflammation in response to carrageenan. In these inflammatory disease models, we evaluated *SmKI-1* effect on neutrophil and our results demonstrate this molecule is able to inhibit neutrophil migration and function, regulating inflammation.

Keywords: *Schistosomamansonii*, inflammatory responses, neutrophil

Support: FIOCRUZ, CAPES

PHYSALINS AS IMMUNOMODULATORY DRUGS

Vinicius Pinto Costa Rocha¹; Ivone Maria Ribeiro²; Therezinha Tomassini Coelho Barbosa² and Milena Botelho Pereira Soares¹

1- Fundação Oswaldo Cruz. Centro de Pesquisa Gonçalo Moniz. Salvador, BA, Brasil

2- Fundação Oswaldo Cruz. FarManguinhos. Rio de Janeiro, RJ, Brasil

ABSTRACT: Physalins are secosteroids purified from *Physalisangulata*. Our group has demonstrated the immunomodulatory activity of these molecules in different immuno-mediated diseases models. These molecules are able to reduce the activity of macrophages, the production of TNF- α and nitric oxide, and protect the animals in a model of endotoxic shock mediated by LPS. Moreover, physalins inhibit lymphocytes activation and xenograft rejection. Recently, we demonstrated that physalin F reduces the production on IL-1 β , in a caspase-1 independent pathway, and the production of IL-12, by peritoneal macrophages. IL-10 is increased after physalin F treatment. However, the treatment of IL-10^{-/-} animal did not block the immunomodulatory effect, suggesting that not only IL-10 production induced by physalin F is important to modulate the immune response. Because, physalins are steroidal molecules, our hypothesis is that physalin F may act through nuclear receptors. To this end, we performed a receptor translocation assay to evaluate the activation of glucocorticoid (GR) and vitamin-D (VDR) receptors. Our results shown that physalin F does not activates GR, but induces VDR translocation to the nuclei. Further research is ongoing to validate the VDR as the pharmacological target of physalin F as well as to evaluate the genes modulated by this molecule.

Keywords: Physalis angulate. Physalin. Immunomodulatory

Support: Fundação Oswaldo Cruz; Conselho Nacional de Desenvolvimento Científico e Tecnológico.

DISCENTES

A MISSENSE-TYPE VARIANT, RS41347648, DECREASES RISK OF ATOPY IN BRAZILIANS BUT NOT ASTHMA

Talita S. Jesus¹, Helena Pitangueira¹, Gabriela P. Pinheiro², Álvaro A. S. Cruz², Ryan S. Costa¹, Camila A. Figueiredo¹

¹Laboratório de Imunofarmacologia e Biologia Molecular, Instituto de Ciências da Saúde, Universidade Federal da Bahia, Bahia, Brasil; ²Programa para o Controle da Asma na Bahia (ProAR), Universidade Federal da Bahia (UFBA), Bahia, Brasil.

Introduction: Asthma is a chronic disease of lungs and it is frequently associated with a Th2 inflammation where IgE and inflammatory mediators are released in the presence of common allergens and among the mediators involved are the cysteinyl leukotrienes (CysLTs) - LTC₄, LTD₄ and LTE₄. CysLTs are linked to bronchoconstriction, airway hyperresponsiveness, and eosinophilia. CysLTs can bind to the Cysteinyl leukotriene receptor type 2 (CysLTR2) and activate the symptoms described above. Thus, polymorphisms in *CYSLTR2* may be associated with asthma phenotypes, especially those related to the Th2 pathway. In this study, we explored the role of a rare variant, rs41347648 which has been already linked to asthma and atopy in several populations but never described in Brazilians. **Objective:** To evaluate the association between a rare genetic variant in *CYSLTR2* (rs41347648) with asthma and atopy in a Brazilian cohort. **Methods:** Genotyping was performed using an Illumina panel and carried out in 1,096 participants from Programa de Controle da Asma Bahia (ProAr). Logistic regressions for asthma and atopy markers (skin prick test) were performed using PLINK 1.9 software adjusted for sex, age, smoking, BMI (body mass index) and ancestry markers. **Results and Discussion:** This is a missense-type variant where the amino acid valine is replaced by a methionine. The frequency of the variant in the study population is very low only 1.23%, despite that the G allele of the variant was negatively associated in the dominant model with skin prick test to at least one mite (OR: 0.23: 0.07-0.73) and negatively associated with skin prick test to at least one of the main allergens in our region (0.45: 0.12-0.73). This result was different from other studies where this same variant was correlated with a higher risk of atopy. The variant was not associated with asthma and other atopic markers, possibly due to low frequency. **Conclusion:** The variant was negatively associated with atopy markers, however further studies conducted with a larger number of subjects are needed in order to increase the statistical power and investigate the real impact of this variant on asthmatic individuals.

Keywords: Asthma, rs41347648, *CYSLTR2*.

Support CAPES, CNPq, FAPESB, PROAR.

AGATHISFLAVONE INCREASES THE ASTROCYTIC POPULATION IN THE SUBVENTRICULAR ZONE AND MODULATES REACTIVE GLIOSIS *IN VIVO*

Juliana Helena Castro e Silva¹, Francesca Pieropan², Andrea Rivera², Arthur Morgan Butt², Victor Diogenes Amaral da Silva, Silvia Lima Costa¹; Department of Biofunction, Health Sciences Institute, Federal University of Bahia, Brazil;

²School of Pharmacy and Biomedical Sciences, University of Portsmouth, United Kingdom.

Introduction: The Subventricular Zone (SVZ) is a neurogenic niche that persists in adult life where neural stem cells (NSCs) give rise to interneurons and glial cells in the brain, and the neurogenesis in this niche is stimulated by growth and transcription factors and occurs after brain injury, for example. In brain injury and other neuroinflammatory conditions, a coordinated inflammatory response of glial cells is a common pathological finding known as reactive gliosis, a factor that might impair the neuroregeneration. In this context, immunoregulatory drugs can be adjuvant therapies. **Objectives:** The aim of this work was to evaluate the potential of the neuroprotective biflavonoid agathisflavone in modulating neurogenic populations in the Subventricular Zone (SVZ) and modulating the reactive gliosis *in vivo*. **Methods:** For this purpose, C57/BL6 hGFAP-EGFP aged 8 to 11 days (P8-P11) were subjected to two intracerebroventricular injections per day with agathisflavone (100 µM in 2 µL PBS / injection) or

PBS + 0.1% DMSO (vehicle) (2 μ L / injection) for 3 days. On the 4th day, the animals were sacrificed and brain fixed tissue analyzed by immunohistochemistry to characterize astrocytic (hGFAP-EGFP⁺ or GFAP⁺) and young proliferating migratory neurons (DCX⁺Ki67⁺) response in the SVZ and astrocytic and microglial (Iba-1, CD206⁺, CD16/32⁺) response in the injured and uninjured cortical regions. **Results and Discussion:** The results showed that animals treated with agathisflavone presented an increased number of hGFAP-EGFP astrocytes in the SVZ domains (dorsal, lateral and horn) without, however, inducing a significant change in the number of proliferating migrating neurons. Additionally, the injection of agathisflavone induced a reduction in the expression of the GFAP protein in the cortical region of the lesion caused by injections of the flavonoid or PBS + DMSO only (control), a marker of astrocytic reactivity. In this region, as well as the non-lesioned site, treatment with agathisflavone also induced a reduction in the number of microglia altered the expression of microglial reactivity markers. **Conclusions:** Together with previous work, our data indicates that agathisflavone can be a potential agent to treat brain disease controlling gliosis and favoring neural tissue regeneration.

Keywords: agathisflavone; subventricular zone (SVZ); neurogenesis; reactive gliosis.

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ANTIGENIC REACTIVITY OF RPKNG, RSPAC, RSODC AND RNaNH IN A GOAT AND SHEEP SERUM

Ramon Mendes dos Santos^{1,2}, Silvana B. Marchioro^{1,6}, Caio Lopes Borges Andrade^{1,2}, Rogério Conceição Reis^{1,2}, Maria Izabel Cerqueira^{1,3}, Hévlyn Ribeiro de Araújo^{1,3}, Marcos Borges Ribeiro^{1,4}, Roberto Meyer^{1,5}, Songeli Menezes Freire^{1,6}

1 - Membro do Laboratório de Imunologia e Biologia Molecular (LABIMUNO) da UFBA, Bahia / Brasil. 2 - Aluno do Programa de Pós Graduação em Imunologia PPGIm. 3 - Aluno da Universidade Federal da Bahia. 4 - Professor Assistente da UFBA (UFBA). 5 - Professor Titular da UFBA. 6 - Professora Adjunto da UFBA.

This work was carried out at the Laboratório de Imunologia e Biologia Molecular (Labimuno) of the Universidade Federal da Bahia (UFBA), Bahia-Brazil

Introduction: *Corynebacterium pseudotuberculosis* is the gram positive bacillus which causes caseous lymphadenitis (CL), disease characterized by cutaneous granuloma formation. This disease causes significant socioeconomic losses in the northeast region of Brazil. The search for biomolecules that can be used for the efficient diagnosis and vaccine to CL is necessary for the control of this diseases.

Objectives: Evaluate the antigenic potential of rSodC, rPknG, rNanH and rSpaC in serum of sheep and goat experimentally infected with three *C. pseudotuberculosis* strains.

Material and Methods: Twenty six animals were experimentally infected with 1 x 10⁷ cells of three different *C. pseudotuberculosis* strains: CAP76 or CAP21 to infect goats and VD57 to infect sheep. Sera from whole blood was collected at 0, 14, 60 and 180 or 190 days after infection. For expression of SodC, PknG, NanH and SpaC recombinant proteins, a commercial expression vector of the “pD444-NH Bacterial Expression Vectors” line marketed by DNA2.0 IncUSA was used. Recombinant plasmids were transformed into *E. coli* BL21 Star and purified using affinity chromatography. Purified recombinant proteins were submitted to 12% SDS-PAGE, then Western blot performed for the antigenicity reaction with sheep or goat pools sera and anti-goat or sheep IgG-peroxidase-conjugated-antibody (Sigma, EUA) diluted at ratio according established protocols. Revelation with 4-chloro- α -naphthol.

Results and Discussion: All recombinant proteins were expressed and successfully purified with the bands on the gel corresponding to the molecular weight of the proteins. The antigenicity reaction revealed that sera from goat infected with CAP21 and CAP76 strains were able to recognize the rSodC and rPknG proteins. This reaction were detected at 14 days after infection remaining at least until 180 or 190 days. While sera from sheep infected with VD57 strain recognized only the rSodC protein. No reaction was observed with the proteins rNanH and rSpaC and with animals serum from the control group (not infected). Although there is availability of in house CL diagnosis test

it is limitations, the SodC and also PknG can be useful in more reliable protocols.

Conclusions: rSodC is a good candidate to be used in the diagnosis test for infection by *C. pseudotuberculosis* in sheep and goats serum samples.

Keywords: *Corynebacterium pseudotuberculosis*, SodC, PknG, caseous lymphadenitis, immunoreactivity antigenicity

Support: Laboratório de Imunologia e Biologia Molecular (Labimuno), Fundação de Apoio à Pesquisa e à Extensão (FAPEX), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)

ASSESSMENT OF THE VIABILITY OF CORYNEBACTERIUM PSEUDOTUBERCULOSIS UNDER DIFFERENT STRESS CONDITIONS

Flávia Martins da Silva¹, Suzana T. Cunha Lima², Roberto Meyer³

¹Doctoral Student of the Postgraduate Program in Immunology – Institute of Health Sciences, UFBA, Salvador, Bahia, Brazil, ²Adjunct Professor, Department of Biointeraction – Institute of Health Sciences, UFBA, Salvador, Bahia, Brazil, ³Adjunct Professor, Researcher and Coordinator of the Bioprospecting and Biotechnology Laboratory (LaBBiotec) of the Institute of Biology / UFBA, Salvador, Bahia, Brazil, ³Professor, Department of Biointeraction – Institute of Health Sciences, UFBA, Salvador, Bahia, Brazil.⁴

Introduction: This work deals with studies related to *Corynebacterium pseudotuberculosis*, a intracellular bacteria that is the etiologic agent of Caseous Lymphadenitis in goats and sheep. This disease harms meat, milk and wool production in several countries, including Brazil. However, studies that searches for identification of molecular factors involved in virulence and pathogenicity during the infection that promotes resistance to Several tresses found in host are still scarce. The discovery of the antigenic properties of proteins may help tounder stand the pathogenicity and factors related to resistance of *C. pseudotuberculosis*. Heat shock proteins (HSPs) have demonstrated an important role of these molecules in increasing microbial resistance under stress conditions during infection, as well as being immunologically important because they are recognized by the host and there fore capable of inducing cellular and humoral immunity response in mammals. **Objectives:** The aim of this research was to identify and evaluate the expression of possible genes of HSPs in *C. pseudotuberculosis* that could contribute to understand the virulence and pathogenicity mechanisms of this pathogen. **Methods and Results:** Different stress conditions were used in vitro to evaluate *C. Pseudotuberculosis* resistance. Cultivation under stress conditions of three different trains used: T1 (attenuated), ER1409 (virulent) and CapJ4 (76) (strong biofilm producer). One colony from each strain was seeded in solid BHI, and from it, pre-inocula in 20 mL of liquid BHI medium plus Tween® 80 at a final concentration of 0.05% were prepared. After 24 hours of grow that 37° C undershaking, part of the cultures were re-inoculated (1: 100) in 100 ml BHI medium plus Tween® 80 (0.05% final) and incubated again at 37° C. The culture was monitore duntil the beginning of the stationary phase (OD600nm = 0.2). The samples were centrifuged and the bacterial pellets were induced to the acid stress in BHI medium add edof (hydrochloric acid with pH adjusted to 5.0 and 6.0), the thermal stress (40°C and 43°C), the osmotic stress increasing concentrations NaCl (1M to 2M) the nitrosative stress at increasing concentrations (5mM to 7Mm) and oxidative stress at increasing concentrations of H2O2 (10mM to 40mM). Strains were submitted to stress for 15, 30 and 45 minutes. All conditions were evaluated in triplicate. The viability oft hestrains was evaluated under stress conditions on BHI agar for 48 hours and cell grow thunder optical densitometry using 10⁻⁴, 10⁻⁵ and 10⁻⁶ serial dilutions. **Conclusion:** As preliminary results, the obtained optical density readings point to a stabilization of growth when the bacteriais subjected to acid, temperature, osmotic and oxidative stress for the ER1409 and CapJ4 (76) strains. These strains were more resistant to the imposed medium, despite presenting a slight loss of replicative potential, which was observed through the survival rate in relation to the control sample. However, these conditions did not inhibit bacterial growth, demonstrating the adaptive potential of *C. pseudotuberculosis* to stress response in adverse conditions. This knowledge is important for understanding the molecular mechanism occurring in the infectious process in goats and sheep.

Keywords: Caseous Lymphadenitis; *Corynebacterium pseudotuberculosis*; Hsps; Stress.

ASSOCIATION OF RETN GENE POLYMORPHISM WITH ASTHMA - EFFECT MODIFICATION BY ABDOMINAL OBESITY

Raísa S. Coelho^{1,2}, Ana Paula C. Melo^{1,2}, Hátilla dos S. Silva², Helena M. P. Teixeira^{1,2}, Jamille S. Fernandes^{3,4,5}, Gabriela P. N. Pinheiro⁵, Adelmir S. Machado⁵, Álvaro A. Cruz⁵, Camila A. Figueiredo^{1,2}, Ryan S. Costa^{1,2}.

¹ Programa de Pós-Graduação em Imunologia, Instituto de Ciências da Saúde (ICS), Universidade Federal da Bahia (UFBA), Salvador, Bahia, Brasil; ² Laboratório de Imunofarmacologia e Biologia Molecular (IMUNOBIO), UFBA, Salvador, Bahia, Brasil; ³ Centro de Ciências Biológicas e da Saúde, Universidade Federal do Oeste da Bahia, Barreiras, Bahia, Brasil; ⁴ Serviço de Imunologia, Hospital Universitário Professor Edgard Santos, Universidade Federal da Bahia (UFBA), Salvador, Bahia, Brasil; ⁵ ProAR - Núcleo de Excelência em Asma, UFBA, Salvador, Bahia, Brasil.

Introduction: Asthma and obesity are chronic diseases with increasing prevalence that, besides environmental and genetic factors, have inflammation as a common link. Accordingly, cytokines secreted by adipose tissue cells with receptors expressed in the lung are pointed at the link between the immune regulation involved in the pathogenesis of both diseases. Variations in the *RETN*, have been associated with their unbalanced serum levels and consequent metabolic dysfunction that promote impact on asthma. **Objectives:** To investigate the association between variants in the *RETN* with asthma and how the abdominal adiposity modifies that association. **Material and Methods:** The study involved 796 individuals, followed by ProAR. Asthma was defined according to GINA and abdominal obesity was defined by WHtR, according to WHO. Genotyping was performed using Illumina Infinium kit Multi-Ethnic AMR/AFR-8. Logistic regression was performed to identify associations between variants with asthma, stratifying the population by WHtR. **Results and Discussion:** After adjustment for confounding parameters, no significant associations were observed in the general study population and in individuals without abdominal obesity. However, in individuals with abdominal obesity the rs3745367 (allele G) was negatively associated, in the dominant model, with asthma (OR: 0.63 95%CI: 0.41-0.98). The G allele is also associated with lower gene expression of resistin in lung tissue, according to GTex. The GG genotype has recently been associated with a lower serum resistin level. We believe that adiposity acts as an inflammatory trigger, activating the genetic predisposition for the overproduction of resistin, which contributes to the increased risk of airway inflammation, a hypothesis that is related to the risk allele (allele A) in our population. The AA genotype has been described in a positive association with obesity and the A allele also with insulin resistance, metabolic conditions often related to high serum levels of adipokine. **Conclusions:** Our results demonstrate the modifying effect of abdominal obesity on the observed association between a variant in the *RETN* with asthma. Functional studies are needed to clarify the inflammatory hypothesis of the associations. Thus, we will measure serum resistin and *RETN* expression in individuals with asthma and to relate it to the observed variant.

Keywords: Asthma. Obesity. Resistin. Genetic.

Support: FAPESB.

ASSOCIATION OF VARIANTS IN GENES OF THE GLUCOCORTICOID PATHWAY WITH LACK OF CONTROL IN PATIENTS WITH SEVERE ASTHMA

Maria Borges Rabêlo de Santana¹; Helena Mariana Pitangueira Teixeira¹; Hátilla dos Santos Silva¹; Álvaro A. Cruz²; Camila Alexandrina Figueiredo¹; Ryan dos Santos Costa¹

¹ Laboratório de Imunofarmacologia e Biologia Molecular, Instituto de Ciências da Saúde, Universidade Federal da Bahia, Salvador, Bahia, Brasil. ² Programa para o Controle de Asma na Bahia (ProAR), Universidade Federal da Bahia (UFBA), Bahia-Brasil.

Introduction: Asthma is a chronic respiratory disease and can be characterized as a obstructive condition in which the inflammation observed plays an important role in increasing airway hyperresponsiveness. There is a heterogeneity of immunological profiles in asthma and a great heterogeneity in the disease in relation to sub-phenotypes, intensity and severity of symptoms, in addition to the therapeutic response. In this context, glucocorticoids are used to reduce

inflammation and consequently reduce symptoms and exacerbation. Despite being a widely used therapy, there is variability in the response to this medication and genetic mechanisms may partially explain such variation in the therapeutic response. **Objective:** To investigate the association of variants in genes whose expression is altered by glucocorticoids with the lack of control in patients with severe asthma. **Material and Methods:** The study was composed of 363 participants who have severe asthma and are accompanied by the Program for the Control of Asthma and Allergic Rhinitis in Bahia (ProAR), residents of the city of Salvador. Asthma control in these patients was assessed using the ACQ6, which is validated in Brazil. DNA was extracted from peripheral blood and genotyping was performed using the Infinium Multi-Ethnic Global chip. The selected genes showed altered expression after exposure to glucocorticoids in two previous studies. Quality control was applied to the variants considering the frequency of the smallest allele, genotyping rate and Hardy-Weinberg balance. The association analysis was performed in the R software using the GENESIS package. Age, sex and the first main component were included as covariables. **Results and Discussion:** 368 genes were evaluated, totaling 10772 variants after quality control. Five variants were found in five different genes suggestively associated with lack of control in severe asthma, three positively associated (in the *FRMD4B*, *SEMA3A* and *FMN1* genes) and two negatively associated (in the *IL6ST* and *BCL2* genes). **Conclusions:** The variants in *FRMD4B*, *SEMA3A* and *FMN1* genes are risk factors for the control of severe asthma while variants in *IL6ST* and *BCL2* genes are protective factors. Future studies are needed both to validate the findings here and to elucidate a possible functional impact of these variants.

Keywords: Glucocorticoids, asthma, variants.

Support: CAPES, FAPESB, CNPq.

ASSOCIATION OF VARIANTS IN THE *PPARY* GENE WITH OBESITY IN A BRAZILIAN POPULATION

Ana Paula C. Melo¹; Helena Mariana Pitangueira Teixeira¹; Raísa Santos Coelho¹; Neuza Maria Alcantara-Neves¹; Maurício Lima Barreto^{2,4}; Ryan dos Santos Costa; Laise C. Pinto³; Camila A. Figueiredo¹

1. Instituto De Ciências Da Saúde, Universidade Federal Da Bahia, Salvador - Ba - Brasil; 2. Instituto De Saúde Coletiva, Universidade Federal Da Bahia, Salvador - Ba - Brasil; 3. Universidade Federal Da Bahia, Salvador - Ba - Brasil; 4. Escola De Nutrição, Universidade Federal Da Bahia, Salvador - Ba - Brasil; 4. CIDACS - Centro de Integração de Dados e Conhecimentos para Saúde – FIOCRUZ; Programa de Pós-Graduação em Imunologia PPGIM- Laboratório de imunofarmacologia e biologia molecular- Salvador/Bahia/Brazil.

Introduction: Obesity is a chronic disease with an increased risk of comorbidities such as cancer and asthma. Obesity has been considered a low-grade inflammatory disease, directly related to insulin resistance and type 2 diabetes mellitus. Peroxisome proliferator-activated receptor gamma (PPAR γ) is a regulator of lipid and glucose metabolism. Dysregulation of PPAR γ is linked to the development of obesity, type 2 diabetes, atherosclerosis and other disease conditions. PPAR γ regulates the expression of numerous genes involved in lipid metabolism, including apoA2, acyl-CoA synthetase and lipoprotein lipase (LPL). It also controls the expression of the fatty acid carrier protein 1 (FATP-1) and CD36, both involved in the uptake of lipids by adipocytes. **Objective:** To evaluate whether there is an association between PPAR γ gene polymorphisms and obesity in Brazilian children. **Methods:** The study comprised 1004 children between 4-11 years. Genotyping was done using the Illumina 2.5 Human Omni bead chip. Logistic regression was used to assess the association between IMC and the PPAR γ gene variations in PLINK 1.07 software. The multivariate analysis was carried out adjusting for sex, age and ancestry markers. **Results and Discussion:** From 1,010 children included in this study, 15.5% (156) had overweight. In addition, 59% of the obese children were male and had an average age of 5 years. There were overall statistically significant differences for age, but not for sex, between cases and controls. Four SNVs in PPAR γ were associated with obesity, three of them negatively associated with obesity using an additive model (rs4135268 (G allele, OR: 0.45 CI 95%: 0.22-0.92), rs13083375 (T allele, OR: 0.44 CI 95%: 0.21-0.94), rs13064760 (T allele, OR: 0.45 CI 95%: 0.21-0.94) and one positively associated with obesity in the XXX model (rs12485478 (G allele, OR: 1.17 CI 95%: 1.17-2.97)). **Conclusion:** The SNVs rs4135268, rs13083375, rs13064760 and rs12485478 in PPAR γ are associated with obesity in Brazilian Children. Further studies are needed to better understand and elucidate the mechanisms whereby such SNVs are involved with obesity in Brazilians.

Keywords: children, obesity, inflammatory gene; **Support:** Fapesb

CHARACTERIZATION OF mi-RNAS IN THE PHENOTYPIC DYSREGULATION OF GLIOBLASTOMA AND MICROGLIAL CELLS AND AS TARGETS OF ANTITUMORAL FLAVONOIDS

Karina Costa da Silva¹, Balbino Lino dos Santos¹, Dora Brites², Silvia Lima Costa¹

¹Neurochemistry and Cell Biology Laboratory, Biochemistry and Biophysics Department, Federal University of Bahia, Bahia, Brazil; ²Instituto de Investigação do Medicamento da Faculdade de Farmácia da Universidade de Lisboa, Portugal.

Introduction: The glioblastoma (GBM) is the most frequent cerebral tumor with a poor prognostic and short life time. Besides that, it is difficult treatment, which is aggressive and of reduced effectiveness due to chemio- and immunoresistant. Recently, the microRNAs's (post-transcriptional and non-coding agents) have been describe as having important role in the prognosis of GBMs. The flavonoids apigenin and bis-apigenin have been shown to inhibit GBM cell proliferation and invasion, in association with the modulation of the inflammatory profile of microglia. In this context, knowledge of the effect of these molecules on the modulation of miRNA expression is of great value, as well as understanding the relationship with the reversal of the tumor phenotype and modulation of the microglia inflammatory phenotype that favours block age of tumor cells proliferation. **Objectives:** This project aims to characterize the involvement of onco- and inflammo-miRNAs in the phenotypic dysregulation of GBM and microglia cells and as targets for flavonoids with antitumor action. As specific Objectives we seek to identify the role miR-155/-21/-124/146a in the phenotypic dysregulation of human GBM (U87, GL15, U373) and microglia (CHME3) cells isolated and in cocultures, as well as during direct cell-cell communication (glioma/microglia co-cultures) by the analysis of its profile in these cultures. In addition, we aim to test the efficacy of the apigenin and bis-apigenin flavonoids in the modulation of onco-miRNAs, recovery of the "responder" microglial phenotype and in the reversal of the astrocytic GBM malignant phenotype. **Methods:** We Direct and indirect interaction will be adopted in isolated and in GBM/microglia co-culture models. Immunocytochemistry will be adopted to evaluate proliferation morphology and phenotype. Moreover, cell viability/death will be measured by staining with the stain of Propidium iodide (necrosis) in association with Annexin-5-FITC (apoptosis). Exosomes will be isolated from the GBM/CHME3 co-culture medium by differential ultracentrifugation to characterize mi-RNA's through the RTqPCR reaction using primers for the 155/-21/-124/146a mi-RNA's. **Expected results:** With the results obtained, it will be possible to characterize the effects of apigenin and bis-apigenin on modulation of onco and inflammo miRNAs expression and the relation between anti-glioma and immunomodulatory effects of these flavonoids in view to contribute to future therapeutic strategies.

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CHARACTERIZATION OF THE GLIAL RESPONSE ASSOCIATED TO NEUROPROTECTION INDUCED BY THE FLAVONOID AGATHISFLAVONE IN VITRO MODELS OF BRAIN INJURY.

Verônica Moreira de Sousa¹, Cleonice Creusa dos Santos¹, Áurea Maria Alves Nunes¹, Juliana Helena Castro Silva¹, Jorge Mauricio David², Maria de Fátima Dias Costa¹, Arthur Morgan Butt³, Victor Diógenes Amaral¹, Silvia Lima Costa¹

¹Laboratory of Neurochemistry and Cell Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil. ² Department of General and Inorganic Chemistry, Institute of Chemistry, Federal University of Bahia, Brazil. ³School of Pharmacy and Biomedical Sciences, University of Portsmouth, United Kingdom.

Introduction: Brain injury is a major cause of death and disability in humans and animals. A cascade of events at the molecular level and biochemical changes begins minutes after the initial injury, such as cellular hyperexcitability, astrogliosis and glial scarring, edema, hypoxia/ischemia, oxidative stress and inflammation, involving immunoprotective glial cells, which in turn can contribute to induce the expansion of the primary lesion. Thus, the development of drugs that can reduce the damage caused by the encephalic injury is extremely important. Previous studies, demonstrated that the flavonoid agathisflavone modulates the astrocytic response (astrogliosis) and the formation of the glial scar, favoring the migration of astrocytes and neurons to the injury site, and stimulating the restoration of the neural network, effects associated with increased expression of the neurotrophic factors NGF

and GDNF. However, the mechanisms of glial response involved is not yet fully understood. **Objectives:** The present study aims to characterize the effect of the flavonoid agathisflavone on the activation of astrocytes and microglia in an in vitro model of brain injury. **Methods:** Brainmixed culture (glia/neurons) will be obtained from Wistar rats (7-9 days old) and maintained in supplemented DMEM/F12. After 3 days in vitro, culture will be maintained in control conditions or pre-treated (1-hour before the injury) with agathisflavone (1 μ M), and then the cultures will be subjected or not to a mechanical injury with the aid of a 200 μ L sterile polystyrene pipette tip. After 24 hours, cultures will be processed for experimental analysis. Neuronal integrity will be assessed by the Fluoro-Jade-B reagent and by immunocytochemistry (ICQ) for β -tubulin III. The morphology, glial reactivity and inflammatory profile will be analyzed by ICQ for the astrocyte markers GFAP, GS, and for the microglia markers Iba-1, CD68 and CD206, and by measuring mRNA expression for of TNF, IL1 β , IL-6, IL10, TGF β and arginase inflammatory markers by RT-qPCR. **Expected results:** The clarification of how this compound acts in the integration of neuroimmune signals in conditions of diseases characterized by glial reactivity and neurodegeneration, such as encephalic injury, will contribute to the development of new or combined therapies for this pathology and other related disorders.

Keywords: neuroinflammation, microglia, astrocyte, Agathisflavone, neuroprotection **Support:** FAPESB (INT 016/2016); CAPES (PGCI Proc. - 88881.117666/2016-01); INCT Nacional Institute for Translational Neuroscience and INCT for Excitotoxicity and Neuroprotection (MCTI/CNPq).

CHARACTERIZATION OF THE IMMUNOLOGICAL MECHANISMS INDUCED IN VITRO BY THE SM29 ANTIGEN IN MACROPHAGES OF ASTHMATIC INDIVIDUALS

Luís Eduardo Ribeiro^{1,2}; Tarciano Nascimento^{1,2}; Dário Pascali^{1,2}; Gabriela Pimentel Pinheiro⁶; Diego Mota Lopes^{1,2}; Jordana Batista^{1,2}; Tarcísio Almeida^{1,2}; Sérgio C. Oliveira³; Edgar M. Carvalho^{2,4}; Álvaro Augusto Cruz⁶; Luciana S. Cardoso^{1,2,5}

¹ Programa de Pós-graduação em Imunologia, PPGIm, ICS/UFBA; ² Serviço de Imunologia, Hospital Universitário Professor Edgard Santos – HUPES/UFBA; ³ Departamento de Bioquímica e Imunologia, Instituto de Ciências Biológicas, UFMG-MG, Brazil; ⁴ Centro de Pesquisas Gonçalo Moniz, FIOCRUZ-Ba, Brazil; ⁵ Departamento de Análises clínicas e toxicológicas, Faculdade de Farmácia, UFBA. ⁶ Programa para o Controle da Asma na Bahia – ProAR/UFBA.

Introduction: Chronic respiratory diseases are some of the leading causes of illness and death in the world, such as asthma that affects more than 350 million people worldwide. Evidence has been accumulating that chronic helminth infection, particularly *Schistosoma* spp. or parasite products, is capable of modulating the inflammatory response. **Objective:** To characterize the immunological mechanisms induced by recombinant *Schistosoma mansoni* Sm29 antigen (rSm29) *in vitro* in M1 and M2a and M2c macrophages of individuals with asthma. **Materials and Methods:** Macrophages of individuals with asthma were differentiated in M1 and M2a by the addition of IFN+LPS and IL4+IL13, respectively. The cultures were then stimulated with Sm29. Since Sm29 is able to induce high amounts of IL-10 in previous studies, we tested if this antigen is able to differentiate macrophages into M2c population. The frequency of macrophages producing TNF and IL-1 β was evaluated by flow cytometry analyses. The levels of IL-10 in cultures supernatants stimulated by Sm29 antigen were evaluated by sandwich ELISA. **Results and Discussion:** The presence of rSm29 reduces the frequency of M1 and M2a macrophages in the culture upon differentiation. And preliminary results demonstrate that the reduction in frequency of the M1 and M2a populations may be related to the increase in M2c population. There is a reduction in the production of proinflammatory cytokines (TNF and IL1 β) by M1 macrophages stimulated with rSm29. In macrophage cultures of asthmatic patients stimulated with rSm29 in the presence of IFN- γ and in the presence of IL-4 and IL-13, an increase in IL-10 production was observed when compared to cultures without stimulation in the same differentiation conditions. In cultures stimulated with rSm29, the frequency of M2c correlated positively with the concentration of IL-10 measured in the supernatant of these cultures. **Conclusion:** Preliminary results demonstrate the ability of rSm29 antigen to regulate the M1 and M2a macrophages that is involved in inflammatory response of asthmatic individuals, as results of the up-regulation of IL-10 production. The rSm29 antigen appears to be a feasible candidate for developing a therapeutic strategy for the treatment of this disease.

Keywords: asthma, Sm29, macrophages. **Support:** FAPESB and CNPq.

CHARACTERIZATION OF THE NEUROPROTECTIVE AND ANTI-NEUROINFLAMMATORY EFFECTS OF FLAVONOID AGATHISFLAVONE (APIGENIN AND BIS-APIGENIN): ROLE OF TRYPTOPHAN CATABOLISM

Deivison Silva Argolo¹, Gizelle Alves Pina¹, Sílvia Lima Costa¹, Maria de Fatima Dias Costa¹.

¹ *Neurochemistry and cell biology laboratory. Federal University of Bahia,*

Introduction: The nervous system is a complex tissue characterized by its cellularity with specific and distinct functions in relation to other tissues in the body. Astrocytes and microglia make up glia, cells with characteristics responsible for maintaining tissue homeostasis and favoring a microenvironment for the better functioning of neurons, which in turn are responsible for synaptic communication. Under conditions of stress and inflammation, the cells of the central nervous system (CNS) position themselves to trigger an effective immune response, which may involve biochemical mechanisms such as the release of nitric oxide, stimulation of apoptotic pathways and activation of catabolic pathways, example of the tryptophan pathway. Tryptophan catabolism produces cinurenines that regulate homeostasis within nervous tissue. In vitro models have been used to verify the role of this pathway, and it has recently been shown that in a parasitic infection of neuron / glia co-cultures, the inflammatory stimulus activated the production of quinolinic acid, a catabolite that has an affinity for NMDA neuronal receptors. In turn, flavonoid phytochemicals, have shown neurogenic and antineuroinflammatory actions on nervous tissue, by modulating glial cells. **Objective:** to correlate the antineuroinflammatory action of flavonoid agathisflavone with tryptophan catabolism in nervous system cells subjected to inflammatory stimuli. **Material and Methods:** Primary cultures of rat cerebral cortex (P 0-2) will be subjected to treatment with INF1 β and LPS subsequently treated with agathisflavone flavonoids (apigenin and bis-apigenin) followed by removal of the culture medium to be filtered (Millipore 0.22 μ m) and used to evaluate tryptophan catabolites by high performance liquid chromatography (HPLC). The morphology and reactivity of astrocytes, microglia and neurons will be investigated respectively by immunocytochemistry (ICQ) using glial fibrillar acid protein (GFAP), the ionized calcium binding adapter molecule 1 (Iba-1) and β tubulin. To evaluate the expression of enzymes in this pathway, qPCR will be used. **Perspective:** It is hoped that the inflammatory process can be associated with the stimulation of the production of quinolinic acid and the anti-inflammatory action of flavonoid agathisflavone, can be related to the release of cinurenic acid, providing neuronal preservation and bringing therapeutic potential for neuropsychiatric diseases, associated with neurodegeneration such as Parkinson's disease, Alzheimer's, among others. **Keywords:** neuroinflammation, neuron, microglia, astrocyte, Agathisflavone, neuroprotection.

Support: FAPESB.

CIRCUMVENTING ANTIMONIAL THERAPEUTIC FAILURE IN LEISHMANIA BRAZILIENSIS INFECTIONS BY TARGETING ABC TRANSPORTERS

Marina Borges Rabelo de Santana, Edgar Marcelino de Carvalho Filho, Lucas Pedreira de Carvalho

Laboratório de Pesquisas Clínicas, IGM, Fiocruz, Bahia, Brasil.

Introduction: Cutaneous leishmaniasis (CL), caused by *Leishmaniabraziliensis*, is a disease with a wide spectrum of clinical presentations, characterized by the presence of one or more ulcers with high edges. The most important limitations of leishmanicidal drugs are the high rate of treatment failure, the emergence of drug-resistant parasites and the abandonment of treatment by patients.

The host genes associated with drug resistance, such as those of the ABC transporter family (ABCB1 and ABCC1), responsible for the efflux of drugs, are more expressed in lesions of patients with CL when compared to the skin of healthy individuals. The higher expression of these proteins may therefore be associated with the therapeutic failure of the leishmanicidal compounds. Consequently, the use of drugs that inhibit ABC transporters (Verapamil, Probenecid or Lovastatin), could prevent the efflux of medications such as pentavalent antimonial (SbV), the medication preferably used in Brazil to treat CL, thus leading to its accumulation in the host cell and increasing its parasitocidal activity. **Objectives:** The objective of this project is to compare the activity of ABC transporters in individuals with CL or early cutaneous Leishmaniasis (ECL) who have failed SbV therapy with the activity of ABC in

individuals who have healed after treatment. In addition, we will test whether inhibitors of ABC transporters increase the leishmanicidal efficacy of the pentavalent antimonial as well as its influence on cytokine production.

Methods: We are cultivating macrophages infected with *Leishmania brasiliensis* strains obtained from aspirates from lesions of patients with CL or ELC who have healed and have failed treatment with SbV through the use of a technique of flow cytometry to calculate the parasitocidal activity of drugs and by counting intracellular amastigotes in cells. In addition, we will verify the activity of ABC in uninfected and infected macrophages in the presence of ABC inhibitors in conjunction with SbV.

Conclusions: Through these results, it is possible to think about the association of SbV with the inhibitor that presents better results, thus reducing the costs with new therapy courses for individuals who fail and investing in promoting the population's awareness about the highest cure rates and the treatment effectiveness even in the most recent phase.

Keywords: *Leishmania brasiliensis*, ABC transporters, cutaneous leishmaniasis.

Support: Capes, IGM-Fiocruz Bahia

COMBINED ADJUVANT THERAPY INVOLVING BCG AND IMIQUIMOD INCREASES THE SURVIVAL OF C57BL/6 MICE DURING EXPERIMENTAL MELANOMA

Maiara Bonfim^{1,2}, Amanda Silva^{1,2}, Davi Salles¹, Rosa Pinho³, Jose Mengel^{3,4}, Fabiola Cardillo¹.

¹Gonçalo Moniz Research Institute. Oswaldo Cruz Foundation, LAPEM, Salvador-Ba, Brazil. ²Federal University of Bahia (UFBA), PPGIm, Salvador-Ba, Brazil. ³Oswaldo Cruz Foundation, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, Brazil. ⁴Faculty of Medicine of Petrópolis, FMP-FASE, Petrópolis, Rio de Janeiro, Brazil.

Introduction: The study of adjuvant therapies has become increasingly relevant in efforts to treat cutaneous tumors like melanoma effectively. Imiquimod (IMIQ) induces an efficient antitumor immune response by activating the Toll-like receptor seven pathway (TLR7). Another immunotherapy is to use *Bacillus Calmette-Guérin* (BCG) for an effective antitumor response. The present study aims to use new tools to evaluate the combined adjuvant effect of BCG and IMIQ on antitumor activity. **Methods:** C57Bl6 mice were inoculated with B16F0 tumor cells subcutaneously at 5×10^4 cells/20 μ L. Subsequently, mice were treated with 10 μ L of IMIQ at 50 mg/mL twice daily. Mice received BCG in situ at the concentration of 1×10^7 /60 μ L, ten days after tumor cell inoculation. Tumor growth and mortality were monitored, and splenic cells from experimental groups were evaluated by flow cytometry on the 18th after B16F0 cell-grafting. Experimental groups used: 1- Naïve (control) mice. 2- Mice that received BCG and IMIQ (IMIQ+BCG). 3- Mice injected with tumor cells (B16F0). 4- Mice challenged with BCG and treated with IMIQ (B16F0+IMIQ+BCG).

Results: The combined treatment protocol B16F0+IMIQ+BCG resulted in significantly increased survival compared to B16F0 mice ($p=0.0001$; Log-rank test). In addition, significantly reduced tumor growth was seen in B16F0+IMIQ+BCG compared to B16F0 on days 10 ($p=0.0115$; Mann-Whitney), 12 ($p=0.0008$; Mann-Whitney), 15 ($p=0.0434$ Mann-Whitney), 18 ($p=0.0219$; Mann-Whitney) and 20 ($p=0.0406$; Mann-Whitney). B16F0+IMIQ+BCG and IMIQ + BCG (without tumor cells) groups have presented increased CD4+ T cells, NK, and NKT splenic cell-numbers, compared to the B16F0 group (Mann-Whitney test $p=0.0286$). For the CD8+ splenic T cell-number, the B16F0, B16F0+IMIQ+BCG, and IMIQ+BCG groups are different when compared to each other (Kruskal Wallis, $p=0.0177$). There was a trend in splenic cells to sustain the number of regulatory T cells (Treg) and myeloid-derived suppressor cells (MDSC) in the studied groups. **Conclusions:** The combined adjuvant treatment of IMIQ+BCG increased the longevity and tumor restraintment in an experimental murine model of melanoma. Increased number of CD4+ T cells, NK and NKT cells, and the maintenance of Treg and MDSC splenic cells are related to the immune response against melanoma in mice treated with BCG and IMIQ.

Keywords: Experimental Melanoma, Imiquimod, BCG, NK Cells, NKT Cells

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CYTOKINE PROFILE INDUCED BY *DERMATOPHAGOIDES PTERONYSSINUS* IN WHOLE BLOOD CELL CULTURE FROM TEENAGERS IN SCAALA 2013

Flávia de Araújo Sena¹, Emília Maria Medeiros de Andrade Belitardo¹, Alana Alcântara Galvão¹, Laure Laine dos Santos de Jesus¹, Daniel dos Santos Rocha¹, Anaque de Oliveira Pires², Gerson de Almeida Queiroz², Álvaro Augusto Souza da Cruz Filho³, Maurício Lima Barreto^{4, 5}, Camila Alexandrina Viana de Figueiredo², Neuza Maria Alcântara Neves¹

¹Departamento de Biointeração, Laboratório de Alergia e Acarologia, Universidade Federal da Bahia, Bahia, Brasil. ² Departamento de Biointeração, Laboratório de Imunofarmacologia e Biologia Molecular, Universidade Federal da Bahia, Bahia, Brasil. ³ ProAR, Faculdade de Medicina, Universidade Federal da Bahia (UFBA), Salvador, Bahia, Brasil. ⁴ Instituto de Saúde Coletiva, Universidade Federal da Bahia (UFBA), Salvador, Bahia, Brasil. ⁵ Centro de Integração de dados e Conhecimentos para Saúde (CIDACS), Fiocruz, Bahia, Brasil).

Introduction: Dust mites are important cause of allergy in the World, being one of the main source of sensitization to IgE and a risk factor to allergic diseases. Among them, *Dermatophagoides pteronyssinus* is the most important source of inhaled allergens worldwide. **Objectives:** This study aim to investigate the cytokine profile induced by *D. pteronyssinus* extract (DpE) in whole blood cells' culture supernatants from teenagers participating in SCAALA Program 2013 (Social Changes Asthma and Allergy in Latin America) according to asthma and atopy status. **Methods:** Asthma outcome was evaluated using an ISAAC phase II questionnaire translated to Portuguese. Serum sampling was used for detection of allergen-specific IgE by ImmunoCAP (Phadia/ThermoFischer, Massachusetts, USA). As ample of blood collected for each participants was used for 120 hours whole blood cells culture, at 5% CO₂ stimulated with DpE extract. IFN- γ , TNF α , IL-5, IL-13, IL-17 and IL-10 cytokines were measured in the cells supernatants by Luminex (The MILLIPLEX[®] Human Cytokine/Chemokine, Merck KGaA; Darmstadt, Germany) in 440 of 985 blood donor. Statistical analyses were done using SPSS 22.1. Non-parametric tests (Kruskal Wallis and Mann-Whitney) were used. **Results/Discussion:** From the 440 participants whose cytokine dosages were obtained, 205 were atopics, 21 asthmatics, 12 atopics asthmatics. Atopic patients had the highest production of IL-5 (atopic median: 1.34, non-atopic: 0.62 $P = 0.0001$) and IL-13 (atopic median: 3.76, non-atopic: 2.59 $P = 0.026$). The increases of sIgE also increased the median of these cytokines. Both cytokines, IL-5 and IL-13, are Th2 type and *D. pteronyssinus* allergens are involved in Th2 polarization response resulting in atopy and allergy development. No statistically significant difference in cytokine production was observed between the asthmatic and non-asthmatic groups. **Conclusions:** Higher levels of Th2 cytokines were observed in DpE stimulation of total blood cells in atopic teenagers; however, no difference in cytokine production was observed in asthmatics compared to non-asthmatic population. This may be due to the reduced number of asthmatics in the present study. New analyses will be made in order to verify the other stimuli used in cell cultures and to use a statistical approach that best suits the data analyzed.

Keywords: Dust mite, Atopy, *Dermatophagoides pteronyssinus*, Asthma; sIgE;

Support: FAPESB, CNPq

DYNAMICS OF SEROCONVERSION AND IMMUNE CELL RESPONSE AS MARKERS FOR DIAGNOSIS AND PREDICTORS OF PROGNOSIS IN SARS-COV 2 INFECTION

Isa Rita Brito de Morais, Alex José Leite Torres.

Laboratório de Imunologia e Biologia Molecular – ICS/UFBA, Salvador, Bahia, Brasil.

Introduction: SARS (severe acute respiratory syndrome) is an infectious disease that represented a major threat to international public health in 2003, affecting 12 countries, with the coronavirus (SARS-CoV) being identified as its etiological agent, reappearing in 2012 in the Middle East. In December 2019, the city of Wuhan, capital of Hubei province in China, became the center of a new outbreak of pneumonia attributed, this time, to a new strain of coronavirus (SARS-CoV-2), transmitted by airways, now called, by the World Health Organization (WHO), as Coronavirus 2019 (COVID-19), quickly reaching pandemic status. The characteristics of seroconversion in SARS-CoV-2 are not well defined, as they demonstrate a significantly idiosyncratic relationship with the patient in view of his

immune response, suggesting an important influence linked to interfering factors in the protection of viral infections between different expressions of ancestry. Mechanisms of action of cells and the dynamics of their expressions during immune activation have demonstrated, in several studies since the isolation of coronaviruses, important actions as diagnostic markers and, mainly, prognoses that, if identified, can contribute to the evolutionary prevention of the disease. **Objective:** To characterize specific markers of the humoral and cellular immune response for SARS-Cov2, which determine indexes for the evaluation of the host's diagnosis and prognosis. **Materials and Methods:** 100 patients tested positive for SARS-Cov2 will participate in the study, being divided into four groups according to mild, moderate and severe clinical conditions, in addition to a control group of seronegative individuals. Patients will come from diagnostic testing centers in the cities of Salvador and Feira de Santana, Bahia. After signing the Free and Informed Consent Form, samples of nasal / oropharyngeal secretion and 4.5 ml of blood will be collected for the characterization of the cellular immune response, evaluation of seroconversion and autoantibodies, in addition to the identification and genotyping of ancestry markers. This project will be submitted to the Research Ethics Committee of the "Instituto de Ciências da Saúde da Universidade Federal da Bahia", according to Resolution 466/2012 of the National Health Council, and the volunteers will be informed verbally and in a written document.

Keywords: SARS vírus, Coronavírus infections, seroconversion.

Support: MCTIC/CNPq/FNDCT/MS/SCTIE/Decit Nº 07/20 - registro401727/2020-3.

EFFECT OF *SCHISTOSOMA MANSONI* SM29 ANTIGEN ON MACROPHAGE INFECTIVITY BY *LEISHMANIA BRASILIENSIS*

Natália Michelly Brandão Mendonça¹; Jordana Batista Santana¹; Tarciano Nascimento Pereira¹; Luís Eduardo Viana¹; Nestor Guerrero Gutiérrez^{1, 2}; Luciana Santos Cardoso^{1, 2, 3}.

¹Programa de Pós-Graduação em Imunologia. Universidade Federal da Bahia-UFBA. Salvador/Bahia. Brasil. ²Serviço de Imunologia. Hospital Universitário Professor Edgar Santos (HUPES), UFBA Salvador/Bahia. Brasil. ³Departamento de Análises Clínicas e Toxicológicas, Faculdade de Farmácia, UFBA. Salvador/Bahia. Brasil.

Introduction: Leishmaniasis is an endemic disease in South and Central America, Africa and Asia, caused by a variety of species of parasites of the genus *Leishmania*. Currently, 88 countries with tropical and sub-tropical climate are affected by leishmaniasis. The immune response to this parasite is of the Th1 type, which is important for the activation of macrophages and elimination of *Leishmania*, but it is also the main responsible for the pathogenesis of cutaneous disease, mainly related to tissue damage. On the other hand, antigens derived from parasites with a modulatory potential of the immune response, such as the Sm29 antigen of *Schistosoma mansoni*, have been evaluated for the potential to regulate the exacerbation of the immune response in immune-mediated diseases. **Objective:** To evaluate the effect of the *S. mansoni* Sm29 antigen on the infectivity of macrophages derived from monocytes in vitro infected with *L. braziliensis*. **Methodology:** The monocytes will be cultured in the presence of M-CSF for differentiation in to macrophages and then infected with *L. braziliensis* promastigotes and stimulated with the Sm29 antigen. The number of infected macrophages, the frequency of amastigotes per macrophage, as well as the expression of the enzymes iNOS and arginase will be evaluated by RT-PCR. The levels of cytokines TNF, IL-12 and IL-10 in the culture supernatant will also be analyzed. The results of this work will assist in understanding the mechanisms involved in the regulation of the immune response induced by the Sm29 antigen in leishmaniasis, as well as assessing whether this antigen influenced the infectivity of the parasite and the macrophages ability to kill leishmania.

Keywords: Leishmaniasis. Sm29. Macrophages.

Support: CAPES / CNPq / INCT.

EFFECTS OF ASC CONDITIONED MEDIA IN TISSUE REGENERATION

Brysa Mariana Dias Silveira^{1,2}; Songeli Menezes Freire^{1,2}; Vitor Antonio Fortuna^{1,2}

¹Programa de Pós-Graduação em Imunologia, Instituto de Ciências da Saúde (ICS), Universidade Federal da Bahia (UFBA), Salvador, Bahia, Brasil; ²Laboratório de Imunologia, Departamento de Biofunção, ICS, UFBA, Salvador, Bahia, Brasil.

Introduction: Chronic leg ulcers (CLU) are very common with an estimated prevalence of 0.6 to 5% among patients over 65 years of age. CLUs are recalcitrant, cause a low quality of life and often lead to lower extremity amputation, representing both a significant health risk and a large economic burden. Adipose derived-mesenchymal stromal cells (ASC) are a potential alternative for treatment of CLUs. These cells secrete cytokines, growth factors, and bioactive molecules responsible for the effects of skin repair and regeneration. A promising strategy to enhance the secretory profile of ASC is the optimization of its angiogenic and regenerative potential through external stimuli. **Objectives:** the present study evaluated the effects of normoxia and hypoxia preconditioning on the ASC secretome and analyzed the expression of soluble mediators involved in the tissue repair process. **Materials and Methods:** ASC were isolated from liposuction samples, subjected to culture in normoxic and hypoxic conditions for 48 hours and evaluated for their angiogenic and regenerative potential. **Results and Discussion:** The ASC secretome preconditioned in normoxia and hypoxia showed in its composition the markers of cell regeneration and other growth factors involved in angiogenesis and tissue repair. In vitro analysis demonstrated that both conditioned media (CM) exerted anti-apoptotic, pro-migratory and angiogenic effects in HUVECs, with better pro-angiogenic performance in cells treated with CM in normoxia. Analysis in a murine model of wound healing showed improvement in the closure of wounds treated with the conditioned means in normoxia and hypoxia. **Conclusion:** Both pre-conditioning regimes in normoxia and hypoxia induced the regenerative capacity in the analyzed ASCs. Considering that normoxia pre-conditioning presented better performance and is more practical to obtain, hypoxia pre-conditioning is not necessary.

Support: FAPESB, CNPq and PIBIC-UFBA.

Keywords: ASC, chronic ulcers, cell therapy.

EFFECTS OF FLAVONOID RUTIN ON GASTROINTESTINAL FUNCTION AND INTEGRITY IN AN EXPERIMENTAL MODEL OF PARKINSON'S DISEASE

Livia Bacelar de Jesus, Annyta Fernandes Frota, Fillipe Mendes Araújo; Rafael Leonne Cruz de Jesus, Victor Diogenes Amaral, Darizy Flavia Silva, Marcelo Biondaro Goes, Gyselle Chrystina Baccan, Silvia Lima Costa.

Laboratório de neuroquímica e Biologia Celular – LabNq, Instituto de Ciências da Saúde, Universidade Federal da Bahia, Bahia, Brasil.

Introduction: Parkinson's disease (PD) is considered the second most prevalent neurodegenerative disease in the world. Studies suggest that the enteric nervous system (ENS) may also be involved in the neurodegenerative process underlying PD. The ENS is responsible for controlling intestinal motility and secretion, the involvement of ENS has been shown to be important in the pathophysiology of PD. Another interesting fact is that natural substances, like the flavonoids, can lower the risk for the development of PD. **Objective:** To evaluate the effect of flavonoid rutin on gastrointestinal function and structure of rats in a PD model. **Material and Methods:** Male Wistar rats weighing 250-300g were anesthetized and submitted to unilateral nigrostriatal injection of 6OHDA (21µg) and submitted to oral treatment (gavage) with rutin (10mg/Kg) for 14 days. To confirm damage rats were submitted the rotation test induced by apomorphine (3mg/kg, i.p.). The gastrointestinal transit was evaluated before euthanasia by gavage of 0.5mL 6% Carmine red. The fecal pellets were collected and monitored for 12h. On the 15th day the rats were anaesthetized and Ileum segments were collected and submitted to a histopathological protocol and stained with hematoxylin/eosin. For tissue contraction assays segments of ileum were placed in organ baths containing Krebs solution and maintained at 37°C and bubbled with 95% O₂/5% CO₂. Carbacol and nitric oxide donor was used to assess tissue responsiveness (10⁻¹⁰-10⁻⁴M), in addition to KCl 80mM. **Results and Discussion:** The rats in the 6OHDA+rutina group exhibited a significant increase in fecal water content (20%), increased fecal production and improvement in gastrointestinal transit time of approximately 1 hour when compared to the 6OHDA group. It was

observed that apparently the treatment with rutin caused an increase in the reactivity of the ileal smooth muscle to muscarinic activation, suggesting reduction in relaxation mediated by nitric oxide signaling pathway. Moreover, histopathological analysis showed an increase in the cell body of paneth cells in the ileum segments of animals in the 6OHDA+rutin demonstrating a greater participation of innate immunity. **Conclusion:** The results showed that treated with flavonoid rutin appear to improve gastric motility and increase contractility of the ileal segment in parkinsonian rats. Expansion of the study group is necessary to confirm these findings. Future perspectives include analyzes of fecal microbiota and immunohistochemistry for enteric glial cells.

Keywords: Enteric nervous system, Parkinson's disease, Rutin. **Support:** FAPESB

AGING AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE: THE ROLE OF THE ENDOCRINE-IMMUNE CROSSTALK

Fabíola Ramos Jesus¹, Fabine Correia Passos¹, Margarida Célia Neves², Antônio Carlos Lemos²,
Gyselle Chrystina Baccan¹

¹Laboratório de Neuroendocrinoimunologia, Instituto de Ciências da Saúde, Universidade Federal da Bahia, Bahia, Brasil; ²-erviço de Pneumologia, Ambulatório Magalhães Neto do Complexo HUPES, Bahia, Brasil.

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a respiratory disease with airflow limitation, chronic inflammation, and the presence of emphysema in the lungs, caused by the inhalation of noxious particles or gases. Age has been recognized as a risk factor for developing of the disease and studies have shown that COPD patients exhibit an acceleration of the aging process when compared with individuals without COPD. Old age COPD patients could have an additional increase in the production of inflammatory cytokines in pulmonary and plasma level. During aging, there is also important changes in the endocrine system with decrease of in the secretion of dehydroepiandrosterone sulfate (DHEAS) hormone and growth hormone (GH). In previous studies we have shown that the endocrine-immune crosstalk could be explain the sex differences found in COPD patients, which is other risk factor for COPD. **Objectives:** we propose to investigate the associations between endocrine and immune senescence in COPD patients and the relevance of this crosstalk for COPD. **Material and Methods:** Individuals with COPD and without COPD (controls), aged between 50 and 80 years, will be recruited in the COPD at the Pneumology Service of the Edgard Santos University Hospital—Federal University of Bahia, and from a public school that offered an adult education program, respectively. Both groups will be divided according to age, considering the adult group composed of individuals aged between 50 to 64 years old and elderly group, aged 65 to 80 years old. After medical evaluation and inclusion in the study, tests will be carried out to assess COPD and determine the severity of the disease, nutritional assessment, blood collection for laboratory tests, application of questionnaires. The DHEA and GH hormones will be quantified using the chemiluminescence technique and the cytokines will be evaluated in the serum and quantified by the flow cytometry technique.

Keywords: COPD, immunosenescence, hormones

Support: FAPESB

EVALUATION OF ANTIOXIDANT MECHANISMS OF THE FLAVONOID AGATHISFLAVONE AGAINST NEUROINFLAMMATORY DAMAGE

Janaina Ribeiro Pereira Soares¹; Silvia Lima Costa¹; Juciele Valéria Ribeiro de Oliveira¹

¹Laboratory of Neurochemistry and Cellular Biology, Department of Biophysics and Biochemistry, Institute of Health Sciences, Federal University of Bahia, Salvador-Bahia 40.110-100, Brazil

Introduction: Oxidative stress and neuroinflammation are critical features involved in the pathophysiology of neurodegenerative diseases (NDD). Glial cells play a fundamental role in the control of neuroinflammation, modulation of homeostasis and in neuroprotective and neurotoxic mechanisms, which result in loss of structure and neuronal degeneration. In this context, there is a need for effective and complementary therapies to treat and / or mitigate the

progression of NDD. Polyphenolic compounds like flavonoids are promising candidates as adjuvants for NDD therapy due to their well described antioxidant and anti-inflammatory activities. The biflavonoid agathisflavone, derived from the Brazilian plant *Poincianella pyramidalis*, demonstrated significant neuroprotective and antineuroinflammatory activities *in vitro*, with potential in acting as a modulator of antioxidant pathways in neuroinflammatory conditions. **Objectives:** This project aims to evaluate *in vitro* the antioxidant mechanisms of action of agathisflavone, associated with the control of the glial inflammatory response and neuroprotection. As specific Objectives, we seek to analyze in cultures of dissociated cerebellar subject to inflammatory damage, to identify the enzymatic pathways modulated by the agathisflavone, and relation with astrocyte and microglia inflammatory profile. **Methods:** Cerebellar primary cultures will be obtained from 8 days old Wistar rats. Three days cultures will be treated or not with agathisflavone (1-10 μ M) and, one hour later, submitted or not to inflammatory damage with LPS (1 μ g/mL) or IL-1 β (10 ng/mL). Twenty-four hours later, different approaches will be adopted for assessing neurons integrity, glia phenotype, free radical levels, and antioxidant systems activity. The integrity of neurons will be analyzed by immunocytochemistry (ICC) for specific structural markers (β -Tub III), and astrocyte and microglia reactivity by ICC for structural markers (GFAP and Iba-1, respectively) and analyzing the expression of growth factor and inflammatory cytokines by RT-qPCR. SOD, CAT, GST and GST enzymatic activities, the levels of reactive oxygen species (iNOS and H₂O₂/peroxidase), redox reactions (FRAP) and free radical capture (FRAP, and DPPH) will be determined by colorimetric assays and Western blot. **Expected results:** With the results obtained, we seek to characterize the antioxidant mechanisms of the flavonoid agathisflavone against neuroinflammatory damage, contributing to studies that help the development of new treatments for NDD.

Keywords: agathisflavone; antioxidant, neuroinflammation.

Support: FAPESB (APP0107/2016; INT 016/2016); CAPES (PGCI Proc. - 88881.117666/2016-01); Nacional Institute for Translational Neuroscience and INCT for Excitotoxicity and Neuroprotection (MCTI/CNPq).

EVALUATION OF IMMUNOMODULATORY EFFECTS OF SELENIUM DIOXIDE IN MICROGLIAL RAT CELL CULTURES INFECTED WITH *NEOSPORA CANINUM*

Brenda Valerio Souza^{1,2}, Ana Elisa Del'Arco Vinhas Costa^{1,2}, Maria de Fátima Dias Costa², Silvia Lima Costa², Alexandre Moraes Pinheiro¹

¹Laboratory of Biochemistry and Veterinary Immunology, Department of Environmental, Agrarian and Biological Sciences, Federal University of Recôncavo da Bahia, Cruz das Almas, Bahia, Brazil. ²Laboratory of Neurochemistry and Cellular Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil.

Introduction: *Neospora caninum* is an intracellular obligatory protozoan capable of infecting several species of animals. This protozoan has a tropism for the cells of the Central Nervous System (CNS), which can cause degeneration of neurons, astrocytes and microglia. Therefore, elements that can contribute to the neuroprotection of glial cells are sought, reducing deleterious effects caused by the parasite on the host. Selenium dioxide (SeO₂), derived from Selenium (Se), has immunostimulating, antioxidant and anti-inflammatory properties, and can be supplemented to increase the immune response against damage. **Objectives:** Evaluate the immunomodulatory effects of SeO₂ in microglial rat cell culture infected with *N. caninum*. **Methods:** Microglia primary cell culture of the cortex of newborn Wistar rats (0-2 days) will be cultivated. Concomitant to this, tachyzoites of the *Nc*-Bahia strain will be grown in Vero cells supplemented with RPMI 1640 medium. Microglial cells will be treated with SeO₂ at a concentration of 0, 4 μ M and incubated for 24 hours. After that, the microglial cell culture will be infected with *N. caninum* tachyzoites in a 1: 1 proportion of cell/ parasite remaining in the culture for 72 hours. The evaluation of cell viability and toxicity will be provided by the MTT method and dosage of the enzyme Beta-glucuronidase, respectively. Nitric oxide levels will be measured using the Griess method. Glutathione peroxidase (GPX), an important antioxidant enzyme, will be measured before and after modulation with SeO₂ in microglial cultures infected with the parasite. As microglial morphological changes, they will be evaluated by immunocytochemistry through the labeling of Iba-1 (ionized calcium-binding adapter molecule-1) and BrdU (bromodeoxyuridine), markers of microglial activation and microglial proliferation, respectively. The quantification of these markers will be assessed by Immunoblotting. Parasitic quantification will be specified by counting tachyzoites, before and after modulation by SeO₂, and dosing of pro-inflammatory cytokines by the ELISA method

(Enzyme-Linked Immunosorbent Assay). **Expected Results:** It is expected that modulation by SeO² will contribute to the neuroprotection of microglia in the infection by *N. caninum*.

Keywords: Neosporosis; microglial activation; antioxidant system; selenium dioxide.

Support: CAPES

EVALUATION OF MAPK38, JNK AND ERK1 / 2 SIGNALING PATHWAYS IN CHRONIC PERIODONTITIS

Rebeca Pereira Bulhosa Santos¹; Patrícia Mares De Miranda¹; Michele Miranda Lopes Falcão^{1,2}; Soraya Castro Trindade^{1,2}

¹Postgraduate Program in Immunology, laboratory of immunology and molecular biology. Federal University of Bahia - UFBA. Salvador/Bahia. Brazil; ²Program of Biotechnology, health Department. State University of Feira of Santana - UEFS. Feira of Santana/Bahia. Brazil.

Introduction: Periodontitis is a multifactorial immuno-inflammatory disease whose primary etiological is related to a dysbiotic biofilm on the dental surface. Porphyromonasgingivalis is a Key pathogen in the dysbiosis, having a central role in the disease progression due to a several of virulence factors, such as HmuY and K gingipains, which can elicit the immune response by activating neutrophils, dendritic cells and macrophages. The macrophage response occurs through activation of intracellular signaling pathways, especially the MAPK pathways, which are crucial due to its ability to phosphorylate a network of proteins that lead to cellular proliferation, differentiation, inflammation and apoptosis. Three families make up the MAPK pathways: ERK, JNK and MAPK p38. **Objectives:** To evaluate in macrophages the signaling pathways MAPK38, JNK and ERK1/2 in periodontitis. **Methods:** This research is based on an experimental study with 60 volunteers (30 with chronic periodontitis and 30 without periodontitis), who will be selected at the dental clinic of the Universidade Estadual de Feira de Santana. PBMCs will be cultured, with and without inhibition for MAPK p38, JNK and ERK 1/2 pathways and stimulated by the sonicated extract, rHmuY and the P. gingivalis K peptide (Kgp12) of P. gingivalis. The measurement of cytokines in the culture supernatant will be done by flow cytometry. The data obtained will be evaluated using the ANOVA tests and the Games-Howell post-hoc tests. **Expected results:** Thus, this study is expected to contribute to a better understanding of the role of MAPK pathways in the induction of periodontal inflammation by Porphyromonasgingivalis.

Keywords: Porphyromonasgingivalis; Signaling pathways; Macrophages; Gingipaina; HmuY.

Support: CAPES; LABIMUNO;PPGIm;NUPPIM.

EVALUATION OF MICROBIOLOGICAL AND IMMUNOLOGICAL MARKERS IN THE ASSOCIATION BETWEEN CHRONIC PERIODONTITIS AND METABOLIC SYNDROME.

Patricia Mares de Miranda, Rebeca Pereira Bulhosa Santos, Michelle Miranda Lopes Falcão, Johelle De Santana Passos Soares, Soraya Castro Trindade¹

¹Department of Health, Dentistry, Feira de Santana State University, Bahia, Brazil.

Introduction: Metabolic Syndrome (MetS) is a chronic and progressive disease related to pathophysiological changes caused by central fat deposition and insulin resistance. Currently, it contributes to increased cardiovascular morbidity and mortality and type 2 diabetes mellitus. Regarding the factors associated with MetS, some investigations have indicated that its development depends on a complex interaction between genetic predisposition, lifestyle, and socio-demographic factors, as well as health-disease conditions such as insulin resistance, centralized obesity, hypertension, low HDL-cholesterol levels and inflammatory diseases. Periodontitis is a chronic inflammatory process in response to bacterial antigens from the dental biofilm, resulting in loss of tooth support tissues, alveolar bone resorption and periodontal pockets formation, which may lead to loss of the unit dental. Explanatory theories for

the association between periodontal disease and MetS have also been presented, migration of buccal bacteria and their byproducts into the circulatory current, with systemic dissemination of inflammatory mediators, such as interleukins (IL-6, IL-1 β ,) and TNF- α may establish a chronic systemic inflammation. Thus, increased production of circulating metabolites would be related to the causal process of MetS. However, the specific cellular and molecular mechanisms for this association remains unclear. **Objective:** To investigate the association between microbiological and immunological markers in patients with the diagnosis of MetS and chronic periodontitis. **Material and Methods:** In this is a case-control study, the microbiological biofilm will be collected from the participants and genotyping will be performed by qPCR to verify the presence and association of periodontopathogens and MetS. In addition, flow cytometry immunoassay will be performed to verify the concentration of Th1, th2 and Th17 profiles cytokines in Porphyromonasgingivalis antigen-stimulated peripheral blood mononuclear cell culture supernatant from individuals with and without MetS. To evaluate the humoral immune response, an enzyme immunoassay (ELISA) will be used to evaluate salivary IgA levels and IgG serum levels specific to antigens present in the sonicated extract of Porphyromonasgingivalis in the comparison groups. **Expected Results:** The possible association between the immunological and microbiological markers of PD and MetS can contribute to explain the relationship these two chronic diseases.

Keywords: metabolic syndrome, Periodontitis, Immunoglobulin G, Immunoglobulin A

Acknowledgment: CAPES, FAPESB, LABIMUNO(ICS-UFBA), PPGIm(ICS-UFBA).

EVALUATION OF THE NEUROPROTECTOR POTENTIAL OF FLAVONOIDS BIS-APIGENIN AND APIGENIN ON AMYOTROPHIC LATERAL SCLEROSIS MODELS

Rodrigo Barreto Carreira¹, Victor Diógenes Amaral da Silva¹, Ravena Pereira Nascimento¹, Lucas Matheus Gonçalves de Oliveira¹, Ellen Cristina Vale Silva, Clarissa Schitine¹, Maria de Fátima Dias Costa¹, Cleide dos Santos Souza², Emiliano Trias³, Luis Barbeito³, Sílvia Lima Costa¹

¹Department of Biochemistry and Biophysics, Laboratory of Neurochemistry and Cell Biology, Institute of Health Sciences, Federal University of Bahia, Brazil; ²Sheffield Institute for Translational Neuroscience, The University of Sheffield, United Kingdom; ³Laboratory of Neurodegeneration, Institut Pasteur Montevideo, Uruguai.

Introduction: Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterised by progressive death of the upper and lower motor neurons leading to the loss of motor function. This disease has a prevalence of approximately 0.6 to 2.6 per 100.000 people, typically fatal within 3 to 5 years of symptom onset. There is no known cure yet, and the current treatments extend the life expectancy only a few months. Indeed, the causes of ALS is unknown there is established that among the pathophysiologic aspects of the ALS are the glutamate-mediated excitotoxicity, oxidative stress and neuroinflammation. Previous research demonstrated in vitro that agathisflavone (bis-apigenin) protects cerebral neurons from inflammatory and glutamate-mediated excitotoxicity. In addition, it was observed that in vitro monomeric apigenin protected cells against induced models of neurodegeneration through immunomodulation of glial cells profile. **Objectives:** The aim of this project is to characterize the neuroprotector outline of flavonoids agathisflavone and apigenin in ALS models through assessing its effect in aberrant glial cells (Aba); evaluating the motor neuron protection from damage related to ALS; and investigating the flavonoids neuromodulation by assessing the expression and the secretion of cytokines and chemokines from microglial cells. **Methods:** Will be used Sprague-Dawley SOD1G93A rats as ALS disease model. The anti and pro inflammatory glial cells profile will be assessed by immunohistochemistry of spinal cord sections from treated rats; the motor neuron protection will be evaluated through determining the number and measuring the length of the ChAt+ neurons from treated rats; and the cytokines and chemokines expression and secretion will be determined in treated microglial culture cells derived from ALS. **Expected Results:** With the development of this project, it is expected to characterize the neuroprotection profile of the flavonoids under study in an ALS neurodegeneration model, with emphasis on its anti-inflammatory mechanisms and in a translational perspective for future therapeutic application.

Keywords: Amyotrophic lateral sclerosis, agathisflavone, apigenin, neuroprotection, immunomodulation.

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EVALUATION OF THE THERAPEUTIC POTENTIAL OF MESENCHYMAL CELLS THAT OVEREXPRESS IGF1 ON SKELETAL MUSCLE INJURY INDUCED BY INOCULATION OF BOTHROPS SNAKE VENOM

Kaenna Baraúna Campos¹, Clara Macêdo Mimoso¹, Luciana Lyra Casais-e-Silva^{1,2}, Simone Garcia Macambira^{1,3,4}

¹Programa de Pós Graduação em Imunologia – Instituto de Ciências da Saúde/Universidade Federal da Bahia.

²Departamento de Biorregulação, Laboratório de Neurolimnocrinologia e Toxinologia (LABNIET) – Instituto de Ciências da Saúde/Universidade Federal da Bahia. ³Departamento de Bioquímica e Biofísica - Instituto de Ciências da Saúde/Universidade Federal da Bahia. ⁴Laboratório de Engenharia Tecidual e Imunofarmacologia – Instituto Gonçalo Moniz/FIOCRUZ/Bahia.

Introduction: Skeletal Muscle (SM) regeneration depends on highly complex mechanisms involves different cell types which of them with its own spatial and temporal kinetics. For small muscle injuries, the remodeling process is mainly guide by satellite cells. For massive muscle lesion besides the recruitment of these stem cells, inflammatory cells, fibroblasts, vascular cells and myogenic one are activated. The process is exacerbated and the scar tissue is formed by active fibroblasts, compromising muscle function and structure. Many cytokines and growth factors releases by these cells contribute to healing process such as IGF-1 that is very important to SM regeneration by stimulating protein synthesis, promoting cell activation, differentiation and hypertrophy. However this regenerative potential is limited and overwhelmed demanding therapeutic intervention to avoid functional loss of SM. As Mesenchymal stem cells (MSC) are considered a potential tool for tissue regeneration through paracrine mechanism, so its regenerative capacity could be improved when MSC is overexpressing IGF-1. **Objective:** To investigate the therapeutic potential of MSC overexpressing IGF-1 on SM damage induced by Bothrops venom inoculation in experimental model. **Methods:** C57Bl6 male mice will be inoculated in hind paw gastrocnemius muscle with 50 µg/mL of the total venom. Animals will be separated in 4 groups: control non-inoculated, venom inoculated MSC-IGF-1(105) treated, venom inoculated MSC (105) treated and venom inoculated non treated. Mice will be submitted to several analysis: functional by treadmill test, serum sinflamatory mediators by ELISA, muscle gene expression of cytokines and growth factors by RTqPCR and structural by morphometric evaluation before and after venom inoculation and after cell therapy. Treatment will be in the acute phase of the lesion (6 hafter inoculation) and in the chronic phase (3, 14 and 28 days after inoculation) and euthanized for further evaluations 24 hafter treatment. **Results and Discussion:** It is expected to prove the therapeutic potential of MSC overexpressing IGF-1 and to elucidate the immunomodulatory mechanisms involved. **Conclusion:** Once the effectiveness of this cell therapy is proven, new therapeutic protocols for muscle regeneration can be proposed. **Keywords:** Mesenchymal stem cells; IGF-1; skeletal muscle; tissue regeneration; poison. **Support:** CAPES

EXPRESSION AND IMUNNE RESPONSE TO RESUSCITATION PROMOTING FACTOR OF CORYNEBACTERIUM PSEUDOTUBERCULOSIS

Natália da Rocha Lopes, Luan Santana Moreira, Vitor Cordeiro Pereira, Marcos Borges Ribeiro, Roberto Meyer, Silvana Beutinger Marchioro

Laboratório de Imunologia e Biologia Molecular, Universidade Federal da Bahia – BA, Brasil

Introduction: Resuscitation promoting factors (Rpf) are responsible for bacteria reactivation from dormant state to active status. In *Corynebacterium pseudotuberculosis* genome has already been observed the presence of *rpf* gene, but its importance is unknown yet. In *Mycobacterium tuberculosis*, Rpf are very important and well characterized then, tounderstand how Rpf is involved in patogenesis caused by *C. pseudotuberculosis* is necessary. **Objectives:** Evaluate the expression of Rpf in two different strains (1002 and Cap76) of *C. pseudotuberculosis*, as well as, evaluate the aspects of immune response induced by Rpf recombinant antigen. **Methods:** The Rpf expression evaluation will be done by collecting and samples from the bacteria in different growth phases and subjected to different stress conditions. In each phase, aliquots will be taken and RNA will be extracted for analysis of *rpf* expression by qRT-PCR. Recombinant protein will be produced by plasmid containing *rpf* gene and expressed in *Escherichia coli*. Lastly, indirect ELISA and Western blot method will analyze the response in goat's serum against to rRpf antigen. **Expected results:** It is expected to characterize the expression of *rpf* during the cultivation of different strains of *C. pseudotuberculosis*,

characterizing this expression after the bacteria be subjected to stress factors. It is also expected to characterize the immune response of naturally infected goats to the recombinant Rpf antigen.

Keywords: Rpf; *C. pseudotuberculosis*; recombinant protein.

Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES); Fundação de apoio à pesquisa e extensão (Fapex).

GENETIC VARIANT IN MIRNA4500 ARE ASSOCIATION WITH ASTHMA AND BRONCHODILATOR RESPONSE

Jéssica F de Araújo, Hatilla S. Silva, Raísa S. Coelho, Helena M. P. Teixeira, Álvaro A. Cruz, Camila A. Figueiredo, Ryan dos S. Costa

Instituto de Ciências da Saúde, Laboratório de Imunofarmacologia e Biologia Molecular (IMUNOBIO), Universidade Federal da Bahia, Bahia-Brasil.

Introduction: Asthma is generally characterized as an obstructive airway disease that involves chronic inflammation of the respiratory tract. The main treatment is bronchodilation depending on the B₂-adrenergic (ADRB₂) pathway. The binding of an agonist to the β₂-adrenoreceptor results in the intracellular elevation of cAMP due to the activation of adenylate cyclase, resulting in bronchodilation. The prevalence, severity of asthma and the search for genetic biomarkers for personalized treatment are on the rise. miRNA-4500 has shown to present a possible relevant interference in the interference of the ADRB₂ pathway, which can be regulatory or deregulating and consequently can be a new therapeutic target. Objective: To investigate the association of polymorphisms in miRNAs. 500 gene with asthma and lack of bronchial reversibility in asthmatic individuals. Methods: a study was carried out with 1094 adult individuals living in Salvador from ProAR (Program for the Control of Asthma in Bahia). DNA was extracted from peripheral blood and genotyping was performed using the Infinium Multi-Ethnic Global chip and the genetic data from the miRNA, 4500 were extracted. The analyzes were performed using SPSS to define adjustments for logistic regression. The quality control for all SNPs was performed in stages using PLINK. Results: There are 13 SNPs in miRNA-4500 significantly associated with one of the phenotypes studied. Two SNPs were associated as risk factors for asthma, while four SNPs were associated as protective factors in relation to the lack of reversibility in asthmatic individuals. Considering, five SNPs were considered a protective factor. Most SNPs are intronic. **Conclusion:** Variants in miRNA-4500 may influence the patient's chance of responding to short-acting bronchodilator. A further study will allow a greater elucidation of the impact of these variants, which the patient's chance of responding to the short-acting bronchodilator. Further studies will allow a greater elucidation of the impact of these variants, which may contribute to a more effective and personalized therapeutic response.

Keywords: asthma, β₂-adrenergic pathway, miRNA therapeutic response.

Support: CNPq.

HETEROLOGOUS PRODUCTION OF RECOMBINANT SCHISTOSOME ELASTASE

Carolina Orrico Melo Ferreira de Jesus^{1,2}; Beatriz de Souza Santos², Carina Da Silva Pinheiro³; Barbara Castro-Pimentel Figueiredo^{1,2}.

¹ Postgraduate Program in Immunology, Federal University of Bahia - UFBA. Salvador/Bahia. Brazil; ² Serviço de Imunologia do Complexo Hospitalar Universitário Professor Edgard Santos (Com-HUPES), Federal University of Bahia - UFBA. Salvador/Bahia. Brazil; ³ Postgraduate Program in Biotechnology, Federal University of Bahia - UFBA. Salvador/Bahia. Brazil.

Introduction: *Schistosoma mansoni* is the parasite that causes schistosomiasis, a disease occurring in a large endemic in Brazil, which reports close to seven million infected individuals. *S. mansoni* parasite presents a complex life cycle and infection of vertebrate hosts occurs through the active penetration of cercariae through the skin. This process involves the vibratory action of cercaria's tail and also the emptying of the acetabular glands, which promotes the secretion of

lytic proteases that assist in the penetration of host intact skin. Previous studies have characterized several proteins in cercariae secretion, being the serine protease elastase (*SmCE*) the most abundant protein and also the most important protease in active penetration of skin. In addition, cercariae antigens are identified as possibly responsible for immediate immune response after host infection, especially in individuals that have not had previous contact with *S. mansoni* antigens. **Objective:** Perform a functional study of *SmCE* enzyme and evaluate its effect on cell activation and cytokine production in uninfected individuals. **Material and Methods:** Experiments were designed in order to heterologously produce cercaria most abundant elastase isoform, *SmCE* 1a. After that, its enzymatic characterization was carried out using chromogenic substrate for elastase. **Results and Discussion:** As a result, recombinant *SmCE* was expressed Rosetta *E. coli* strain. After purification, the obtained protein was submitted to enzymatic tests. Considering the conditions tested up to now, the best activity was obtained using the 20 µg of protein, after 360 min of incubation with the substrate at 37 °C, at pH 9.0. **Conclusion:** Further experiments will outline *SmCE* 1a functionality in buffer containing Ca²⁺. In addition, we intend to test the effect of elastase activity inhibitors, such as tosyl-L-phenylaminechloromethyl ketone (TPCK) and elafine, as well as the *SmKI-1* protein from *S. mansoni*, recently characterized as a neutrophilic elastase inhibitor. Still, we intend to study the effect of *SmCE* effect on cellular activation and cytokines production by peripheral blood mononuclear cells from uninfected individuals, for a better comprehension of cercarial dermatitis mechanisms.

Keywords: *SmCE*; elastase; *S. mansoni*; cercaria.

Support: Fapesb, CNPQ.

HOMER2 GENE VARIANTS ARE ASSOCIATED WITH BDR IN ASTHMATICS

Helena M.P. Teixeira^a, Hátilla Santos^a, Ana Paula Castro^a, Talita S. Jesus^a, Maria B. R. de Santana^a, Gabriela P. Pinheiro^b, Álvaro A. S. Cruz^b, Ryan S. Costa^a, Camila A. Figueiredo^a

^aDepartamento de Biorregulação, Laboratório de Imunofarmacologia e Biologia Molecular, Instituto de Ciências da Saúde, Universidade Federal da Bahia, Bahia, Brasil. ^b Programa para o Controle da Asma na Bahia (ProAR), Universidade Federal da Bahia (UFBA), Bahia, Brasil.

Introduction: Asthma is a complex, heterogeneous and variable disease, usually characterized by chronic inflammation of the airways. The first line of treatment for asthma rescue is the use of bronchodilator. HOMER2 is postsynaptic density scaffolding protein which is a member of homer family and regulates G-protein-coupled receptors such as β₂ adrenergic receptor, and aids in coupling of surface receptors. **Objectives:** To identify whether genetic variants in the *HOMER2* gene are associated with bronchodilator response (BDR) in an admixture population with asthma. **Methods:** We performed an association test to identify genetic variants that may contribute to differences in acute BDR to inhaled β₂-agonists, characterized by the change in forced expiratory volume in one second (FEV₁). Single-nucleotide variants (SNVs) in *HOMER2* were genotyped with the Multi-Ethnic Global Array (Illumina) in 716 individuals with asthma from the Programa de Controle da Asma e da Rinite Alérgica Bahia (ProAR). We used logistic regression models adjusting for age, sex, body mass index (BMI), FEV₁ pre-bronchodilator, asthma severity, and genetic ancestry. **Results and Discussion:** We identified seven SNVs in the *HOMER2* associated with BDR. Three variants, rs3784377 (G, OR: 0.62, IC: 0.46-0.83), rs12148275 (A, OR: 0.63 IC: 0.47-0.84), rs11393166 (C, OR: 0.64 IC: 0.47-0.85), were negatively associated with BDR which means that individuals who have the alternative allele have less chance of responding to bronchodilator. Four variants, rs2667385 (G, OR: 1.32 IC: 1.01-1.72), rs115483400 (C, OR: 1.51 IC: 1.14-2.00), rs1256439 (A, OR: 1.67 IC: 1.28-2.18), rs78086831 (G, OR: 2.42 IC: 1.04-5.59) were positively associated which means that they are more likely to respond to the bronchodilator. Variants in the *HOMER2* gene have already been associated with FEV₁ / FVC rate and vital capacity (FVC). This gene has also been reported as a negative regulator of T cell activation through NFAT. **Conclusions:** These findings suggest the *HOMER2* variants associated with BDR could be involved lung function and immunological pathway, and consequently influence in some way the smooth muscle relaxation that occurs in asthma. Our study expands the understanding of pharmacogenetic analyses provided potentially new insight into biological mechanisms associated with BDR in admixture populations.

Keywords: HOMER2, BDR, asthma, immunogenetics.

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IDENTIFICATION OF NATURAL POLYPHENOL AND SYNTHETIC DERIVATIVES AS NEW CANDIDATES FOR THE TREATMENT OF SARS-COV2 INFECTIONS BASED ON THEIR NEUROPROTECTIVE IN PRECLINICAL MODELS OF NEUROINFLAMMATION.

William Douglas Lacerda Novais, Clarissa Schitine, Juciele Valéria Oliveira, Maria de Fátima Dias Costa, Balbino Lino dos Santos, Ravena Pereira Nascimento, Victor Diógenes Amaral da Silva, Silvia Lima Costa

Laboratório de Neuroquímica e Biologia Celular, Departamento de Bioquímica e Biofísica, Instituto de Ciências da Saúde, Universidade Federal da Bahia (UFBA), Brazil.

Introduction: Since the beginning of the COVID-19 pandemic, the number of cases has increased exponentially. In the most severe cases of the disease, patients have a severe acute respiratory syndrome, which can progress to severe pneumonia and even multiple organ failure. In addition, the nasal route is one of the main pathways for the virus to enter the body, thus causing neurological impairment of the central nervous system (SCN). In addition, studies have shown the possibility of brain regions infected with SARS-CoV2 to induce reactive astrogliosis and microglia activation, placing the modulation of the glial inflammatory response as a strategy to contain neurological damage and subsequent damage in other systems. **Objectives:** The present study has as objective to identify natural polyphenols and synthetic derivatives as new candidates for the treatment of SARS-CoV2 infections based on their neuroprotective effects in preclinical models of neuroinflammation associated with viral infection. **Methods:** Initially, a panel of 5 natural flavonoids and 10 synthetic heterocyclic derivatives will be tested in concentrations ranging from 0.1 to 10 μ M in dissociated midbrain cultures subjected (or not – control) to inflammatory damage with IL1- β (10 ng / mL), IFN- γ (100 U / mL) and/or LPS (10 μ g / mL) associated with virus infection, and also with recombinant viral protein (100 nM / mL). In order to analyze the neuroprotective effect of these compounds, experimental tests of cell viability and neuron integrity will be carried out by MTT test, Alamar-Blue staining and FluorJade-B staining. The compound that present low neuron toxicity and the best neuroprotector profile against inflammatory damages, will be tested in dissociated and organotypic midbrain cultures, aiming to characterize the inflammatory profile and glial response. For This, immunocytochemistry for astrocyte (GFAP) and microglia (Iba-1) marker will be performed and RT-qPCR for inflammatory cytokines and growth factors. **Expected Results:** With the development of of this project It is expected to determine new neuroprotective compounds, purified from the regional flora or its derivatives, against inflammatory damage associated with viral infection in the CNS and their potential use as adjuvants in the treatment of diseases of this nature.

Keywords: neuroinflammation, neuroprotection, COVID-19, flavonoids, synthetic heterocyclic compounds.

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IMMUNOLOGICAL CHARACTERIZATION OF PATIENTS WITH DIAGNOSIS OF COVID-19 AND RELATIONSHIP WITH MARKERS OF VASCULAR INFLAMMATION AND NEUROINFLAMMATION

Nívia Nonato Silva¹, Maria de Fátima Dias Costa¹, Victor Diógenes Amaral da Silva¹, Clarissa Schitine¹, Balbino Lino dos Santos¹, Ravena Pereira Nascimento¹, Vitor Antônio Fortuna², Silvia Lima Costa¹

¹Laboratory of Neurochemistry and Cellular Biology, Institute of Health Sciences, Department of Biochemistry and Biophysics, Federal University of Bahia, Bahia, Brazil. ²Laboratory of Immunology and Molecular Biology, Institute of Health Sciences, Federal University of Bahia, Bahia, Brazil.

Introduction: Coronavirus disease 2019 (COVID-19) has now spread quickly worldwide. In addition to major respiratory distress, characteristic neurological manifestations are also described, for example, encephalitis as well as reactive astrogliosis and microglia activation. Furthermore, histopathological studies have emphasized the crucial role of endothelial cells in severe SARS-CoV-2. Events like, venous thrombotic, pulmonary embolism, with elevated D-dimer and coagulation activation are highly prevalent in COVID-19 patients. **Objectives:** The study will aim to characterize the immunological profile of patients diagnosed with COVID-19 and the relationship with vascular and

neuroinflammatory markers as a basis for prospecting for new therapeutic approaches. Methods: In the present study, ECA2 and GFAP levels will be analyzed by ELISA, as well as the profile of total leukocytes in blood samples of infected patients. On the other hand, the gliomodulatory effect of a panel of natural flavonoids and synthetic derivatives will be tested in cultures of human astrocytic cells subjected to inflammatory damage associated with virus infection. Cell viability will be measured using the MTT assay and AlamarBlue blue reagent. Astrocyte activation markers, as well as the inflammatory cytokines and vascular factors will be tested by immunocytochemistry and/or RT-qPCR. Expected Results: Characterization of the inflammatory profile, astrocytic response and vascular markers associated with SARS-CoV-2 in view of translation of possible candidates for treatment of SARS-CoV-2. Keywords: COVID-19, astrocyte, neuroinflammation, vascular endothelium. **Support:** FAPESB (APP0107/2016; INT 016/2016 - Indirect Support); INCT Nacional Institute for Translational Neuroscience and INCT for *Excitotoxicity* and Neuroprotection (MCTI/CNPq); CAPES (MPhil fellowship).

IMMUNOLOGICAL RESPONSE LIVER MITOCHONDRIAL OXYGEN CONSUMPTION OF BROILERS FED SUPPLEMENTED ZINC DIETARY

Tatiane Almeida Viana Lopes¹; Jerônimo Ávito De Brito²; Alexandre Moraes Pinheiro².

1-Programa de Pós-Graduação em Imunologia, Instituto de Ciências da Saúde (ICS), Universidade Federal da Bahia (UFBA), Salvador, Bahia, Brazil; 2- Laboratório de Bioquímica e Imunologia Veterinária, Universidade Federal do Recôncavo da Bahia – (UFRB) Cruz das Almas, Bahia, Brazil

Introduction: Zinc (Zn^{2+}) is a trace element that is involved in several numerous biological functions due to it is a cofactor of a large number of enzymes. It has antioxidant effect and is crucial for the development of the immune system. In broilers, the immune response can be influenced by the nutritional levels or diet ingredients. **Objectives:** The aim of this study was to evaluate the effect of supplementing diet supplemented with Zn^{2+} on cellular and humoral responses and mitochondrial metabolism in broilers. **Material and Methods:** A total of 1, 248 day-old broilers was randomly distributed to one of 6 dietary treatments: T1- Control (Basal diet without supplement al zinc); T2 (50mg/Kg of zinc oxide); T3 (100mg / Kg of zinc oxide); T4 (25 mg / Kg of Zincglycinate –Zn Gly); T5 (50 mg/ Kg of Zn-Gly) and T6 (100 mg/Kg of Zn-Gly). Each treatment was replicated in 48 cages of 26 broileres per cage in a period of 38 days. A peripheral mononuclear cells culture was performedat 12 days of age, in 6 birds per treatment, to verify the production of nitric oxide andthe MTT test. In addition, the assessment of liver oxygen consumption andthe response of cutaneous basophils in response to phytohemagglutinin-P test and measurement of the weight lymphoid organs (spleenand Bursa of Fabricius), at 21, 28 and 31 days of age respectivelywith 8 birds per treatment. **Results and Discussion:** Nitric oxide production in response to LPS increased in most treatments with zinc, especially (T6). Through the MTT test, greater cell proliferation can be observed in treatments (T3) and (T4) compared to the control. There was no significant difference between treatments in the response of cutaneous basophilostrophy to hemagglutinin. However, a significant effect was observed on the relative weight of the Bursa of Fabricius with the supplementation of the organic form of zinc ($p < 0.05$) (T4). **Conclusions:** The results suggest that supplementing the diet of broilers with zinc maybe beneficial to the immune system of these animals mainly using the organic source of this mineral, the Zn^{2+} glycinate.

Keywords: immune system, broilers, zinc.

Support: CAPES; UFRB.

IMMUNOMODULATION OF THE ETHANOLIC EXTRACT OF *PHYALIS ANGULATA* ON MICRÓGLIA CELL CROPS INFECTED BY *NEOSPORA CANINUM*

Washington Santos Antunes^{1,2}, Silvia Lima Costa², Alexandre Moraes Pinheiros¹.

¹Veterinary Biochemistry and Immunology Laboratory, Federal University of Recôncavo da Bahia, Bahia, Brazil.

²Neurochemistry Laboratory, Neurochemistry Laboratory, Federal University of Bahia, Salvador, Bahia, Brazil.

Introduction: Neosporosis is a disease caused by the intracellular protozoan *Neospora caninum*, which can affect various species of animals, including companion and production animals, causing reproductive disorders, neuromuscular changes. In the host, the parasite can infect different tissues, however, they have tropism for tissues of the central nervous system (CNS), where tissue cysts are observed more frequently. There is no effective treatment for neosporosis. The parasite induces a Th1-type response, which causes the synthesis and release of pro-inflammatory molecules. Regulatory cytokines can reshape the Th1 to Th2 response, contributing to the non-progression of tissue damage caused by the mediators of the Th1 response. *P. angulata* is a plant with important pharmacological properties, such as anti-inflammatory, antioxidant and neuroprotective action. **Objectives:** Evaluate the effects of the crude ethanolic extract of *Physalis angulata* (EEPA) in cultures of microglial cells infected with tachyzoites of *N. caninum*. **Methods:** EEPA will be produced by the stems of the *P. angulata*, properly cleaned and macerated in ethanol. The microglia cells will be obtained from the cortex of newborn mice. The cells will be exposed to EEPA in different concentrations for 24h and then will be infected with *N. caninum* tachyzoites for 72h. The cytotoxicity of EEPA will be determined using the 3-(4, 5-dimethylthiazolyl)-2, 5-diphenyltetrazolium (MTT) assay. The changes and microglial proliferation will be assessed by immunostaining of the calcium binding adapter molecule 1 (IBA-1) and the cell proliferation marker, 5-bromo-2'-deoxyuridine (BrdU) synthetic thymidine nucleotides. IBA-1 expression will be evaluated using the Western blotting technique. The level of nitrous oxide will be determined by measuring the nitrite using the Griess method. TNF levels will be determined using the sandwich ELISA assay method using a commercial kit (Invitrogen, Canada). The results will be analyzed by the statistical program GraphPadPrism 5.10 (California, USA) and the data will be expressed in mean \pm mean standard error of the evaluated parameters. **Expected results:** Identify a fraction of the extract of *P. angulata* capable of promoting an immunomodulatory action in the microglial cells of rats, in the face of experimental infection by the protozoan *N. caninum*.

Keywords: Central Nervous System, Neosporosis, Microglial cells, Phytotherapeutic.

Support: CAPES.

INFLUENCE OF TEMPERATURE AND ANTIPYRETIC USE ON CELL VIABILITY IN PRIMARY CNS CROPS OF NEONATE RATS

Itamara Raquel dos Anjos, Silvia Lima e Costa¹, Clarissa Schitine, Denis de Melo Soares.

¹Laboratory of Neurochemistry and Cell Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil.

²Department of Medication, Faculty of Pharmacy, Federal University of Bahia, Brazil.

Introduction: Several neuropathological manifestations can be characterized by oxidative stress and exacerbated inflammatory response. One constituent part of the inflammatory process is the occurrence of fever, especially in the acute phase of several infections in which there are pyrogenic stimuli. The febrile symptom is, represented by the controlled rise in temperature and has a relevant role in the immune system stimulation. Neurogenesis occurs in two main regions: the subventricular zone (SVZ) of the lateral ventricle and the subgranular zone (SGZ) of the hippocampal dentate gyrus (DG). The process is a highly complex, with multistep that begins with the proliferation of progenitor cells, is followed by commitment to a neuronal phenotype and ends with the existence of a newly functioning, integrated neuron. Fever induced by viral infections could compromise cell migration, proliferation and differentiation, causing irreversible damage during CNS formation and maturation. Therefore, in pregnant woman, fever could compromise neural formation and cause several neurological pathologies to the embryo. In this context, it is necessary to study drugs that have neuroprotective potential and could prevent these clinical manifestations.

Objectives: This work will evaluate the influence of high temperature and the use of antipyretics on inflammatory and cellular responses in the main neurogenic niches of CNS. **Material and Methods:** Primary cultures of two different brain regions, the subventricular zone and the hippocampus, from C57BL/6 mice which will be prepared. The cultures will be carried out at different developmental stages and will be subjected to induction of several range of thermal stress and subjected to treatment with antipyretic. After this, biological tests will be performed to assess astroglial reactivity, cell viability, cell proliferation, cell differentiation death. Moreover, the expression of inflammatory and regulatory interleukins during the process will be measured. Results: It is expected that we can characterize both inflammatory events, as well as the neurogenesis process through exposure to elevated temperatures and the possible protective effect that can be caused by the modulation generated by antipyretics in the CNS development stages. In addition, we aim to elucidate these effects on neural formation.

Keywords: Neurogenesis. Heat stress. Antipyretic. Neuroinflammation.

Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES.

INFLUENCE OF TRYPANOSOMA CRUZI COINFECTION ON THE IMMUNE RESPONSE AND CLINICAL OUTCOME OF PATIENTS WITH CUTANEOUS LEISHMANIASIS FROM THE ENDEMIC AREA OF CORTE DE PEDRA-BAHIA, BRAZIL

Mônica Sousa Pita^a, Andréa Santos Magalhães^{a, c}, Lucas Pedreira de Carvalho^{a, b, c}

^aImmunology Service, University Hospital, Universidade Federal da Bahia, Brazil, ^bPostgraduate Program in Immunology, Universidade Federal da Bahia, Brazil, ^cClinical Research Laboratory (LAPEC), Gonçalo Moniz Institute, Fiocruz-Bahia, Brazil.

Introduction. American Tegumentary Leishmaniasis (ATL) is a disease that presents wide complexity in different aspects, and may result from the interaction between the patient's immune response, the genetic characteristics of the species involved in the infection, epidemiological aspects of the endemic area and possible coinfections. In several areas of Latin America, the geographical distribution of cutaneous leishmaniasis overlaps with areas of transmission of *T. cruzi* ranging from 12 to 70% of patients with clinical symptoms for leishmaniasis. (Gil, José.F., 2016). A higher T cell differentiation profile has been observed in patients with cutaneous and mucosal leishmaniasis infected with *T. cruzi* when compared to patients only infected with *Leishmania* (Bracco, María M. de Elizalde de. 2016). **Objectives.** To assess whether the immune response of patients with cutaneous leishmaniasis caused by *L. braziliensis* and co-infected by *T. cruzi* is associated with the poor clinical outcome. **Material and Methods.** This is a case-control study in which patients with cutaneous leishmaniasis caused by *L. braziliensis*, living in an endemic area of Corte de Pedra, Bahia, were recruited. Two-hundred serum were evaluated for specific IgG *T. cruzi* proteins by ELISA technique. **Results and Discussion.** Twenty patients who were coinfecting and twenty patients only infected with *Leishmania* were evaluated. Coinfected patients had higher IgG1 and IgG3 antibody titers compared to patients only infected with *Leishmania*. In addition, among patients who failed the first leishmaniasis treatment cycle, IgG3 levels were higher in co-infected patients compared to those infected only by *L. braziliensis*. **Conclusions.** These results indicate that coinfection may interfere with the individual's immune response to Leishmania infection. **Keywords:** leishmaniasis, Chagas disease, coinfection.

Keywords: Leishmaniasis, symptoms, coinfection.

Support: National Institute of Science and Technology - Tropical diseases (INCT-DT).

LYMPHOCYTE PROFILE IN ACUTE MYELOID LEUKEMIA AT DIAGNOSIS AND AFTER INDUCTION THERAPY

Reis R, Santos MM, Santos AS, Santos HHM, Santos LS, Almeida BL, Peralva CMS, Meyer R, Freire SM

Laboratório de Imunologia e Biologia Molecular – ICS-UFBA, Salvador - Brazil

Introduction: The role of the immune cells in hematological neoplasms is not fully understood of ar. Since the cytolytic activity of Natural Killer (NK) cells and the interaction of B and T lymphocytes seem to inhibit the development and progression of neoplastic cells, this study aimed at analyzing the distribution of subsets of lymphocytes in individuals with Acute Myeloid Leukemia (AML) at diagnosis and after induction therapy. **Methods:** This preliminary study included 13 participants diagnosed with new AML. Peripheral blood samples were collected at diagnosis and at day 21 after initiation of induction therapy. The lymphocytes' subsets were analyzed using the FACS Canto II™ flow cytometer and the Infinicyt™ software. **Results:** The median percentage of T lymphocyte after induction (25.76%) was higher than at diagnosis (10.86%). The median CD4/CD8 ratio was also increased after induction (1.87) compared to the diagnosis (1.37). On the other hand, the median percentage of B lymphocytes and NK cells, respectively, was higher at diagnosis (1.66% and 2.40%) compared to the end of induction therapy (0.09% and 1.17%). **Discussion:** The cell-mediated immune response plays a key role in fighting neoplasms. The infiltration of lymphocytes with in the tumor microenvironment has been associated with a better prognosis and therapeutic response. In this study, the increased amount of T lymphocytes at the end of induction highlights its importance in the anti-leukemic response. According to Park et al. (2018), an increase of NK cells (≥5%) in the blood is associated with an improved survival, as patients with a low percentage of NK cells also tend to have higher rates of relapse. A decrease in the number of B lymphocytes was also observed. This subtype of cells may reflect the overall health of the bone marrow, and it is associated with better prognosis as well. **Conclusion:** In AML, the distribution of lymphocyte subsets differs at diagnosis and after induction therapy. These partial findings, in association with other immunological, clinical factors and additional molecular characteristics, may contribute to a better understanding and in the role of the immune system in the progression and clinical outcome of patients with this hematological neoplasm.

Keywords: Acute Myeloid Leukemia, Lymphocyte, Induction Therapy

Support: CAPES

MODULATORY EFFECTS OF MAGNETIC STIMULATION IN ASTROCYTES: A NEUROINFLAMMATORY STUDY

ANA ELISA DEL'ARCO^{1, 2, 3}; SILVIA LIMA COSTA³, DEIVISSON SILVA ARGOLO^{1, 3}; GIZELLE ALVES PINA³; MARIA DE FÁTIMA DIAS COSTA³; ALEXANDRE MORAES PINHEIRO²

¹Postgraduate Program in Immunology, Federal University of Bahia; ²Biochemistry and Immunology Laboratory, Federal University of Recôncavo of Bahia; ³Neurochemistry Laboratory, Federal University of Bahia

Introduction: Magnetic stimulation (MS) is a technique based on electromagnetic theory and has been studied to treat psychiatric and neurologic disorders and to assess the cognitive function of nervous system. Many researches have been produced to achieve this knowledge, but few works were developed to know the cellular effect in inflammation of central nervous system. **Objectives:** The aim of this study was to investigate the role of magnetic stimulation in a neuroinflammation model in astrocytes. **Material and Methods:** Astrocytes were obtained from the cortex of newborn rats (<48 h) and the culture was maintained in supplemented DMEM (Dulbecco's modified Eagle's medium). After 10 days, the microglial cells were removed and astrocytes were plated in 24 wells plates. Cultures were treated with 1 µg/mL of LPS diluted in culture medium. Cultures without LPS were maintained as control. After 6 hours of treatment, MS treatment was performed in the cultures in room temperature with intensity of 0, 62T, at 10 Hz for 30s with repetitive pulse. This procedure was repeated once a day for 3 days and plates without MS treatment were used as control. Cytotoxicity was determined using MTT and nitric oxide (NO) tests, and the cells were photographed in contrast phase microscope. **Results and Discussion:** The MTT results shown MS groups with lower viability: less 5, 46% in astrocytes plus MS, and less 13, 44% in LPS plus MS group. The production

of NO ($\mu\text{g} / \mu\text{g}$ of protein) was 5, 98 x10⁻⁵ in the control (astrocytes only), 4, 94x10⁻⁴astrocyte plus MS, 1, 54x10⁻²toLPS and 9, 2x10⁻³to LPS plus MS. The difference was statistically significant between the groups: astrocyte and LPS with their respectively MS group. Studies of the cultures images suggest a decrease in gliosis in LPS group after magnetic stimulation treatment. **Conclusion:** MS reduces nitric oxid production and gliosis in astrocyte inflammation model. The reduction of viability could suggest a decrease of immune activated cells, controlling the inflammation. **Keywords:** MTT, nitric oxid, repetitive magnetic stimulation. **Financial Support:** CAPES, FAPESB, CNPq, INCT.

NANOVACIN DEVELOPMENT USING RECOMBINANT PROTEINS OF *CORYNEBACTERIUM PSEUDOTUBERCULOSIS* LINKED TO POLYMERIC NANOPARTICLES

Vitor Cordeiro Pereira, Natália da Rocha Lopes, Luan Moreira Santana, Vagner de Oliveira Machado,
Marcos Borges Ribeiro, Roberto Meyer, Silvana Beutingier Marchioro

Postgraduate Program in Immunology, Federal University of Bahia; Immunology and Molecular Biology Laboratory,
Federal University of Bahia

Introduction: Caseous lymphadenitis (CLA) is a contagious infectious disease caused by *Coryne bacterium pseudo tuberculosis*. This disease leads to impacts in Brazilian agribusiness and, indirectly, public health. It is characterized by chronic clinical signs such as suppurative abscesses in subcutaneous tissue, lymph nodes and vital organs. The control of the disease by means of vaccines is fundamental, but this control is affected by limitations of protection of the current vaccines, which motivate the development and production of efficient vaccines and with a higher degree of protection. Objective: To evaluate the immune protective capacity of recombinant antigens (NanH and PknG) of *C. pseudo tuberculosis* linked to polymeric nanoparticles of tri-methylene carbonic polyacetic acid (PLDLA-co-TMC/Twenn 80). **Method:** Synthetic version of genes encoding proteins of *C. pseudo tuberculosis*, with optimized codons for expression in heterologous systems and cloned into *Escherichia coli* vector for the production of the proteins. Nano vaccines formulations will be synthesized via interfacial deposition with changes in the organic/aqueous phase and characterized in terms of their size, stability and surface load. BALB/C mice will be grouped in seven experimental groups to evaluate the immunogenic potential of nanovaccines. **Expected results:** We intend to find significant results in the immune protection with the nanovaccines against *C. pseudo tuberculosis*. Indirect ELISA analyzes will evaluate the production of specific IgM and IgG antibodies against vaccine antigens in the immunized groups. Levels of gamma interferon and cytokines will quantify in each experimental group to determine the profile of immune response induced by the nanovaccines.

Keywords: Caseous lymphadenitis, reverse vaccinology, nanovaccines

Support: Labimuno/ICS/UFBa, Fapex, Capes

NICOTINE INHIBITS AMINOCHROME-INDUCED *IN VITRO* CYTOTOXICITY: PERSPECTIVES FOR APPLICATION IN PARKINSON'S DISEASE

Érica Novaes Soares¹; Ana Carla Costa¹; Cleonice Creusa dos Santos¹; Maria de Fátima Dias Costa¹; Yussef Tsabl²;
Silvia Lima Costa¹; Victor Diogenes Amaral da Silva¹

¹Laboratory of Neurochemistry and Cell Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil. ²Department of Pharmacology, Howard University College of Medicine, 520 W Street NW, Washington, DC 20059, USA

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder that affects brain tissue, especially midbrain dopaminergic neurons. The loss of dopaminergic neurons result in low levels of dopamine and motor symptoms such as dyskinesia, muscle stiffness, posture instability and tremors at rest, which appear after years of degenerative processes and can be preceded by non-motor symptoms such as olfactory and mood disorders. Studies have been suggested aminochrome as an endogenous neurotoxin responsible for the dopaminergic neuron degeneration in PD. It is a natural molecule in dopaminergic neurons derived from dopamine oxidation that has been used as inductor of

PD study model. On the other hand, studies have been demonstrated that nicotine protects neuronal cells against aminochrome-toxicity. **Objective:** The aim of this study was to evaluate the effect of nicotine on neuroprotection and glial cell response in *in vitro* model of Parkinson's disease induced by aminochrome. **Methodology:** Primary microglia cultures was obtained from neonatal Wistar rats (0-2 days) cortex and mixed primary cultures was obtained from Wistar rat embryos (15 - 16 days) midbrain as described in the approved protocol CEUA 127A/2017 for animal use in experimental procedure. The mixed primary cultures were treated with 25 μ M aminochrome and/ or 0.01 μ M or 1 μ M nicotine for 48 h. Cell viability was performed by propidium iodide test and cell morphology was analyzed by Rosenfeld's staining. The primary culture of microglia was treated with nicotine at concentrations of 0.01 μ M, 0.1 μ M, 0.5 μ M and 1 μ M and the cell morphology was analyzed by phase contrast. **Results:** It was observed that 25 μ M aminochrome induced cell death in primary cultures, moreover 0.01 μ M and 0.1 μ M nicotine prevents the cell damage induced by aminochrome. It was observed in the microglia culture that the treatment with 0.01 μ M nicotine showing branched morphology. **Conclusion:** We concluded that nicotine is not cytotoxic at 0.01 μ M or 0.1 μ M in primary midbrain culture or microglial culture, moreover it protects cells neural cells against aminochrome cytotoxicity. We suggest that more studies must be performed to characterize the mechanism of nicotine action and its effect in glial cells. At the end of the analysis, we expect characterize the effect of nicotine in glial cells and mechanism involved in its protective effect against aminochrome.

Support: FAPESB, CAPES and CNPQ.

Key-words: Nicotine, aminochrome, midbrain, glial cells.

PERIPHERAL BLOOD CD4⁺ T CELLS PROFILE IN SICKLE CELL DISEASE PATIENTS WITH OSTEONECROSIS

Paula Braga Daltró^{1,2}; Vitor Antonio Fortuna^{1,2}; Roberto José Meyer Nascimento^{1,2}.

¹Post-graduation Program in Immunology, Health Science Institute (ICS), Federal University of Bahia (UFBA), Salvador, Bahia, Brazil; ²Immunology and Molecular Biology Laboratory, ICS, UFBA.

Introduction: Osteonecrosis (ON) is a chronic severe complication in sickle cell disease (SCD) resultant of microcirculatory obstruction by sickled erythrocytes leading to bone infarction. Cytokine and T helper cells (TCD4⁺) play an important role in ON pathophysiology and has been reported to be important in SCD. Cytokine and T helper cells (TCD4⁺) profile from SCD/ON patients peripheral blood (PB) remains a challenge. **Objective:** Here we aimed to assess peripheral blood mononuclear cells (PBMC) TCD4⁺ phenotype from SCD, SCD/ON and non-SCD (nSCD). **Material and Methods:** Peripheral blood (PB) from 9 steady state SCD patients, 15 SCD/ON patients and 19 healthy controls CD4⁺T cells derived from PBMC were analyzed for CD4, CD8, CD45RA, CD45RO surface molecules and Th1/Th2/Th17 (in activated PBMC) phenotype. **Results and Discussion:** We found that PB of SCD patients with or without ON presented significantly reduced TCD4⁺, TCD8⁺ and TCD4⁺ naïve cell frequencies [for TCD4⁺ (T helper) and TCD8⁺ (T cytotoxic) co-expressing CD3 marker. Compared with healthy controls, SCD and SCD/ON patients had a significantly lower median distribution of TCD4⁺ Only SCD subjects had significantly lower median effector T cell proportions than control subjects [21.62% (range 4.84-41.26) vs 10.84% (range 4.33-16.08), $p=0.05$]. We also saw an increase in the number of bi-functional IFN- γ ⁺/ IL4⁺ and IL-17⁺/ IL4⁺CD4⁺T cells compared to healthy controls. Co-expression of IL17⁺/IL4⁺ was significantly higher in SCD compared to SCD/ON group ($p=0.0425$). The increase in IL-4 frequency of expression which may suggest a shift in CD4⁺ T cell response, corresponding to a Th2 phenotype. **Conclusion:** Taken together, these data indicate the association of CD4⁺T cells in pathophysiology of osteonecrosis related to sickle cell disease.

Keywords: T helper cells; Osteonecrosis; Sickle cell disease

Support: FAPESB, CAPES, CNPq

POLYMORPHISMS IN *IFI16* GENE ARE ASSOCIATED WITH PERIODONTAL DISEASE IN A POPULATION IN SALVADOR/BA—BRAZIL

Marcia Otto Barrientos^a, Tatiane de Oliveira Teixeira Muniz Carletto^a, Helena M. P. Teixeira^a, Soraya Castro Trindade^a, Álvaro A. S. Cruz^b, Camila A. Figueiredo^a, Ryandos Santos Costa^a

^aBioregulation Department, Immunopharmacology Laboratory of Molecular Biology, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil. ^bProgram of Control of Asthma and Allergic Rhinitis of Bahia (PROAR), Federal University of Bahia, Salvador, Bahia, Brazil.

Introduction: Interferon inducible protein, IFI16, is a protein with 785 amino acids, of quaternary structure, with 3 isoforms that combine to form oligomers. IFI16 has a HIN-200 domain and another pyrine. It is located mainly in the nucleus, being a transcriptional regulator for the activation of NF- κ B activity. One of the functions of this protein is to detect and bind to DNA fragments in the cell cytosol through the HIN-200 domain. Apparently, the presence of cytosolic DNA stimulates the migration of IFI16 from the nucleus to the cytosol to control viral or bacterial invasion, but its route of action is not completely elucidated. The literature shows an association between the gene IFI16 with periodontal disease. This disease characterized by a complex inflammatory process involving pathogenic oral bacteria. **Objective:** The aim of this study is to verify the association of the genetic variants in IFI16 with the presence of periodontal disease. **Methods:** Participating in the Program of Control of Asthma and Allergic Rhinitis of Bahia (ProAR) (n=396), of both sexes, aged ≥ 18 years, were classified for the presence (n=72) or absence (n=324) of periodontitis, according to the criteria of Gomes Filho et al. DNA genotyping used the Infinium Multi-Ethnic Global chip. Statistical analysis used PLINK 1.9 software, logistic regression in three models - additive, dominant and recessive, adjust for smoking habit, age, gender, schooling, obesity, asthma and the main component of sample ancestry, considering the Hardy-Weinberg equilibrium deviation (HWE <0.05) and frequency of the smallest allele (MAF >0.01). **Results and Discussion:** Thers1417805 was associated to severe periodontal disease in the one genetic model evaluated, recessive (OR 3.00, 95%CI 1.05-8.57, p=0.04, p-perm=0.03). IFI16 have role in inflammation and on innate immunity. Their actions are fundamental for homeostasis therefore, variants in the gene for this protein can result in alteration of pathogens, including those affecting the periodontium. **Conclusion:** The genetic variant rs1417805 of the IFI16 is associated with the presence of periodontal disease, in recessive model. It is suggested to increase the statistical power by means of a larger sample to confirm these results.

Keywords: Polymorphism, IFI16, periodontal disease.

Supports: CAPES, UFBA

PRETREATMENT NEUTROPHIL-TO-LYMPHOCYTE RATIO AS PROGNOSTIC PARAMETER FOR SURGICAL RESECTION IN ADVANCED ORAL SQUAMOUS CELL CARCINOMA PATIENTS

Renata Freitas Araujo-Calumby^{1,2}, André Leonardo de Castro Costa³, Anna Beatriz Pereira Simões Alves², Camila da Silva Souza^{1,2}, Daniel Nascimento², Deyse Souza Carvalho da Silva², Geovane de Jesus Santos², Gessualdo Seixas Oliveira Junior², Herval Bruno Moreira dos Santos Filho², Matheus Antônio da Hora Borges², Miguel de Jesus Oliveira Santos², Lucianna Stutz Souza Carneiro de Campos², Vitor Silva de Oliveira², Marcus Antônio de Mello Borba³, Lucas Gomes Silva³, Iguaracyra Araújo³, Rodrigo Tripodi Calumby⁴, Sílvia Lima Costa^{1,2}, Deise Souza Vilas-Bôas^{1,2}

¹Post-Graduate Program in Immunology, Federal University of Bahia (UFBA), Salvador-Bahia, Brazil

²Institute of Health Sciences, UFBA, Salvador-Bahia, Brazil; ³Aristides Maltez Hospital (Liga Baiana Contra o Câncer), Salvador-Bahia, Brazil; ⁴Advanced Data Analysis and Management Laboratory, Department of Exact Sciences, State University of Feira de Santana (UEFS), Feira de Santana-Bahia, Brazil

Introduction: Oral Squamous Cell Carcinoma (OSCC) represents the major oral cavity tumor and presents high aggressiveness and metastatic potential. The use of conventional pretherapeutic assessment of cells and serum markers as adjuvants to improve the clinical management of solid tumors has received increasing attention due to its potential to provide prognostic information, acting as low-cost biomarkers. **Objectives:** To investigate the prognostic value of neutrophils and lymphocytes ratio (NLR), lymphocytes and monocytes ratio (LMR) and platelets and lymphocytes ratio (PLR) in patients who underwent or did not undergo resection surgery in a large cohort of OSCC patients. **Methods:** A total of 433 OSCC patients who were treated between 2008 and 2017 at Department of Head and Neck Surgery of Aristides Maltez Hospital (Salvador, Bahia, Brazil) were enrolled and evaluated retrospectively in this study. **Results and Discussion:** During an average longitudinal follow-up period of circa 30 months, the death event occurred in 52.2% (n = 226) of the cases, death by cancer in 49% (n = 212), locoregional recurrence in 24.5% (n = 106) and metastasis in 13.9% (n = 60). In order to investigate whether NLR, PLR and/or LMR were associated with the clinical outcome of patients with OSCC, univariate and multivariate Cox proportional models were calculated for overall (OS), disease-specific (DSS), locoregional-free (LRF5) and distant recurrence-free survival (DRFS). The univariate analysis identified that both high NLR (≥ 2.1) and PLR (≥ 131.5) or low LMR (< 4.2) were significantly associated with worse OS and DSS ($p < 0.05$) although not associated with LRF5 or DRFS. However, the multivariate analysis showed that only a high NLR presented an independent prognostic value for OS and DSS. Furthermore, patients in advanced stage (III and IV) treated with surgical resection exhibited NLR as a prognostic parameter for OS and DSS. **Conclusions:** The systemic NLR presents potential as predictive factor for survival in OSCC patients and may influence clinical choices in relation to therapeutic interventions for patients with advanced clinical staging.

Keywords: oral cancer, oral squamous cell carcinoma, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio.

Support: CAPES.

POLYMORPHISMS RELATED TO TYPE 2 INNATE LYMPHOID CELLS ARE ASSOCIATED WITH ASTHMA AND ATOPY IN A BRAZILIAN POPULATION

Louise C. de Lima², Álvaro A. Cruz³, Hatilla dos S. Silva², Raísa S. Coelho², Ryan dos S. Costa², Camila A. V. Figueiredo², Vadirene L. Carneiro¹.

¹Department of Life of Sciences, State University of Bahia-Brazil. ²Department of Bioregulation, Laboratory of Immunopharmacology and Molecular Biology, Federal University of Bahia (ICS), Bahia-Brazil. ³Program for the Control of Asthma and Allergic Rhinitis in Bahia (ProAR), Federal University of Bahia (UFBA), Bahia-Brazil.

Introduction: Asthma is a chronic inflammatory disease that impacts the lives of millions of people worldwide. There are several phenotypes and endophenotypes of this pathology, and some are associated with an increase in eosinophils in blood and sputum. This increase may cause greater severity of the disease and studies have shown that this condition may be associated with genes related to type 2 innate lymphoid cells (ILC2). **Objectives:** The purpose of this work is to evaluate the association between polymorphisms in genes related to ILC2 (TSLP, IL25, GATA3 and RORA) with asthma endophenotypes. **Methods:** This is an unconventional case-control study, composed of 364 patients without asthma, 412 patients with mild asthma and 401 patients with severe asthma, over 18 years of age, resident in Salvador-BA and belonging to the Asthma and Rhinitis Control Program Allergic in Bahia (ProAR). Four genes were selected for the study and additive logistic regression models were used for all genes, using the software Plink 1.09. **Results and Discussion:** Eleven SNPs in the studied genes were significantly associated with asthma and atopy variables. rs3806933 and rs11466741 in the TSLP gene demonstrated protective associations with asthma and its severity (OR: 0.79; 95%CI: 0.64–0.96/OR: 0.75; 95%CI: 0.61-0.91). On the other hand, rs263423 and rs263424 in the GATA3 gene, demonstrated risk associations with asthma (OR: 1.29; 95%CI: 1.06-1.57/OR: 1.34; 95%CI: 1.03-1.76) and rs3824662, in the same gene, demonstrated a risk association with atopy (OR: 1.53; 95%CI: 1.03-2.28). rs12899193 in the RORA gene demonstrated a risk association with asthma severity (OR: 1.44; 95%CI: 1.12-1.86), while rs11071557 and rs11071559 of this gene demonstrated protective associations with eosinophilia in asthma (OR: 0.71; CI95%: 0.57-0.89/OR: 0.73; 95% CI: 0.59-0.90). rs10135798, rs1124053 and rs3811178 in the IL25 gene demonstrated risk associations with atopy markers (OR: 2.10; 95% CI: 1.05-4.18/OR: 1.54; 95% CI: 1.04-2.29/OR: 0.66; 95%CI: 0.43-0.99). **Conclusions:** These data demonstrate that variants in the TSLP, IL25, GATA3 and RORA genes cause genetic risk or protection impacts on asthma and its different endophenotypes. However, functional studies are needed to elucidate the mechanisms involved in these results.

Keywords: Phenotypes, Asthma, ILC2, SNPs.

Support: CAPES, CNPq, FAPESB, IMUNOBIO

PROPOSITION OF NATURAL COMPOUNDS AND CHIMERIC PROTEINS FOR NOVEL PROPHYLACTIC METHODS AGAINST *STREPTOCOCCUSEQUI*

Bernardo Mirabal Santos¹; Sarah Pereira Andrade de Souza¹, Igor Batista dos Santos Oliveira¹, Letícia Vivas Carvalho¹, Nubia Seyffert¹; Roberto Meyer¹; Thiago Luiz de Paula Castro¹.

¹Laboratory of Immunology and Molecular Biology - Institute of Health Sciences, Federal University of Bahia, Bahia, Brazil.

Introduction: Equine strangles is a disease that affects the upper respiratory tract, guttural pouch and lymph nodes in horses. The disease is caused by *Streptococcus equi*, a Gram-positive facultative intracellular bacterium. Novel and promising prophylactics are necessary to control strangles dissemination in herds and prevent substantial economic losses worldwide. In the genome era, prospection of therapeutic drugs and vaccine candidates is facilitated by the use of robust bioinformatics approaches. **Objectives:** To prospect natural plant compounds with potential use as drugs against *S. equi* and propose a potentially immunogenic chimeric protein for the development of a vaccine for strangles. **Material and Methods:** Theoretical proteome sequences of 195 *equi* strains were retrieved from the National Center for Biotechnology Information (NCBI) database. Proteins shared by all strains and non-homologous to equine were identified and subjected to prediction of subcellular localization. Cytoplasmatic proteins predicted

to be essential for the bacterium and involved in virulence are being prospected as potential targets for a library of 5, 000 natural plant compounds using AutoDockVina. Proteins likely exposed on the cell surface or secreted to the environment were selected for epitope screening using the IEDB platform. A list of chimeric proteins will be generated using different combinations of epitopes likely recognized by the equine Major Histocompatibility Complex (MHC) I and II. Structural models of these proteins will be predicted using the MHOline platform. Antigenicity, allergenicity, toxicity, physicochemical behaviour, instability, and solubility features will be assessed *in silico*. **Partial and Expected Results:** 247 proteins shared by all 19 *S. equi* strains were found to be not homologous to equine. Out of these, 134 were selected as potential drug targets and are being used for essentiality, virulence involvement and structure prediction. The other 113 proteins were selected as potential vaccine targets. Next, we expect to select natural plant compounds with the best biochemical interactions with the selected protein targets. We also expect to predict the best immunogenic chimeric proteins for future immunization assays against strangles.

Keywords: Equine; Strangles; Bioinformatics; Molecular docking; Natural compounds; Chimeric protein; Subunit vaccine.

Support: CAPES, CNPq, FAPESB.

PROSPECTING FOR *N*-HETEROCYCLIC COMPOUNDS TO CHARACTERIZATION OF ANTIGLIOMA ACTION MECHANISMS IN GLIOBLASTOMA CELLS AND IN INTERACTION WITH MICROGLIA

Jéssika Alves Oliveira Amparo¹, Raimundo Francisco dos Santos Filho², Victor Diógenes Amaral da Silva¹; Silvio do Desterro Cunha², Ravena Pereira do Nascimento¹, Silvia Lima Costa¹

¹Laboratory of Neurochemistry and Cellular Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Bahia, Brazil. ²Research Group in Chemical Synthesis and Molecular Bioactivity, Department of Organic Chemistry, Institute of Chemistry, Federal University of Bahia, Bahia, Brazil.

Introduction: Glioblastoma (GBM) is the most aggressive type of brain tumor that affects the central nervous system (CNS) and present resistance to radiotherapy and chemotherapy, thus remaining with the worst prognosis. Microglia are immuno-effector cells of the CNS, however, they can contribute to the progression of glioma, acquiring immunosuppressive and tumor support properties. In the search for new treatments, enaminone-derived molecules, obtained by organic synthesis using Green Chemistry-based principles, have been proposed as compounds that exert an inhibitory and immunomodulatory potential to glioma cells growth and proliferation. Objective: The aim of this study was to perform a prospection in vitro of the effects of thirty six new enaminone-derived molecules in terms of cytotoxicity and morphological changes of chemoresistant GBM cells, and select best candidates capable to modulate microglial immunosuppressive profile during interaction with GBM cells. Methods: Human GL-15 GBM cells were treated with a panel of 36 enaminone-derived molecules at concentration of 100 μ M or kept in control conditions (0.1% DMSO). The cell viability and morphology were evaluated after 24 and 72 h of treatment by MTT assay and by phase-contrast microscopy. The molecules that followed in the next test met the criteria for stronger effect on cell viability, induction of morphological alterations, efficiency on synthesis and absence of precipitation in organic solvents. Four molecules were selected and tested in GL-15 and C6 GBM cells and also normal glial cells at concentrations of 1, 10, 50 and 100 μ M or kept in control conditions. After selecting the most promising molecule, the proliferation and phenotypic profile of microglia will be evaluated, as well as the profile of inflammatory and anti-inflammatory cytokines secreted in microglia/glioma co-cultures. Results and **Conclusions:** The compounds RRF-D468, RRF-D542 and RRF-D610 induced concentration dependent reduction on viability of glioma cells and morphological changes since 24 h after treatments. However, only the compound RRF-D610 presented selective cytotoxic and morphogenic activity against highly proliferating glioma cells, not affecting the viability of normal glial cells, putting in perspective further studies to investigate immunomodulatory effects during microglia/glioma interactions, to better characterize possible application for GBM adjuvant therapy.

Keywords: Glioma, microglia, nitrogenous heterocyclic compounds, enaminone, cytotoxicity.

Support: CNPq (Proc. 443723/2014-1, partially); INCT - Nacional Institute for Translational Neuroscience and INCT for Excitotoxicity and Neuroprotection (MCTI/CNPq); FAPESB(MPhil fellowship).

Protective and profibrotic cytokines mediated by CD4⁺ T lymphocytes in periportal fibrosis secondary to schistosomiasis

Jordana Batista Santana^{a,b}; Tarcísio Vila Verde S. de Almeida^{a,b}; Diego Mota Lopes^{a,b}; Luís Eduardo Ribeiro^{a,b}; Néstor A. Guerrero Gutierrez^{a,b}; Edgar M. Carvalho^{b,d}; Luciana Santos Cardoso^{a,b,c}.

^aPrograma de Pós-Graduação em Imunologia, Instituto de Ciências da Saúde (ICS), Universidade Federal da Bahia (UFBA), Salvador, Bahia, Brasil; ^bServiço de Imunologia, Hospital Universitário Professor Edgard Santos, HUPES/UFBA, Salvador, Bahia, Brasil; ^cDepartamento de Análises clínicas e Toxicológicas, Faculdade de Farmácia, UFBA, Bahia, Brasil; ^dInstituto Gonçalo Moniz, Fundação Oswaldo Cruz, Salvador-BA, Brasil^d

Introduction: Schistosomiasis is a parasitic disease that affects about 229 million people around the world. During the chronic phase of the disease, fibrosis periportal can occur, which associated with a predominantly Th2 type of immune response. Evidences also suggests that Th1 and Th17 lymphocytes are involved in the development of the disease. **Objectives:** To evaluate the profile of cytokines produced by TCD4⁺ lymphocytes, and the correlations between these cytokines with wall measurement and diameter of the portal vein. **Material and Methods:** A total of 29 individuals living in the endemic area for schistosomiasis, classified according degree of periportal fibrosis were recruited. Lymphocytes were obtained by separation of PBMCs and analyses of surface markers and cytokines were performed by flow cytometry. **Results and Discussion:** We observed an increase in Th2 cytokines IL-4, IL-5, IL-13, and the regulatory cytokine IL-10 in the group with periportal fibrosis when compared to the group without fibrosis or advanced fibrosis. In addition, we observed that all groups of individuals who had some degree of periportal fibrosis present higher frequency of TGF-β⁺CD4⁺ T lymphocytes, compared with those without fibrosis. Analyzing of the ultrasonography parameters individually we found a significant correlation between the frequency of TGF-β⁺ CD4⁺ T lymphocytes and the measurement of the left lobe and the portal vein wall thickness. We also studied the presence of CD4⁺ IL17A⁺ lymphocytes that show an increase in the frequency, however we found a negative correlation with the portal vein wall thickness. **Conclusions:** CD4⁺ T lymphocytes from the group with periportal fibrosis have an increase in the expression of pro-fibrotic cytokines, while higher levels of IL-10, seem to be able to maintain low morbidity in this group. Additionally, the correlation data provide indirect evidence for the role of TGF-β and IL-17A and their association with severe forms of schistosomiasis.

Keywords: Schistosoma mansoni, Periportal fibrosis, CD4⁺ T lymphocytes.

Support: FAPESB

QUANTIFICATION AND COMPREHENSIVE ANALYSIS OF MESENCHYMAL STROMAL CELLS IN BONE MARROW SAMPLES FROM SICKLE CELL DISEASE PATIENTS WITH OSTEONECROSIS

Tiago Oliveira Ribeiro^{1,2}; Songeli Menezes Freire^{1,2}; Vitor Antonio Fortuna^{1,2}.

¹Graduate Program in Immunology, Health Sciences Institute, Federal University of Bahia (UFBA); ²Laboratory of Immunology and Molecular Biology, UFBA, Salvador, Bahia, Brazil.

Introduction: Osteonecrosis (ON) is a frequent complication of sickle cell disease (SCD) and the implantation of bone marrow mesenchymal stromal cells (BM-MSCs) is currently performed to treat early stages of ON. The efficacy of this therapy depends on the quantity of BM-MSCs to induce bone regeneration. CD271 is a cell surface marker that potentially defines a subpopulation of MSC precursors with osteogenic potential. Colony-forming unit assay (CFU) is the conventional method for the quantification of MSC in vitro. Therefore, convenient BM-MSC quantification is a critical factor for cell therapy efficacy. **Objectives:** The objective of this study was to quantify the MSC population in bone marrow aspirate (BMA) and bone marrow mononuclear cell (BMMC) from SCD patients with osteonecrosis (SCD group) and patients with osteoarticular complications not related to SCD (NS group), using flow cytometry for

CD271+CD45^{low} cell phenotype and CFU-F assay. **Materials and Methods:** ICS/UFBA ethics committee approved this study [registration number 11738, SIPAR/MS: 25000.039812/2005–99]. 15 ml of BM aspirate was obtained from 22 patients. Bone marrow mononuclear cells (BMMC) were isolated on a Ficoll density gradient. Immunostaining for CD271+CD45^{low} cells and CFU assay were performed to detect and quantify MSC in BM samples. **Results and Discussion:** The mean total cell number (96.7 ± 53.4 vs 34.8 ± 15.3 cells $\times 10^3$ cells/ μ L, $p < 0.001$) and CFU-F count (1390 [range 15.70 – 7050] vs 42.9 [range 12.10 – 73.80]) in BMMC were significantly higher in SCD than NS patients, respectively. A significant correlation between CD271+CD45^{low} cell number and CFU-F counts was found in SCD ($r = 0.7483$, $p = 0.0070$) and NS ($r = 0.7167$, $p = 0.0370$) BMMC. An age-related quantitative reduction of CFU-F counts and CD271+CD45^{low} cell number was noted. **Conclusion:** We observed that BM samples from patients with SCD-ON have a higher frequency of stromal progenitor cells in BMA and BMMC than samples from NS patients. The CD271+CD45^{low} cell counts showed a positive correlation with the number of CFU-Fs in SCD samples. Thus, this work provides important data for the quick measurement of putative BM-MSCs in **Support** to advanced cell-based therapies for SCD patients with osteonecrosis.

Keywords: bone marrow aspirate, mesenchymal stromal cells, osteonecrosis.

Support: Capes, CNPq.

REVERSE VACCINOLOGY IN MURINE MODEL AND CANINE FOR THE CONTROL OF TOXOCARACANIS INFECTION

DUMAR ALEXANDER JARAMILLO HERNÁNDEZ^{1, 2*}; LUIS FABIÁN SALAZAR GARCÉS¹; CARINA SILVA PINHEIRO¹; NEUZA MARIA ALCANTARA-NEVES¹.

1-Institute of Health Sciences (ICS), Federal University of Bahia (UFBA), Salvador, Brazil; 2- College of Animal Sciences, Faculty of Agricultural Sciences and Natural Resources, University of the Llanos, Villavicencio, Colombia;

*Postgraduate Program in Immunology, ICS, UFBA, Salvador, Brazil.

Introduction: toxocaríasis is a zoonosis of global importance, and has recently been named one of the five most neglected parasitic infections in the USA by the CDC. **Objective:** this research applies the methodology of reverse vaccinology in the murine model and canine with the aim of contributing to the control of toxocaríasis in canines through immunoprophylaxis. **Materials and methods:** preclinical studies determined that two recombinant proteins *T. canis* (rTcVcan and rTcCad) provided significant levels of protection against larval migration in the murine model. These proteins along with three adjuvants (Alhydrogel[®] Th2 profile, PAM3CSK4[®] Th1 profile and Quil-A[®] Th1/Th2 profile) were used for immunization protocol in a murine model of toxocaríasis (112 C57black mice); three blood samples were collected at different times of the experiment to measure through indirect ELISA IgA, IgE, IgG (total, IgG1, IgG2a); at the end of the experiment, splenocytes were cultured to measure cytokines (IL-5, TNF- α and IL-10) in the supernatant, and *T. canis* larvae were quantified in tissues. The best protein+adjuvant pair found in the mice experiment (rTVcan+QuilA[®]) was used to immunize 24 neonatal canines free-*T. canis* experimentally infected with *T. canis*. In this first clinical phase study of the toxocaríasis vaccine, immunoglobulin curves (IgA, IgE, IgG, IgG1 and IgG2), parasite load (eggs in feces) and cytokines of PBMC cultures (IL-4, IL-10, IL-17A and INF γ) were measured through RT-PCR. **Results and Discussion:** rTVcan+QuilA[®] presented a highly significant reduction ($p < 0.0001$) of larvae in brain, with a mixed cytokine profile (Th1/Th2) and important anti-*T. canis* antibody titers (IgG, IgG1, IgG2a) in the murine model. In canines it presented a significant reduction in the parasite load ($p < 0.05$) according to the accumulated count of eggs in feces, as well as a significant reduction in adults excreted in feces. The mixed response of Th1/Th2 cytokines with an adequate level of antibodies (IgG) promoted significant protection of mice and canines against toxocaríasis under controlled laboratory conditions. **Conclusions:** this is the first clinical study in the world of a vaccine with recombinant *T. canis* proteins. A vaccine that has shown promising results in the control of canine toxocaríasis, where the field of public health and the control of human toxocaríasis will surely be positively impacted.

Keywords: Human toxocaríasis, immunoprophylaxis, vaccine, zoonosis.

Support: RENORBIO/CNPq grant and extension resource of the Laboratory of Allergy and Acarology of ICS - UFBA.

RUTIN INHIBITS GLIAL ACTIVATION AND PROTECTS DOPAMINERGIC NEURONS AGAINST 6-OHDA AND AMINOCHROME CYTOTOXICITY IN ANIMAL MODEL.

ARAÚJO, F.M.^{1,2}; FROTA, A.F.²; JESUS, L.B.^{1,2}; MACEDO, T.C.²; SANCHEZ-RODRIGO C.³; MENDES, K.M.F.³; CUENCA L.³; SEGURA-AGUILAR, J.³; COSTA, S.L.^{1,2}; HERRERO, MT; SILVA, V.D.A.^{1,2}.

¹Postgraduate Program in Immunology, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil. ²Laboratory of Neurochemistry and Cell Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil. ³Clinical & Experimental Neuroscience, Department of Human Anatomy & Psychobiology, Institute for Biomedical Research of Murcia (IMIB), School of Medicine, Campus Mare Nostrum, University of Murcia, Murcia Spain

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder marked primarily by motor symptoms such as rigidity, bradykinesia, postural instability and resting tremor associated with dopaminergic neuronal loss in the Substantia Nigra pars compacta (SNpc) and deficit of dopamine in the basal ganglia, however the mechanisms responsible for the neurodegeneration remain unknown. Studies have been suggested aminochrome as an endogenous neurotoxin responsible for the dopaminergic neuron degeneration. The aim of this study was to determine glial reactivity induced by aminochrome in an *in vivo* model of PD and to explore the protective action of flavonoid rutin.

Methods and Results: Experimental procedures were sanctioned by the local animal research ethics committee (protocol CEUA –ICS-UFBA- n°. 011/ 2017). Wistar rats (male, 250-270g) were divided in 6 groups (**1:** saline control, **2:** rutin 10 mg/ kg, **3:** 6-hydroxydopamine 1370, 9 µM **4:** aminochrome 1, 000 µM; **5:** 6-hydroxydopamine (6-OHDA) + rutin and **6:** aminochrome + rutin). The animals were orally dosed with rutin 30 minutes before the stereotaxic injection of aminochrome or 6-OHDA in the striatum and daily orally treated with rutin until the 14th experimental day. After euthanasia, the brains were fixed in 4% PFA, slices were performed in microtome and immunohistochemical analyzes was performed for IBA-1, CD68, GFAP, S100β and Tyrosine hydroxylase (TH) in the striatum and SNpc. We observed that the aminochrome and 6-OHDA were able to generate increase in the total number of microglia, as well as to increase the quantity of activated microglia evidenced by co-localized IBA-1⁺/ CD68⁺ cells. It was also observed that astrocyte activation marked by an increase of co-localized GFAP⁺/ S100β⁺ expression. Dopaminergic neuronal (TH⁺ cells) loss was also observed in the aminochrome or 6-OHDA-treated groups. On the other hand, rutin presented neuroprotective effect by inhibition effects of aminochrome or 6-OHDA in terms of microglial activation, astrogliosis and dopaminergic neuronal loss. **Conclusion:** rutin inhibits glial activation and protects dopaminergic neurons against 6-OHDA and aminochrome cytotoxicity. This is the first evidence of glial response in an *in vivo* model of PD induced by aminochrome. These results improve a new animal model, suggested as a more physiological model of PD and contribute to a development of a new therapeutic agent against neurodegeneration.

Palavras-chave: Parkinson's disease, dopamine, neuroprotection flavonoid.

Support: FAPESB, CAPES, CNPQ and INCT

SCREENING OF MACHINE LEARNING ALGORITHMS FOR THE PREDICTION OF ASTHMA USING GENETIC MARKERS

Luciano Gama da Silva Gomes; Camila Alexandrina Figueiredo; Álvaro Augusto Souza da Cruz Filho; Ryan dos Santos Costa

Institute of Health Science of Federal University of Bahia - UFBA. Salvador/Bahia. Brazil.

Introduction: Asthma is a very heterogeneous chronic inflammatory airway disease. Several genetic variants associated with asthma have been documented in studies of GWAS, but the agreement among studies can be difficult due to the ethnic differences of populations and the complexity of the disease heterogeneity. Advanced artificial intelligence studies are the key to try to decipher patterns for complex decision making. In this sense, machine learning algorithms are useful tools for predicting complex diseases. **Objectives:** This study aims to scan some machine learning algorithms to predict asthma and non-asthma and discuss their particularities. **Material and Methods:** This work is a pilot study in which we used genetic data from subsamples (RORA gene) from a larger genetic bank, which comprises 535 genotyped SNPs (Illumina Multi-Ethnic AMR / AFR Kit BeadChip) of individuals

admitted to the ProAR. All data processing and results generation was performed by R. The tested algorithms were the Naive Bayes classifier and the decision tree: C5.0, 1R, and RIPPER. **Results and Discussion:** Naive Bayes algorithm presented low accuracy of its test prediction (58.50%) when we used all genetic markers. In this sense, the search for more informative markers for prediction is adequate. The C5.0 algorithm showed 97.8% training accuracy, however, its test accuracy drops to 60.89%. At this point, C5.0 signals the main markers used for decision-making. The 1R algorithm returns only one marker that it considers the best to classify the outcome. Because of this, serial analyzes were performed, and from the second onwards the SNP indicated in the previous analysis was previously removed. Of these results, three SNPs shared the findings by C5.0: rs1550225, rs140827468, and rs72750685. There were no similarities in decision-making between sequential 1R analysis and RIPPER. We returned to the analysis with Naive Bayes, however, using only the three SNPs taken together. We observed that the accuracy of the prediction was 73.13%. **Conclusion:** Algorithms work differently, but they can jointly signal genetic markers that can become the focus of other studies.

Keyword: asthma, Machine Learning, prediction, SNP

Support: CNPq.

SEROPREVALENCE OF CASEOUS LYMPHADENITIS IN SMALL RUMINANTS AT SLAUGHTERHOUSE FROM THE STATE OF BAHIA.

Caio Lopes Borges Andrade^{1,2}, Ramon Mendes dos Santos^{1,2}, Rogério Reis Conceição^{1,2}, Hévlyn Ribeiro de Araújo^{1,3}, Maria Isabel Cerqueira^{1,3}, Marcos Borges Ribeiro¹, Roberto José Meyer Nascimento¹, Songeli Menezes Freire^{1,4}

¹Laboratório de Imunologia e Biologia Molecular (LABIMUNO), Instituto de Ciências da Saúde, Universidade Federal da Bahia; ²Programa de Pós Graduação em Imunologia.

Introduction: *Corynebacterium pseudotuberculosis* is a gram-positive pleomorphic bacillus, macrophage facultative intracellular pathogen, which commonly affects ruminants, being responsible for Caseous Lymphadenitis (LC) in goats and sheep. This disease with an endemic character, is widespread in herds throughout Brazil and causes economic losses for producers. Animal diagnosis is relatively simple. However, the treatment and control of LC has low effectiveness. Bacteriological culture from the caseous content, followed by biochemical tests is currently the gold standard. According to data from the Instituto Brasileiro de Geografia e Estatística (IBGE), more than 90% of goat population and 60% of sheep population in Brazil are concentrated in the Northeast region, with emphasis on Bahia and Pernambuco, these herds are mainly intended for the production of meat and leather. As they receive herds from different regions of the state, slaughterhouses represent a crucial point for assessing large contingents from different properties. **Objectives:** Identify the degree of contamination of slaughtered sheep and goats in the state of Bahia. **Methods:** Information on the origin and characteristics of the animals will be recorded during their arrival at the slaughterhouse and before sample collection. With the help of the slaughterhouse staff, samples of blood and necropsy of lymph nodes with alterations will be collected from goats and sheep in the slaughter line. Serum from blood samples will be recovered and an ELISA performed to identify individuals with antibodies to *C. pseudotuberculosis* antigens. Samples with results very close to the cutoff will be confirmed by *Western Blotting*. From the altered lymph nodes, bacterial isolation and identification of possible strains of *C. pseudotuberculosis* will be performed. Generated data will be cataloged and analyzed statistically using Microsoft Excel and Prism-GraphPad. **Expected Results:** Describe the distribution and geographic density of *C. pseudotuberculosis* in the state of Bahia, obtaining a better understanding of the distribution of LC in goat and sheep herds slaughtered in Bahia.

Keywords: *Corynebacterium pseudotuberculosis*, Caseous Lymphadenitis, Slaughterhouses

Support: Universidade Federal da Bahia (UFBA), Laboratório de Imunologia e Biologia Molecular (Labimuno-UFBA), Fundação de Apoio à Pesquisa e à Extensão (FAPEX), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Agência de Defesa Agropecuária da Bahia (ADAB), Ministério da Agricultura Pecuária e Abastecimento da Bahia (MAPA-BA).

SKELETAL MUSCLE INJURY INDUCED BY BOTHROPSLEUCURUS VENON AND TISSUE REPAIR: INFLAMMATORY PROFILE AND MECHANISMS INVOLVED

Clara Macêdo Mimoso¹, Kaenna Baraúna Campos¹, Simone Garcia Macambira^{1,2,3}, Luciana Lyra Casais-e-Silva^{1,4}

¹Programa de Pós Graduação em Imunologia – Instituto de Ciências da Saúde/Universidade Federal da Bahia. ²Departamento de Bioquímica e Biofísica - Instituto de Ciências da Saúde/Universidade Federal da Bahia. ³Laboratório de Engenharia Tecidual e Imunofarmacologia – Instituto Gonçalo Moniz/FIOCRUZ/Bahia. ⁴Departamento de Biorregulação, Laboratório de Neurolimnocrinologia e Toxinologia (LABNIET) – Instituto de Ciências da Saúde/Universidade Federal da Bahia

Introduction: Snakebite envenoming is an important public health problem in tropical regions of the world, due to the number of people affected and the risk of morbidity and mortality. In Brazil, about 90% of snake accidents are caused by Bothrops genus, which envenoming is characterized by systemic alterations (i.e. coagulation disorders, hemorrhage and nephrotoxicity, the main cause of death) and local damage (i.e. persistent inflammation, tissue damage and myonecrosis). In Bahia, Bothrops leucurus species is the main etiological agent. Although antivenom serotherapy is effective in neutralizing systemic effects, the local effects are poorly neutralized, causing irreversible tissue damage. **Objectives:** Characterize the tissue injury evolution and repair development after venom inoculation in skeletal muscle, determining (i) process time course, (ii) tissue functional and structural impairment and (iii) inflammatory mediators involved in tissue lesion and repair. **Methods:** Swiss mice will be inoculated into the gastrocnemius muscle with 50 µg/mL of the total venom. Muscle damage will be assessed by measuring serum creatine kinase at different experimental times (3 and 6 h, 1, 3, 7, 14 and 28 days). Before the inoculation of the venom and during the experimental times, the animals will be submitted to treadmill test and euthanized for histological analysis of the gastrocnemius muscle. The total and differential leukocyte count will be performed using Neubauer's chamber and specific staining, respectively. Muscle fibers will be quantified in the cryopreserved muscle, by immunofluorescence analysis, and the measurement of cytokines will be performed in the serum by ELISA technique. **Results and Discussion:** The results of this research will expand knowledge about the inflammatory response to venom that leads to tissue injury and repair, through immunomodulatory mechanisms characterization, improving the regionalized studies for this species. **Conclusions:** These studies will contribute to elucidate the pathogenesis of inflammation and local necrosis triggered by this venom, in addition to providing information for the development of therapeutic strategies in the management of local injuries due to poisonous snake bites, acting as an adjunct to antivenom serotherapy.

Keywords: Venom; Bothrops; Myotoxicity; Inflammation.

Support: FAPESB.

STUDY OF GLIAL RESPONSE IN A NEW *IN VITRO* MODEL OF CEREBELLAR CELL CULTURE

Santana, L. F., Santos, C. C., Ferreira, R. S., Almeida, A. M. A. N., De Castro, M. V. L., Franchi, M. S., Andrade, G. B., Da Silva, T. M., Costa, S. L* and Silva, V. D. A*

¹Laboratory of Neurochemistry and Cell Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil. ²Postgraduate Program in Immunology, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil.

Introduction: Communication between glial cells and neurons modulate the pattern of neuroinflammatory response. Astrocytes and microglia, are immuno-effector cells in the Central Nervous System (CNS), when they suffer insult they become activated and add neuroprotective or neurotoxic response profiles of type A1-A2 / M1-M2. **Objectives:** In this study, we evaluated the pattern of glial response after inflammatory induction with LPS in a new model of primary cerebellar cell culture. **Methods:** We used primary cerebellar culture, grown in a medium supplemented with growth factors B27, bFGF, Insulin, PDGF-AA and factors released in the conditioned medium, later exposed to LPS and neuron integrity analyzes by staining with Fluoro Jade B (FJB) and immunocytochemistry for β-TubIII neurons, GFAP astrocytes and Iba1 microglia markers. **Results and Discussion:** It was observed that LPS induced neurodegeneration characterized by an increase in FJB⁺ cells and loss of β-TubIII expression, activation of the glial response by increasing the percentage of GFAP⁺ and Iba1⁺ cells, as well as morphological changes. **Conclusions:** Thus, we suggest the new

study model as a useful tool to study neurodegenerative diseases associated with neuroinflammation, since we characterize an evident glial response to the inflammatory stimulus induced by LPS and evident neuronal loss.

Keywords: Neuroinflammation, invitrostudymodel, glia, cerebellum.

Support: FAPESB, CAPES, CNPq.

STUDY OF THE FLAVONOID RUTIN EFFECT ON ANTI-INFLAMMATORY AND ANTIVIRAL RESPONSES IN DIFFERENT BRAIN REGIONS DURING DEVELOPMENT.

Rosiméire Oliveira Torres¹, Silvia Lima Costa and¹ Clarissa de Sampaio Schitine¹

¹Laboratory of Neurochemistry and Cell Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil.

Introduction: Neurogenesis is a constitutive process that occurs in two main regions: the subventricular zone (SVZ) of the lateral ventricle and the subgranular zone (SGZ) of the hippocampal dentate gyrus (DG). The subventricular zone (SVZ) generates neurons that migrate through the rostral migratory current (RMS) to the olfactory bulb (OB) to act as interneurons. Anomalies in the processes of cell proliferation, migration and differentiation may be involved with the emergence of neurodegenerative diseases. In addition, the recent coronavirus pandemic outbreak (COVID-19) poses an important and urgent threat to global health. In addition to the systemic symptoms caused by COVID19, many patients develop severe neurological symptoms. And how the long-term consequences of neurological damage of an inflammatory nature contributes to the development of neurodegenerative diseases are largely unknown. Flavonoids are polyphenolic compounds that can reduce inflammation, promote cognition prevent cancer and promote antiviraleffects. The flavonoid rutin participates in the activation of cascades of neuroprotection and differentiation, and has functions in the regulation of cell proliferation and differentiation events in models of neurogenic niches, being possible pro-cognitive candidates and potential therapeutic agents for oxidative and neurodegenerative processes. In addition, it has antiviral effects, so rutin is a strong candidate for prospecting antiviral drugs including the new coronavirus. **Objectives:** To evaluate the effect of f rutin on cell proliferation, differentiation, and its influence on astrocytic and microglial reactivity, cell viability, using specific markers, and measuring inflammatory response indicators in control, under excitotoxicity stimulation, and preclinical models of SARS- CoV-2 infection. **Material and Methods:** Our study model involves cell cultures from different brain regions (cortex, SVZ, and hippocampus), prepared from C57BL / 6 mice. The cultures will be carried out at different developmental stages embryonic, postnatal, and adult animals. Expected results: characterization of the rutin functions on cell proliferation and differentiation in culture models of SVZ, cortex, and organotypic cultures of the hippocampus at different stages of development and its anti-inflammatory, antioxidant mechanisms, as well as its possible antiviral activity for clinical strategy proposals against different neuropathologies including SARS-CoV-2 infection. **Keywords:** Neurogenesis; rutin; SARS-CoV-2. **Support:** Capes.

STUDY OF THE MOLECULAR MECHANISMS ASSOCIATED WITH ANTIGLIOMA AND IMMUNOMODULATORY EFFECTS OF FLAVONOIDS RELATED TO INTERACTION WITH AHR

Monique Reis de Santana¹, Ravena Pereira do Nascimento¹, David Gilot², Silvia Lima Costa¹

¹Programa de Pós-Graduação em Imunologia, Instituto de Ciências e Saúde (ICS), Laboratório de Neuroquímica e Biologia Celular, Universidade Federal da Bahia (UFBA), Bahia, Brazil; ²NSERM U1242, Université Rennes 1, France.

Introduction: Glioblastoma (GBM) is the most common and aggressive neoplasm in the primary brain tumor, presenting high cell proliferation, with infiltrative and invasive characteristics, that favors these tumor to have a great recurrence after treatment. Many mechanisms potentially involved in the tumor recurrence have been described, and between them the BRAF-V600E mutations have been associated to tumorigenesis and most commonly found in brain tumors such as GBM. Recently, BRAF mutation was identified as a marker for a small subset of infiltrating gliomas in adults and appears to be related to chemo and immunoresistance. Moreover, a study demonstrated that

the transcription factor arylhydrocarbon receptor (AhR) is constitutively activated in tumor cells, promoting the differentiation of melanoma cells and increased expression of BRAF I resistance genes, putting AhR antagonism as a target in cancer chemotherapy. The anti-tumor potential of flavonoids and the anti-inflammatory activity in human glioma cells has been investigated and the pharmacological potential of these drugs have encouraged studies in alternative therapy for malignant gliomas. **Objectives:** This study aims to better define the antitumor mechanisms of flavonoids and association of its antiglioma activity with the capacity to acts as AhRantagonists. **Material and Methods:** Natural flavonoids, whose anti-glioma effects have already been demonstrated, will be tested as ligands of AhR, and the more actives in AhR selectivity will be chose to investigate effects during microglia/GBMcells interaction by using methodological approaches in the field of cell and molecular biology, based on cell culture models. **Expected Results:** The characterization of the molecular mechanisms of flavonoids is expected at the end of this study, featuring a possible antagonistic effect on AhR and its role in chemosensitivity, to sustain their application as adjuvant for GBM treatments.

Keywords: glioma; flavonoids; AhR, immunomodulation; microglia

Support: CAPES, CNPq e FAPESB

STUDY OF VARIANTS IN THE IL17 GENE IN DIFFERENT PEDIATRIC ASTHMA ENDOPHENOTYPES, INCLUDING GLUCOCORTICOID RESISTANT ASTHMA.

Saulo Ferreira de Assis, Laura Maria de Lima, Belizario Facury Lasmar, Ryan dos Santos Costa.

Departamento de Biorregulação, Laboratório de Imunofarmacologia e Biologia Molecular (IMUNOBIO) – Instituto de Ciências da Saúde da Universidade Federal da Bahia (ICS/UFBA). Centro Multidisciplinar de Asma de Difícil Controle (CEMAD) da Universidade Federal de Minas Gerais (UFMG).

Introduction: Asthma is a chronic disease that presents heterogeneity in clinical and functional aspects, being characterized by inflammation of the lower airways whose development depends on the interaction between environmental and genetic factors. Usually, asthma symptoms are well controlled with medium or low doses of inhaled corticosteroids, but approximately 5% of asthmatics do not have a good response, requiring high doses of inhaled corticosteroids in addition to associations with other drugs to obtain or not clinical control. Among patients with severe asthma, approximately 10% of them, although using high doses of inhaled corticosteroids associated with a second controlling drug, are unable to obtain clinical control. **Objectives:** The aim of this study is to investigate the association of variants of the IL17 gene with the different pediatric asthma endophenotypes, including glucocorticoid-resistant asthma. **Material and Methods:** The study population includes individuals with severe asthma, severe refractory asthma, mild asthma and healthy controls who will be evaluated for clinical parameters, lung function, atopy markers, response to glucocorticoid treatment, among others. The polymorphisms in the IL17A and IL17F gene will be genotyped. **Results and Discussion:** Preliminary results from nine patients, among them, four with severe uncontrolled asthma and five with severe controlled asthma showed that there is a relationship between SNP rs3819024 for IL-17th with the severity of asthma. **Conclusions:** Therefore, the study will advance the understanding of the inter-individual variability of asthma.

Keywords: IL17, severe asthma, resistance to glucocorticoids.

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THE FLAVONOID AGATHISFLAVONE MODULATES MICROGLIAL ACTIVATION AND PRESENTS NEUROPROTECTIVE EFFECTS IN VITRO MODEL OF NEUROINFLAMMATION.

Balbino Lino dos Santos^{1,2}, Cleonice Creusa dos Santos¹, Victor Diogenes Amaral da Silva^{1,3}, Sílvia Lima Costa^{1,3,4*}

¹Laboratory of Neurochemistry and Cellular Biology, Institute of Health Sciences, Av. Reitor Miguel Calmon S/N, Federal University of Bahia (UFBA), Salvador, Brazil, ²College of Nursing, Federal University of Vale do São Francisco (UNIVASF), Petrolina, Brazil, ³INCT for Excitotoxicity and Neuroprotection (INCT-EN, BR), Porto Alegre, Brazil, ⁴Instituto Nacional de Ciência e Tecnologia em Excitotoxicidade e Neuroproteção (INCT)—Translational Neuroscience (INCT-TN, BR), Porto Alegre, Brazil.

Introduction: Neuroinflammation is one of the mechanisms responsible for the emergence of neurodegenerative diseases, as it acts by interfering with the morphology and activation of CNS cells, with emphasis on the inflammatory profile assumed by the microglia, and the neural damage caused by its inflammatory mediators. Some classes of flavonoids extracted from plants have shown anti-inflammatory effects in in vitro and in vivo models of studies.

Objectives: Here, we studied the anti-inflammatory and immunomodulatory effect of agathisflavone, a flavonoid derived from *Poincianella pyramidalis* (Tul.), in a model of neuroinflammation induced by lipopolysaccharide (LPS), in primary microglia cultures. **Results and Discussion:** we observed that the inflammatory stimulus with LPS induced the primary microglial culture to assume an activated cellular state with an inflammatory profile characteristic of M1 (increase in CD68 - inflammatory marker), confirmed by the phenotypic changes with rounder or amoeboid cells. However, when treated with agathisflavone, there was positive regulation of CD206 (anti-inflammatory marker M2) and negative regulation of CD68, as well as proliferation and prevalence of more branched-looking microglia, thus demonstrating the tendency of cells to assume an anti-inflammatory state. **Conclusions:** Thus, these data reinforce the anti-inflammatory activity of flavonoid, highlighting it as a promising molecule for the treatment or prevention of neurodegenerative diseases.

Keywords: Neuroinflammation, Neuroprotection, Anti-inflammatory, Flavonoids.

Support: CAPES

THE GLUCOCORTICOID RECEPTOR CONTRIBUTES TO REDUCTION OF LPS-INDUCED GLIAL REACTIVITY IN VITRO BY AGATHISFLAVONE

Áurea Maria Alves Nunes Almeida¹, Cleonice Creusa dos Santos¹, Glorieni Carvalho de Jesus¹, Larissa Pedreira da Silva¹, Verônica Moreira de Souza¹, Ana Elisa Del'Arco Vinhas Costa¹, Balbino Lino dos Santos¹, Victor Diógenes Amaral da Silva¹, Suzana Braga de Souza¹, Sílvia Lima Costa¹

¹Laboratory of Neurochemistry and Cell Biology, Department of Biochemistry and Biophysics, Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil.

Introduction: Neuroinflammation is a characteristic of neurodegenerative diseases, resulting from the release of proinflammatory molecules by glial cells. The co-occurrence of chronic dysregulation of inflammatory and stress responses in neurodegenerative and psychiatric disorders suggests the participation of the glucocorticoid receptor (GR) in the etiology of neurodegeneration. The biflavonoid agathisflavone is an apigenin dimer, with neurogenic, neuroprotective and anti-inflammatory actions demonstrated in in vitro models of glutamate-induced toxicity, neuroinflammation and stroke. In previous studies, our group demonstrated that agathisflavone mediates neuroprotection against glutamate excitotoxicity via estrogen receptor, a transcription factor sharing structural and functional properties with glucocorticoid receptor. The mechanisms mediating agathisflavone action are still poorly understood. **Objectives:** The aim of this study was to investigate whether the anti-inflammatory action of agathisflavone is mediated by GR. **Methods:** An in vitro model of lipopolysaccharide (LPS; 1 µg/mL) induced neuroinflammation was performed in primary cultures of astrocytes and microglia from the cortex of neonatal Wistar rats. Cells were treated with LPS, in association or not with agathisflavone (1 µM), in the absence or presence of mifepristone (RU486; 1 µM), a GR antagonist. The cytotoxicity of these substances in this in vitro model was evaluated by the MTT assay. Glial reactivity, an indicator of inflammatory profile, was evaluated by immunocytochemistry against astrocyte and

microglia markers, GFAP and Iba-1, respectively. Cell proliferation was evaluated by immunocytochemistry against bromodeoxyuridine (BrdU). Results: No decrease in mitochondrial activity was caused by the substances tested in the MTT assay, suggesting they are not cytotoxic in the tested concentration ranges. Astrocyte proliferation and relative GFAP expression increased in response to LPS treatment, but not in response to co-treatment with agathisflavone and/or RU486. Microglial proliferation was reduced following treatment with both LPS and agathisflavone, which was inhibited in the presence of RU486. These results suggest that agathisflavone modulates microglial proliferation via GR after inflammatory stimulation. The mechanisms of agathisflavone action would be further elucidated by studies characterizing the molecular and gene expression profile of glial cells.

Keywords: neuroinflammation, glucocorticoid receptor, microglia, astrocyte, Agathisflavone, neuroprotection.

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THE USE OF TUMOR ANTIGENS IN THE IMMUNIZATION OF ANIMALS CHRONICALLY INFECTED WITH *TRYPANOSOMA CRUZI* PREVIOUSLY TREATED WITH ADJUVANTS

Amanda Silva^{1,2}, Davi Salles¹, Maiara Bonfim^{1,2}, Jose Mengel^{3,4}, Fabiola Cardillo¹.

¹Gonçalo Moniz Research Institute, Oswaldo Cruz Foundation, LAPEM, Salvador-Ba, Brasil. ²Federal University of Bahia (UFBA), PPGIm, Salvador-Ba, Brazil. ³Oswaldo Cruz Foundation, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, Brazil. ⁴Faculty of Medicine of Petrópolis, FMP-FASE, Petrópolis, Rio de Janeiro

Introduction: Infection with *Trypanosoma cruzi* (*T. cruzi*) is associated with unregulated autoimmunity and severe tissue damage. The disease usually presents an initial acute phase, followed by an indeterminate or a chronic phase.

Objectives: This investigation aimed to analyze whether the associated administration (or not) of alpha-tocopherol or tumor antigens (ags) modulate the tissue damage found in muscles of animals chronically infected with *Trypanosoma cruzi*. Besides, this study is to verify if tumor antigens could induce immunosuppression to regulate immune responses. **Methods:** Mice were immunized with *T. cruzi* adsorbed in alpha-tocopherol or Al₃OH and infected with *T. cruzi*. Then, mice were also immunized with melanoma B16F0ags. Splenocytes were cultured with (or without) Concanavalin A (Con A). T cells were stained for intracellular cytokines (IFN γ , IL10) and membrane LAP labeling. In all experimental groups, inflammatory infiltrates in the heart, and skeletal muscles were evaluated by histopathological analysis. **Results:** Chronically infected animals previously treated only with alpha-tocopherol presented lower inflammation in striated and skeletal muscles infiltrates than untreated chronically infected animals ($p=0,0286$, Mann Withney test, $n=4$). These results were similar when 50 or 1000 forms of *T. cruzi* were used for the infection. Subsequently, after alpha-tocopherol immunization and injection with B16F0ags, results indicated immunomodulation that is probably related to a nonspecific immune response, because of the previous treatment with alpha-tocopherol. A decrease in CD4⁺ and CD8⁺ T cells producing IFN γ , IL10, and LAP were observed *ex vivo*, after Con A stimulation. Contrarily, chronically infected animals that did not receive alpha-tocopherol previously (but were immunized with the B16F0ags) had higher percentages of cytokine-producing T cells compared to animals without alpha-tocopherol injection. After B16F0ags injection, inflammatory infiltrates in striated or skeletal muscles were not different between the experimental groups evaluated. **Conclusion:** Chronically infected mice that received alpha-tocopherol before the injection of B16F0ags lead to the establishment of a regulated immune response. After the injection of B16F0ags, in the absence of the previous alpha-tocopherol in chronic mice, cytokine levels were increased upon Con A stimulation of splenocytes.

Keywords: *Trypanosoma cruzi*, adjuvant effect, melanoma antigens, immunomodulation.

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ZIKA VIRUS SINGULAR PEPTIDE PRODUCTION FOR THE DEVELOPMENT OF SEROLOGICAL IMMUNOASSAYS AND EVALUATION OF IMMUNE RESPONSE

Rafael Ribeiro Mota Souza^{1, 3}, Isabela Brandão Peixoto¹, Rejane Hughes Carvalho^{1, 2}, Gubio Soares Campos¹, Roberto José Meyer Nascimento³, Silvia Ines Sardi¹

¹Laboratory of Virology, Health Science Institute, Universidade Federal da Bahia, Brazil. ²Gonçalo Moniz Institute (FIOCRUZ), Bahia, Brazil. ³Laboratory of Immunology and Molecular Biology, Health Science Institute, Universidade Federal da Bahia, Brazil, Brazil;

Introduction: The rapid spread of Zika virus (ZIKV) in endemic regions where other Flaviviruses have already been established, such as Dengue Virus (DENV), has led to difficulties in accurately diagnosing the infectious agent. Both Flaviviruses present very similar acute symptomatic conditions and high similarity among their viral proteins, what leads to serology cross-reactions between Zika and Dengue, producing false positive results. In addition, studies have demonstrated that antibody-dependent enhancement also increase viremia due to the cross-reaction between the tests. **Objectives:** Based on the demand for more specific antigens, the present project aims to produce non cross-reactive ZIKV antigens for immunodiagnostic and immunomodulation in vivo. **Material and Methods:** Unique epitopes were indentified using bioinformatic tools to analyse amino acids conservance (EBI-MUSCLE-MSA ; Jalview), their similarity (BLASTp/NCBI), and antigenicity (IEDB ; CHIMERA (UCSF)). The production of ZIKV unique antigens was planned and performed on a plamid construction derived from the bioinformatic investigation. Plasmids used in BL21 Star transformation for expression under administration of IPTG. **Results and Discussion:** As preliminary results, bioinformatics analysis identified 3 unique and immunogenic epitopes derived from ZIKV proteins; one from the E protein and two from the NS1. The coding region for the E epitope was used to construct an expression vector containing four in tandem uninterruptedly repetitions of the sequence. The other expression vector was constructed using the two sequences from the NS1 protein. Those two regions were placed in a 3 and 2 intercalated repetition manner. Both vectors were cloned in *E. coli* and were expressed (confirmed by western blot against histag). Future experiments include the evaluation of sensitivity and specificity of the antigens using Dengue and Zika IgG+ sera by ELISA and Western Blot, and the evaluation of humoral immune response in BALB / c mice. **Conclusion:** Overall, the investigation of the ZIKV epitopes based on previous bioinformatic analysis could lead to the elaboration of new tools for immunodiagnosis, provaiding a more accuretedstategies to the survaillance of ZIKV.

Keywords: Zika virus, immunodiagnostic, bioinformatics.

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Universidade Federal da Bahia
Instituto de Ciências da Saúde
Av. Reitor Miguel Calmon s/nº
40.110-100 Salvador, BA – Brasil

