Universidade Federal da Bahia
Instituto de Ciências da Saúde

Volume 16
Número 3 – Suplemento 1
Outubro 2017

Revista de Ciências Médicas e Biológicas

Journal of Medical and Biological Sciences

UNIVERSIDADE FEDERAL DA BAHIA
INSTITUTO DE CIÊNCIAS DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM IMUNOLOGIA

PPGIm
Programa de Pós-graduação em Imunologia

ANAIS DA XVII EXPOPPGIM 2017

ISSN 1677-5090

REVISTA DE CIÊNCIAS MÉDICAS E BIOLÓGICAS

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ANAIS DA XVII EXPOPPGIM 2017
RESUMOS

Revista Ciências Médicas e Biológicas
[Journal of Medical and Biological Sciences]
ISSN 1677-5090

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Normalização bibliográfica: Keite Birne Lira – Universidade Federal da Bahia, Brasil
Editoração: Virgínia Morais
Secretário: Marcelo Andrade Silva Santos
Impressão: Empresa Gráfica da Bahia (EGBA)
Tiragem e Distribuição: 500 exemplares

Apoio: **UFBA/CAPES**

Revista de Ciências Médicas e Biológicas = Journal of Medical and Biological Sciences / Instituto de Ciências da Saúde da Universidade Federal da Bahia. – Vol. 1, nº 1 jul./dez. 2002 –.
Salvador: Instituto de Ciências da Saúde, 2002 –
v. : il.; 30 cm.
Quadrimestral.

ISSN 1677-5090

1. Ciências Médicas – Periódicos 2. Ciências Biológicas – Periódicos.
I. Universidade Federal da Bahia. Instituto de Ciências da Saúde.
CDD – 610.05
574.05
CDU – 61:57(05)

(Elaborada pela Profa. Carmélia Mattos – ICI-UFBA)

Revista de Ciências Médicas e Biológicas

Journal of Biological and Medical Sciences

ISSN 1677-5090

SUMÁRIO

Volume 16 – Suplemento 1 – Outubro 2017

ISSN 1677-5090

Apresentação

O Programa de Pós-graduação em Imunologia (PPGIm) há vinte e oito anos, vem formando recursos humanos de excelência, capacitados para as atividades de ensino e pesquisa em Imunologia e áreas correlatas. O PPGIm tem realizado reuniões científicas anuais visando difusão do conhecimento científico e integração acadêmica com a graduação e a pós-graduação da UFBA e de outras IES.

A ExpoPPGIm, Reunião Anual do Programa, já se tornou um evento tradicional que acontece anualmente desde 2000. Essa reunião tornou-se um fórum de integração de profissionais, pesquisadores e jovens cientistas, alunos de graduação e pós-graduação da UFBA e de outras IES do Estado da Bahia e do Brasil com interesse no amplo domínio da Imunologia. Neste sentido, o objetivo da ExpoPPGIm é divulgar conhecimento científico em Imunologia e áreas correlatas tendo como público alvo estudantes de graduação, pós-graduação e pesquisadores e profissionais da área. Nesta XVII ExpoPPGIm, além de conferências com pesquisadores do Programa e pesquisadores convidados, contamos também com os *workshops* em metodologias envolvendo recentes tecnologias na Imunologia aos participantes interessados, além da sessão de pôsteres e comunicações orais dos melhores trabalhos, incluindo premiações, sendo o melhor trabalho agraciado com a segunda edição do Prêmio Lain Carlos Pontes de Carvalho.

Neste documento, sumarizamos a produção científica gerada para a XVII ExpoPPGIm que teve como tema em 2017 “Explorando o Microbioma”. Assim, pretendemos disseminar a Imunologia, divulgar as idéias e projetos em curso desenvolvidos por docentes e discentes de nosso Programa, bem como, ampliar novas perspectivas, resgatando nossa história e instigando nossa evolução.

Saudações acadêmicas,

Camila A Figueiredo
Coordenadora do PPGIm/ICS/UFBA

LINHA 01: Imunodeficiências e Imunopatologia

CHARACTERIZATION OF THE IMMUNOLOGICAL MECHANISMS INDUCED *IN VITRO* BY THE Sm29 ANTIGEN IN MACROPHAGES OF ASTHMATIC INDIVIDUALS

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Introduction: Evidence has been accumulating that chronic helminth infections, particularly by *Schistosoma* sp or their products, is able to modulate the type 2 inflammatory response in allergic diseases. Studies suggest that M2 macrophages are the main cells present in bronchoaveolar lavage fluid from asthmatic patients. Additionally, these cell populations may contribute to the severity of allergic inflammation with an important role in the pathophysiology of the disease. **Objectives:** The aim of this study is to characterize the immunological mechanisms induced by the recombinant antigen Sm29 from *Schistosoma mansoni in vitro* in macrophages from individuals with asthma. **Materials and Methods** We will evaluate 20 subjects with severe asthma refractory to treatment, 20 with mild / intermittent asthma (both groups uninfected by *S. mansoni*), and 10 healthy controls. The effect of Sm29 antigen on the production of activation markers, cytokines, and metalloproteinases (IL-10, TNF, IL-1β, MMP-2 and MMP-9) by macrophages from these patients will be evaluated as well as the effect of Sm29 on macrophage maturation. We will also evaluate the frequency of Toll-like receptors (TLR) – 2 and TLR-4 after stimulation with Sm29. The mechanisms underlying the induction of regulation by Sm29 antigen *in vitro* in macrophages will be evaluated through the ERK / MAPK protein kinase signaling pathway, as well as the transcription factor NFκB and the adapter protein MyD88. **Perspectives:** The identification and characterization of cellular and immunological mechanisms induced by Sm29 in asthma, as proposed in this study, may contribute to the production of a feasible antigen for use in the control of the exacerbated immune response observed in this disease.

Support: FAPESB and CNPq.

Keywords: asthma, Sm 29, macrophages.

LINHA 01: Imunodeficiências e Imunopatologia

EVALUATION OF REGULATORY T-CELLS (TRegs) EXPRESSION IN HIV-1 / HTLV-1 VIRUS COINFECTION

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Introduction: HIV-1 patients development a higher risk to new infection by HTLV-1. The coinfection HIV-1 and HTLV-1 can to associate a increase to T CD4+ cells counts and to hide AIDS progression. T reg cells are a T CD4+ lymphocytes subsets responsible to produce and proliferation of cytokines and maintenance of immunological tolerance.The T reg cells functions are not clear in the development to HIV and HTLV coinfection and our study aims to clarify the behavior this cells in this moment.**Objectives**: To evaluate T Reg cells expression in the HIV-1 and HTLV-1 coinfection and to compare with cytokines expression. **Materials and Methods**: Five groups will be composed by 10 participants each. One group HIV monoinfected symptomatic for AIDS, other HIV monoinfected asymptomatic, HTLV monoinfected symptomatic and / or asymptomatic and control individuals. 20 ml of peripheral blood in tubes containing anticoagulant k^{3}EDTA will be collected. Immunophenotyping by flow cytometry will be used to perform specifics membrane markers cells. Monoclonal antibodies to CD3+, CD4+, CD8+, CD45+, CD25+ and FoxP3 proteins will be used to determinate the cells profile of the T lymphocytes subpopulations. After wash cells procedure using PBS, the samples will be acquired and analyzed by flow citometry. Cytokines IL-12, IFN-α, IFN-γ, IL-5, IL-10, IL-6, IL-2 e IL-4 will be quantified by flow cytometry also. Expected results: To evaluate T reg cells behavior during HIV/ HTLV coinfection development. **Perspectives**: It's expected to understand the behavior of the virus and the immune system in these patients, and also to raise relevant questions to the development of new research.

Support: FAPESB, LAPI and LABIMUNO

Keywords: coinfection, hiv, htlv, tregs

LINHA 01: Imunodeficiências e Imunopatologia

FUNCTIONAL DETERMINATION OF THE INNATE IMMUNE RESPONSE IN HIV-1 AND HTLV COINFECTION

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Introduction: HIV and HTLV vírus are classified as retrovírus. The first is widespread throughout the world some of the individuals infected by it become ill. The second is more prevalent to some geographic regions, but only 3-5% of those infected by HTLV-I develop disease. Coinfected patients was shown by study in Brazil with prevalence of 1.8% in the HIV general patients. These numbers are 0.28% for pregnant in Bahia and 0,9% to Salvador. To drug users injectables, the prevalence is 25.5% to HTLV-I. The innate response triggers effector mechanisms that restrict infection and activates the adaptive response by completing the elimination of the pathogen or infected cells. HIV-1 and HTLV-1 infects monocytes and dendritic cells in the innate response. **Objectives:** To characterize the expression of the innate immune response in HIV-1 and HTLV-1 virus coinfection. To compare innate immune response between monoinfected and coinfected patients in both viruses. To evaluate the profile of cytokines in coinfection and monoinfections. **Materials and Methods:** Groups of patients of both gender and over 18 years of age, monoinfected by HIV and HTLV under asymptomatic and / or symptomatic conditions will be invited. The patients will be attended at the Bahia Foundation of Infectious Diseases. 20 ml whole blood will be collected to perform the laboratory tests. For determination of the cellular immunophenotypic profile, monoclonal antibodies specific to membrane surface proteins will be used and analyzed by flow cytometry. The innate immune response will be evaluated from the determination of dendritic cells, B1 cells and Natural Killers cells, since they are the main ones involved in the Th1 type response to the virus. Detection of these cells will be characterized by the presence of CD14 + (PE), CD64 + (PE) monoclonal antibodies to monocytes; CD15 + (FITC), CD40 + (PE) and CD1a + (PerCP) for dendritic cells, CD5 + (FITC), CD19 + (PE) for B1 cells producing neutralizing antibodies and Natural Killers cells will be characterized by the presence of CD56 + (PE), CD16 + (FITC), and CD8 – (PerCP); For Anti-CD 45+ (RO) and NAIVE Anti-CD 45 (RA) Memory Cells. Cytokines involved in Th1 immune responses are IFN-α, IFN-γ, IL-2; IL-5, IL-6, IL-10, IL-12. **Perspectives:** This study aims to identify the various aspects of the innate immune response during infection by patients coinfected with HIV-1 and HTLV-1 viruses.

Support: HUPES Complex; LabImuno.

Keywords: Innate Immune Response; Coinfection; HIV; HTLV.

LINHA 01: Imunodeficiências e Imunopatologia

THERAPEUTIC RESPONSE EVALUATION BASED ON IMMUNOLOGICAL PROFILE IN DOGSWITH GENERALIZED DEMODICOSIS

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Introduction: Canine generalized demodicosis is a very common inflammatory skin disease caused by the overgrowth of *Demodex canis*, a mite which belongs to the canine normal skin microbiota. Despite the high incidence, little is known about its pathophysiology, and long treatment protocols based on clinical outcomes coupled with negatives results of parasitological exams of the skin are used as standard procedures. T-cell exhaustion phenotype is characterized by low production of stimulatory cytokines and high levels of suppressive cytokines. Almost all of these changes have been documented in dogs with generalized demodicosis and it is very likely that these dogs suffer from T-cell exhaustion. **Objective:** To assess the need for such prolonged treatment protocol for canine generalized demodicosis based on analysis of immunological markers and measurment of the parasitic load by real-time PCR and compare the results of three treatment protocols, two with Ivermectin and one with an Isoxazoline. **Material and Methods:** Forty dogs of either sex will be included in the study. They will be divided into 4 groups with ten dogs each: Group I (control), consisting of ten healthy dogs without skin lesios; Group II (Ivermectin), ten dogs treated with ivermectin according to a standard protocol; Group III (Ivermectin) with ten dogs treated with ivermectin until the immunological parameters normalize and Group IV (Isoxazoline), with ten dogs treated with a isoxazoline until the immunological parameters normalize. Prior to initiating the therapeutic protocol, blood and skin samples will be collected. The treated patients will be allocated to the groups randomly. Hemogram and biochemistry, CPR and Haptoglobin dosing will be done from blood and cytokines will be analyzed in the skin samples by the ELISA method.The tests will be repeated every 30 days for 3 months in groups II, III and IV. Hemogram and biochemistry, CPR and Haptoglobin dosing will be done from blood and cytokines (IL-2, IL-4, IL-5, IL-10, IL-21, TNF-α and TGF-β) will be analyzed in the skin samples by the ELISA method. **Perspectives:** to verify that treatment interruption can be based on the return to normality of the immunological parameters, reducing treatment costs, side effects and increased treatment efficacy.

Support: Self funded

Keywords: Canine generalized demodicosis

LINHA 01: Imunodeficiências e Imunopatologia

EVALUATION OF THE REGULATORY MECHANISMS INDUCED BY THE RECOMBINANT *Schistosoma mansoni* Sm29 ANTIGEN ON THE LYMPHOCYTES OF PATIENTS WITH ASTHMA

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Introduction: Evidences has been accumulated that chronic helminth infection, particularly by *Schistosoma sp* or parasite products, is able to modulate the type 2 inflammatory response of allergic-based diseases, such as asthma. **Objective:** The aim of this study is to evaluate the mechanisms of regulation induced by the recombinant antigen of *Schistosoma mansoni* Sm29 in vitro in the lymphocytes of patients with asthma. **Materials and Methods:** In this study 20 individuals with mild/moderate asthma, 20 patients with severe refractory asthma to treatment, both atopic and non-infected by *Schistosoma mansoni*, were evaluated in addition to 20 individuals infected with *Schistosoma mansoni* and 10 healthy controls. Evaluation of the IL-10 producing source after stimulation by the recombinant Sm29 antigen in the T ($CD4^+$, $CD8^+$) and B ($CD5^+$ $CD19^+$) lymphocyte population, NK cells, monocytes, NKT cells and dendritic cells will be performed by flow cytometry. The effect of the Sm29 recombinant antigen on the expression of intracellular cytokines (IL-5, IL-13, TGF-β, IFN-γ and IL-17A) and the proliferation of $CD4^+$ T lymphocytes, as well as the IL-10 in the proliferation, activation state and production of intracellular cytokines of lymphocytes after stimulation by this antigen. **Perspectives:** The characterization of the immunoregulatory mechanisms induced by the recombinant antigen Sm29, as proposed in this study, with the potential modulatory of the exacerbated immune response in asthma, whose large scale production is viable, will aid in the development of the control and treatment of this disease.

Support: FAPESB and INCT-DT/CNPq

Keywords: severe asthma, *Schistosoma mansoni* Sm29 antigen, lymphocytes

LINHA 01: Imunodeficiências e Imunopatologia

QUANTITATIVE CHARACTERIZATION OF ILCs FROM INDIVIDUALS BEARING DIFFERENT ASTHMA PHENOPYPES AT SALVADOR, BAHIA, BRAZIL

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Introduction: Asthma is a chronic inflammatory disease of the lower airway. The classical known phenotypes are atopic asthma and nonatopic asthma. The atopic asthma is mediated by genetics factors that lead to a Th2 profile response mediated by allergen agents, such as house dust mite, pollen, and others. The Th2 cells produces interleukins (IL4, IL5, IL9, and IL13) and lead the plasmocytes to produce IgE. These response culminate with the mast cells degranulation, eosinophils activation and the hypersensitivity type 1 response. The nonatopic asthma is caused by the Th1 and Th17 cells profile producing IL17, IL22, IL-12, IFN-γ and TNF that fallow the NK cells, neutrophils and phagocytes activation, leading to bronchial hyperresponsiveness. Recently, the innate lymphoid cells (ILCs) have been associated with asthma, being activated through interleukins produced by epithelial tissue. The ILC-1 is related to asthma associated to virus infection and IFN-γ production; ILC-2 is related to asthma allergenic and produces IL4, IL5, IL9, IL13 and Areg; ILC-3 is related with asthma associated with obesity and it produces IL17A and IL22. **Objectives:** Evaluated quantitatively the ILCs production in individuals from Salvador-Ba with different asthma phenotypes associating this production with immunological and biochemical markers. **Materials and Methods:** 30 individuals will be grouped in 4 groups: 8 individuals bearing atopic asthma; 8 bearing nonatopic asthma; 8 bearing atopy and 6 healthy individuals being a negative control. Asthma characterization will be made by ISAAC (International Study of Asthma and Allergy in Childhood) questionnaire phase III and atopy will be defined as presence of at least one positive test of anti-aeroallergen serum IgE ≥ 0.70 kU/L performed by ImmunoCap. Also, will be performed the skin test, the individual who shows papules bigger than 3 mm compared to negative control will be considered as atopic. The ILCs will be extracted from peripheral blood mononuclear cells. The PBMC will be marked for positive linage exclusion and remarked to detect ILCs and ILC2 following quantification by flow cytometer**.** The ILCs quantifications will be associated with immunological and biochemical markers and sociodemographic aspects of these individuals. **Perspectives:** The purposes of this study is to understand how the ILC production influences the asthma development and the relationship between innate cells and adaptive cells in this disease.

Support: WASP (World Asthma Study Phenotypes).

Keywords: innate cells, atopy, interleukins, immunoglobulin.

LINHA 01: Imunodeficiências e Imunopatologia

DEVELOPMENT OF A QUANTITATIVE DETECTION TEST OF HIV AND HTLV INFECTED CELLS BY IMMUNOPHENOTYPING

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Introduction: HIV infected individuals can be coinfect by other virus, like HTLV 1/2. Both virus presents same transmissions routes, as needles sharing and unprotected sexual contact (KLASE e JEANG, 2013; PILOTI et al., 2013). Clinical complications has been informed in this coinfection and HTLV-1 is associated with AIDS progression (BRITES et al., 2009; BEILKE et al., 2007; CASSEB et al., 2008; REGIS et al., 2009; SILVA et al., 2012). **Methods and results:** Will be collected 10 mL of peripheral blood of pacients with HIV and HTLV in monoinfection and coinfection. Ficoll gradient will isolate mononuclear cells from peripheral blood to flow cytometry. Cytoplasmic virus will be detect by specific probes anti-HIV and anti-HTLV. To determine proviral load, will be used monoclonal antibodies anti-CD4 (APC), anti-CD3(PerCp) and HIV (FITC) probe (to HIV infection) and anti-CD4 (APC), anti-CD3(PerCp) and HTLV (PE) probe (to HTLV infection). The cytokine profile to compare mono and coinfected patients will include IL-12, IFN-α, IFN-γ, IL-5, IL-10, IL-6, IL-2 e IL-4 and it will be done by Cytometric Bead Array. This project was approved by Research Etics Commission (CAAE 56213716.3.0000.5543). We had creat a pacient database after search in pacients treated in c-Hupes and find 174 pacients with HIV/HTLV coinfection. We also colected HIV infected pacients samples and made their viral load. **Conclusions:** The high levels infection of HIV and HTLV in Salvador, Ba, allow criation of a coinfected pacients database with several clinical information as age, sex, proviral load and other infections.

Keywords: Coinfection, immunophenotyping, cytometry

LINHA 01: Imunodeficiências e Imunopatologia

25 Hydroxyvitamin D serum levels are negatively associated with atopy and correlated with specific IgE to *Dermatophagoides pteronyssinus*, but it is not associated with asthma, asthma phenotypes or asthma morbidity.

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Introdution: Recent research's show the vitamin D had beneficial effect in allergic diseases such as asthma. It's known that vitamin D decreases IgE synthesis by inhibiting epsilon germ-line transcription in B cells. Also higher vitamin D serum levels are associated with more asthma control and less use of drugs, including corticotherapy. However, there are not report about the association of vitamin D levels with different asthma phenotypes. Our objective was to investigate the relationship between serum levels of 25 hydroxivitamin D with atopy and asthma, asthma morbidity and asthma phenotypes. **Methods and Results:** 968 individuals aged 11-19 years of a cohort study involving 24 peripheral neighborhoods of the city of Salvador, Northeast, Brazil. The ISAAC phase III questionnaire was replied to identify wheezing/asthma cases. Allergen-specific serum IgE was measured using ImmunoCap (AB, Uppsala Sweden) and serum levels of 25-hydroxy-vitamin D were detected using an inhibitory ELISA (IDS, UK). Atopy was defined as presence of at least one positive test of anti-aeroallergen serum IgE ≥ 0.70 kU/L. To carry out logistic regression analysis, 25 hydroxy vitamin D serum levels were classified in two different forms; insufficiency and deficient grouped in the same class and insufficiency and sufficiency grouped in other same class. Among the 968 participants, 76 (7.85%) reported current asthma, 449 (46.4%) were atopic. Deficiency of vitamin D was present in 200 (20.7%) individuals and 377 (38.9%) had sufficient vitamin D levels. We have found that individuals with deficiency serum vitamin D (less than 20ng/ml) had more chances of being atopic (OR = 1.45 95% CI 1.05-2.00). In addition, we found that in atopic individuals the serum levels of vitamin D levels are negatively correlated with specific IgE to *Dermatophagoides pteronyssinus* (r = – 0,11 p = 0,019). No association was found between asthma and serum vitamin D; however the levels in the healthy individuals was slightly higher than in asthmatic. When we evaluated asthma morbidity based on ISAAC questionnaire, did not find any association with vitamin D serum levels. Furthermore in multinomial logistic regression analysis also did show association of vitamin D with these phenotypes. **Conclusion:** In this study vitamin D was associated with lower risk of atopy but not with asthma. These findings was similar with those found by our group in children of a small city nearby Salvador.

Support: Fundação de Amparo a Pesquisa do Estado da Bahia

Keywords: Atopy, Asthma, Vitamin D.

LINHA 01: Imunodeficiências e Imunopatologia

IMPACT OF PRETHERAPEUTIC LABORATORY VALUES, COMORBIDITIES INDEX, SOCIO-ECONOMIC STATUS AND DEMOGRAPHIC CHARACTERISTICS IN IMMUNOSUPPRESSION PARAMETERS AND PROGNOSTIC OF HEAD AND NECK CANCER PATIENTS

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Introduction: Head and neck squamous cell carcinoma (HNSCC) is the fifth cause of cancer death in the world and patients from lower socio-economic patterns present the worse clinical parameters, including overall survival outcomes. In relation to demographic factors, tabagism and etilism are the major source of associated comorbidities in disease. Besides this, recent studies demonstrated influence of pretherapeutic laboratory values in prognostic of HNSCC patients. **Objectives**: Considering evidences of a highly immunosuppressive microenvironment for HNSCC tumors, the aim of this study is to evaluate the impact of pretherapeutic laboratory values, comorbidities, socio-economic status and demographic characteristics in immunosuppression parameters and prognostic of HNSCC patients. **Materials and Methods**: This study was approved by the Ethics Committee of Health Sciences Institute of the Federal University of Bahia (no 2.214.083). A retrospective cohort of patients treated in Aristides Maltez Hospital (Salvador, Bahia, Brazil) with primary HNSCC of oral cavity, oropharynx and larynx diagnosed between 2006 and 2017 will be constituted. In relation to pretreatment laboratory values, the assessment of cellular and biochemical parameters will include hematologic profile related to red and white blood cells; platelets counting; urea and creatinine levels, caracterization of liver enzymes as alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT) and gamma-glutamyl transferase (gammaGT); lipid profile with total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides; and C-reactive protein (CRP) as an inflammatory indicator. Clinico-pathological parameters as selected treatment, TNM and WHO classification of tumors will be collected. Socioeconomic status, including residence deprivation and place of death will be also analyzed. Finally, the Charlson comorbidity index will be calculated. In 50 patients, the serum (pre existent data) and tumoral levels of the immunosuppressive cytokines IL-10 and TGF-β will be obtained and compared with all data. **Perspectives:** This study intend to clarify if present comorbidities or demographic and socioeconomic peculiarities represent significant omissions in the approach of immunosuppression levels and prognostic of HNSCC patients. In addition, this study will contribute to describe the local geografic epidemiology of HNSCC and for to the construction of state multidisciplinary healthcare politics.

Support: UFBA

Keywords: head and neck cancer, cohort studies, comorbidity, socio-economic status, alcohol drinking/adverse effects

LINHA 01: Imunodeficiências e Imunopatologia

IL4 and IL4R GENE POLYMORPHISMS, ASTHMA AND ATOPY.

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Introduction: It is estimated that asthma affects about 334 million people worldwide and has emerged as a relevant public health problem since it presents high prevalence. This elevation may be linked to environmental factors changes, as well as to genetic factors that may affect asthma and atopy in different populations. Asthma is characterized by chronic inflammation of the airways along with obstruction and hyperresponsiveness associated to the production of inflammatory cytokines, such as IL-4, which play a key role in the pathogenesis of asthma. In this context, genetic variants in the genes interleukin 4 (IL4) and the interleukin 4 receptor (IL4R) may affect this process, and, consequently, modulate inflammation. **Objectives:** To evaluate the association of variants of these genes with markers of asthma and atopy in a Brazilian population. **Materials and Methods:** The study involved individuals from the SCAALA (Social Change, Asthma, Allergy in Latin America) project defined as asthmatic according to ISAAC Phase 2 (The International Study of Asthma and Allergies in Childhood) questionnaire. Skin tests for *Blomia tropicalis* allergen and blood samples collected for anti-*B. tropicalis* IgE assays were performed. The DNA was extracted and genotyped through a commercial Illumina panel (BeadChip Human Omni2.5-8 Kit). Logistic regression analyzes will be performed using PLINK 1.9 software for asthma and allergy markers (skin tests and IgE level), adjusted for sex, age, helminth infections and ancestral markers. Linkage disequilibrium (LD) analysis will be performed in Haploview 4.0 and *in silico* analysis using public databases. **Perspectives:** To identify possible associations of variants in the IL4 and IL4R genes with asthma and atopy to better understand the immunopathological mechanisms involved, as well as to direct new strategies for the treatment of these allergic disorders.

Support: FAPESB and PIBIC-UFBA.

Keywords: Asthma, atopia, IL4, IL4R.

LINHA 01: Imunodeficiências e Imunopatologia

EVALUATION OF THERAPEUTIC POTENTIAL OF MESENCHYMAL STEM CELLS AND CONDITIONED MEDIUM IN THE TREATMENT OF CARDIAC DYSFUNCTION DUE TO OBESITY AND DIABETES MELLITUS TYPE II

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Introduction: Obesity is associated with numerous cardiac complications, including arrhythmias, cardiac fibrosis, remodeling and heart failure. Here we evaluated the therapeutic potential of mesenchymal stromal cells (MSCs) and their conditioned medium (CM) to treat cardiac complications in a mouse model of high-fat diet (HFD)–induced obesity and diabetes type 2 (DM2). To evaluate the therapeutic effects of MSCs and its CM in obese mice due to HFD ingestion. **Methods and Results:** After obesity and DM2 induction and HFD withdrawal, obese mice were treated with MSCs, CM or vehicle. Cardiac function was assessed using electrocardiography, echocardiography and treadmill test. Body weight and biochemical parameters were evaluated. Cardiac tissue was used for real time (RT)-polymerase chain reaction (PCR) and histopathologic analysis. Characterization of CM by protein array showed the presence of different cytokines and growth factors, including chemokines, osteopontin, cystatin C, Serpin E1 and Gas 6. HFD-fed mice presented cardiac arrhythmias, altered cardiac gene expression and fibrosis reflected in physical exercise incapacity associated with obesity and diabetes. Administration of MSCs or CM improved arrhythmias and exercise capacity. This functional improvement correlated with normalization of GATA4 gene expression in the hearts of MSC – or CM-treated mice. The gene expression of connexin 43, troponin I, adiponectin, transforming growth factor (TGF) β, peroxisome proliferator activated receptor gamma (PPARγ), insulin-like growth factor 1 (IGF-1), matrix metalloproteinase-9 (MMP9) and tissue inhibitor of metalloproteinases 1 (TIMP1) were significantly reduced in MSCs, but not in CM-treated mice. Moreover, MSC or CM administration reduced the intensity of cardiac fibrosis. **Conclusion:** Our results suggest that MSCs and CM have a recovery effect on cardiac disturbances due to obesity and DM2, and corroborate to the paracrine action of MSCs in heart disease models.

Support: CAPES,FAPESB, CNPq, and FINEP.

Keywords: cardiac dysfunction, cell therapy, mesenchymal stromal cells, obesity.

LINHA 01: Imunodeficiências e Imunopatologia

IN VITRO OF G-CSF ON DIABETIC CARDIOMYOPATHY USING HUMAN INDUCED PLURIPOTENT STEM CELLS.

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Introduction: Diabetic cardiomyopathy (DCM) is a complication of type 2 diabetes, that leads to pathological remodeling of the heart, with limited therapeutic options available. We demonstrated that granulocyte colony-stimulating factor (G-CSF) is able to accelerate recovery and improve cardiomyocyte (CM) functions in a mouse model of DCM. However, little is known about the mechanisms of action and therapeutic potential of G-CSF in human DCM. In this context, human induced pluripotent stem cells (iPSC) are important tools to study disease mechanisms and to test new treatments for cardiac diseases. To investigate the therapeutic potential and molecular mechanisms of action of G-CSF on DCM using human iPSC-derived CM. **Methods and Results:** Human iPSC cells were generated and differentiated into CM. Differentiated cells were characterized by flow cytometry, electron microscopy, confocal microscopy and qPCR. Human iPSC were successfully differentiated into CM, showing widespread spontaneous beating areas. Different protocols were tested, until high efficiency differentiation (>90% cardiac troponin T-positive cells) was achieved. Immunofluorescence analysis demonstrated positive staining for troponin-T, GATA-4, alpha-actinin and sarcomeric myosin, showing

typical sarcomeric organization, also confirmed by electron microscopy analysis. These results were confirmed at the mRNA level by qPCR analysis, that demonstrated significant increase in the gene expression of troponin-T, GATA-4, and NKX2.5, genes involved in cardiac development. Since DCM is a disease of adult CMs, human iPSC-CMs will be exposed, in the next steps, to maturation medium (containing insulin and fatty acids, but no glucose), followed by a diabetogenic medium, in order to induce cellular alterations. Finally, the effects of G-CSF and the signaling pathways involved will be analyzed. **Conclusion:** Human iPSC can be successfully differentiated into CM for in vitro studies of DCM and may be useful for investigation of the therapeutic effects of G-CSF.

Support: FAPESB, CNPq.

Keywords: G-CSF; Diabetic Cardiomyopathy; Diabetes type 2; Human iPSC.

LINHA 02: Imunologia Aplicada

IMMUNOLOGICAL RESPONSE, MITOCHONDRIAL METABOLISM AND PERFORMANCE OF CHICKENS FED WITH DIET SUPPLEMENTED WITH ZINC

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Introduction: The poultry has grown intensely in Brazil in recent decades, diets for broilers are formulated with ingredients in appropriate proportion to meet the requirements of birds at each stage of creation. Among the components used in formulation are micro-nutrient supplements such as vitamins and minerals. Zinc (Zn^{2+}) is a micromineral that is cofactor of a large number of enzymes. Many of the enzymes of which the ZN^{2+} is cofactor are found in immune cells. Zinc acts as antioxidante by inhibiting the NADPH-oxidase, it also acts as cofactor of superoxide dismutase (SOD). **Objectives:** The objective of this work is to evaluate the effect of supplementation of diets with Zn on the immune system, mitochondrial metabolism and performance of broilers. **Materials and Methods:** 960-day old chicks will be used and will receive corn and soy rations and premix with zinc source (ZnO) supplemented with organic zinc (Mintrex-Zn 15%). Will be used a completely randomized design with 04 treatments (T1:60mg Zn (ZnO); T2: T1 + 25mg Zn-Mintrex; T3: T1 + 50mg Zn-Mintrex and T4: T1 + 75mg Zn-Mintrex) and 08 repetitions. Laboratory analyses will be conducted to evaluate the proliferation of peripheral blood mononucleadas cells, check the occurrence of membrane lesion and nitric oxide production in these cells. The method of converting the MTT [3 – (4,5-dimethylthiazol-2yl) – 2-5-diphenyl-2H-bromo tetrazolate] into formazan and lactate dehydrogenase will also be carried out. Performance characteristics, weight measurement and biometry of organs and digestive attachments and morphometric analysis of the small intestine will be evaluated. In addition, lysosomal activity and mitochondrial metabolism. **Perspectives:** It is expected to determine what effect the diet supplementation of chickens with zinc on the immune system, mitochondrial metabolism and performance of these animals.

Support: UFRB-UFBA.

Keywords: immune system, chickens, micromineral, mitochondrial metabolism

LINHA 02: Imunologia Aplicada

IMMUNOBIOLOGICAL ASPECTS OF MESENCHYMAL STEM CELLS IN ANIMAL MODEL OF DIABETIC FEET ULCERS

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Introduction: Chronic ulcers clinical cases in diabetic patients constitute an important public health problem, presenting higher costs of health services in consequence of the treatment and management of the complications resulting from the inflammatory process. Currently, the mesenchymal stromal cells (MSC) are presented as potential alternatives for cell therapy. These cells secrete cytokines, growth factors, and bioactive molecules responsible for the effects of tissue repair and regeneration. Recently our group demonstrated that MSC from bone marrow have positive effects on healing of lower-limb ulceration. One of the factors involved in this process is the PDGF, being responsible for the recruitment of MSC to the lesion site and subsequent angiogenesis stimulation. Due to the lack of treatment alternatives, it is necessary to search for new strategies to reversal ulcers diabetic patients. **Objectives:** Therefore, the objective of this project is to evaluate the immunobiological and regenerative effects of mesenchymal stem cells in the treatment of lower-limb cutaneous ulcers. **Materials and Methods:** To reach this proposal, MSC will be transfected with PDGF and angiogenesis assays, tissue regeneration and immunosuppression will be performed in order to evaluate their biological activity on the lesion. **Perspectives:** It is expected, therefore, contribute constructively to the scientific community, generating new knowledge, qualifying the professionals for

the elaboration of new strategies that aim to improve the quality of life of diabetic patients, minimizing the cost of and the morbidity and mortality rates of these patients.

Support: FAPESB, CNPq and PIBIC-UFBA.

Keywords: MSC, chronic ulcers, diabetes.

LINHA 02: Imunologia Aplicada

THE STUDY OF *CORYNEBACTERIUM PSEUDOTUBERCULOSIS* VISCERAL DISTRIBUTION OVER 180 DAYS OF AN EXPERIMENTAL INFECTION IN GOATS.

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Introduction: Caseous Lymphadenitis (CLA), caused by *Corynebacterium pseudotuberculosis*, is considered a chronic disease that afflicts goats and sheeps, This disease results in the formation of granulomatous lesions that may be presented in two main forms: external (also known as cutaneous or superficial) and internal (also known as visceral) (BAIRD & FONTAINE, 2008).**Objectives:** The goal of the present work is to evaluate and determine, through 180 days post infection with two *C. pseudotuberculosis* virulent and biofilm producer lineages – a strong (76-CapJ4) and a weak (21-Cap3W) – aspects of the humoral and cellular immune responses and the bacilum distribution in the main affected organs. **Materials and Methods:** 18 Canindé goats of both sexes will be raised at the experimental farm unit (Salinas das Margaridas, Bahia state). Twelve of them will be infected with the two lineages (6 infected with the 76-CapJ4 and the other 6 with the 21-cap3W lineages). The other six animals will be treated as control group and will receive a saline solution inoculum. From peripheral blood samples from goats experimentally infected with *C. pseudotuberculosis* will be evaluated aspects of humoral and cellular kinetics. The kinetics of the appearance of antibodies will be made by ELISA and the cellular reactivity will be evaluated *in vitro*, through a peripheral blood culture, under antigen stimulation of this pathogen. To evaluate the distribution of the microorganism in the affected viscera will be performed by fluorescence microscopy analysis, from fragments of lymph nodes, lungs, kidneys, liver and spleen, included in resin and cut (about 5µm) in cryostat. For the immunohistochemical study, the samples collected in the anatomic-pathological examination of the animals of the groups will be submitted to the preparation of histological sections according to standardized protocol in the Laboratory of Immunology and Molecular Biology (ICS-UFBA). the histological sections will be made in duplicate. **Perspectives:** CLA is highly frequent and it is estimated the majority of the flocks are infectd by *C. pseudotuberculosis*. There is a relation of the disease with low flock sanity, genetic profile and, mainly, with a low level of disease understanding of the producers. Thus, it is very important to know the immunological mechanisms as well as the host-parasite relationship in order to improve diagnostics, disease control and the development of new vaccines.

Suport: Labimuno, Fapex

Keywords: *Corynebacterium pseudotuberculosis*; Caseous Lymphadenitis; Biofilm; Immunohistochemistry.

LINHA 02: Imunologia Aplicada

EVALUATION OF THE IMMUNE RESPONSE TO RECOMBINANT HUMAN PDGF FOR THE TREATMENT OF CHRONIC CUTANEOUS ULCERS IN DIABETIC MICE

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Introduction: *Diabetes mellitus (DM) has become a serious disease that affects approximately 415 million people worldwide. People with DM have a 15% to 25% chance of developing a diabetic foot ulcer (DFU) during their lifetime. In the field of regenerative medicine for the treatment of chronic cutaneous ulcers, the clinical use of recombinant growth factors has been considered as a new and promising therapeutic alternative and only recombinant human PDGF (rh-PDGF) has demonstrated sufficient DFU repair efficacy to earn Food and Drug Administration (FDA) approval.* **Objectives:** *The goal of this project is to evaluate the immune response of rh-PDGF for use in biological activity assays in preclinical models of chronic cutaneous ulcers in mice and study the involved molecular mechanisms in tissue repair.* **Materials and Methods:** *Initially diabetes will be induced in mice by high dose of streptozotocin (STZ). After, full-thickness surgical wounds will be generated on the back of the mice for the chronic ulcer development and rh-PDGF will be administered intradermally. In vitro and in vivo biological activity, safety and toxicity assays, lymphocyte proliferation assays and pro/anti-inflammatory cytokine dosing will be performed***. Perspectives:** *We hope to obtain information on the efficiency of rh-PDGF injection in reducing the inflammation of diabetic ulcers and to elucidate the regenerative, angiogenic and immunological mechanisms of the therapeutic action of rh-PDGF in animal models of diabetic foot ulcer.*

Support: CNPq, FAPESB.

Keywords: Cell therapy, recombinant human PDGF, diabetic chronic ulcers, wound healing.

LINHA 02: Imunologia Aplicada

THE ROLE OF TOLEROGENIC DENDRITIC CELLS IN ATOPY

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Introduction: The dendritic cells (DCs) play an important role in the immunity, acting as a link between innate and adaptative immune systems, mediating the immune response including immune tolerance. Tolerogenic DCs have a lower capacity for induction of T cell proliferation, increased production of IL-10, and induction of regulatory T cells, potentially helping to treat immune mediated illnesses such as asthma and autoimmune diseases. **Objectives:** To study *in vitro* the role of tolerogenic dendritic cells in atopic individuals. **Materials and Methods:** This is a case-control study, composed of 20 volunteers, among them ten are healthy controls and ten are atopic. Atopy will be defined by positive skin prick test for environmental aeroallergens and by the presence of serum specific IgE for Phadiatop and *Blomia tropicalis* extract, detected by immunocap (Thermo Scientifica Phadia, AB, Uppsala Sweden). Dendritic cells will be induced from peripheral blood mononuclear cells (PBMCs) collected from participants with IL-4 and GM-CSF cytokines and will be sensitized with the extract of *B. tropicalis*, rTtFBPA (recombinant *Trichuris trichura* fructose bisphosphate aldolase), rTtMIF (recombinant *T. trichura* macrophage inhibitory factor), rTcCYS (recombinant Toxocara canis cystatin), and TLR 1/2 and 2/6 agonists. For the generation of tolerogenic dendritic cells, 10^{-6}M dexamethasone will be added to cells cultivated at the third day. Tolerogenic dendritic cells will be co-cultured with the participants' PBMC. The supernatants will be collected in 24h for the cytokines IL-12p70, IL-10 and TNF-alpha and 120h for IL-5 and IL-13 by ELISA (Kit eBioscience, San Diego, USA). **Perspectives:** To know the potential of dendritic cells for treatment

of allergic diseases and its immunomodulatory potential. The use of autologous dendritic cells in the treatment of asthma and other allergic diseases may result in an allergen-specific desensitization without necessarily having effects on the immunity of the individual. The treatment would then occur in the mechanism associated with the disease and not in its effects.

Support: FAPESB, CNPq

Keywords: Tolerogenic dendritic cell, allergy, atopy

LINHA 02: Imunologia Aplicada

ADAPTIVE IMMUNE RESPONSE FROM IgE ANTIBODIES IN CHRONIC HEPATITIS C

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Introduction: Hepatic C has a high prevalence rate worldwide. According to the World Health Organization (WHO, 2014), about 185 million people are infected with HCV in various populations distributed in different geographic regions. It is considered the greatest cause of liver disease in the world, with the possibility of developing cirrhosis or hepatocellular carcinoma, causing approximately 350,000 deaths each year. The detection of the presence of IgG antibodies to epitopes of core structural proteins, and non-structural (NS3 and NS5) is the basis of the standard serodiagnosis used in clinical laboratory and blood banks in the serological screening of donor candidates. However, the negativity of this IgG antibody response is not a parameter for monitoring the sustained virological response after antiviral treatment. The investigation of the immune response mediated by IgE antibodies to viral antigens in chronic hepatitis C has been neglected, with only rare reports on it. **Objective:** To develop and standardize ELISA tests with individual viral antigens to investigate the adaptive immune response mediated by IgE antibodies. **Materials and Methods:** 150 patients with anti-HCV IgG and HCV-RNA, without treatment, will be included. As controls will be used 150 healthy individuals from the same local population, negatively screened for anti-HCV IgG antibodies and RNA of this virus. In the IgE antibody test, the primary reaction will be performed with serum depleted of IgG due to the previous treatment with Sepharose – G Protein, while the secondary reaction will be conducted with anti-IgE monoclonal antibody conjugate. Serum levels of the cytokines IL-2, IL-4, IL-6, IL-10, TNF-α, IFN-γ and IL-17A of seropositive and seronegative patients for subclasses of IgG antibodies and IgE antibodies will be determined with the immunoassay multiparameter. **Perspectives:** The best knowledge of the adaptive immune response of IgE antibodies in chronic hepatitis C and its importance for patients infected with HCV during the treatment. Information about the importance of IgE immunoassays with the different viral antigens tested with a view to the serological diagnosis of this disease may also be obtained, including evaluating its usefulness in the follow-up of antiviral treatment and its importance for improving the quality of life of individuals infected with HCV.

Support: CAPES and CNPq

Keywords: hepatitis C, serodiagnosis, immunoglobulin E.

LINHA 02: Imunologia Aplicada

THE USE OF BCG VACCINE INCREASES SPLENIC CELL-NUMBERS THAT IS RELATED TO GREATER SURVIVAL IN A MODEL OF MELANOMA TUMOR GRAFTED INTO THE PINNA OF THE EAR OF C57BL/6 MICE

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Introduction: BCG is an attenuated *Mycobacterium bovis* vaccine that induces a non-specific increase of immune responses that can be essential for an effective antitumor response. As BCG is a promising immunostimulant. Our

aim is to test BCG as an adjuvant to anti-melanoma therapy. In this study, we evaluated tumor growth and survival of C57BL/6 mice grafted with B16F0 melanoma tumor cells into the pinna of the ear with the *in vivo* addition of BCG, locally. **Methods and Results:** Each animal received $5x10^4$ of B16F0 in 0.020mL intra-ear (i.e.). BCG were injected at $1,2x10^7$ /0.060mL *in situ* (i.e.) 10 days after tumor injection. Additional groups have received only tumor cells or only BCG, and a non-manipulated control group was also used. Tumor growth and mortality of the animals were monitored daily. Later on, splenic cells from experimental groups were evaluated by flow cytometry from day 11 to 18 after B16F0 cell-grafting. After inoculation of BCG *in situ* there was a remarkable reduction in tumor growth when compared to control group that received only tumor cells. Increased survival rates were observed in mice which received BCG($p < 0.0001$; Log-Rank test). In B16F0 control group, mice begin to die first compared to B16F0+BCG. Statistical difference in tumor size between groups was observed on the 18th day after injection of the tumor ($p=0.0298$, Mann-Whitney). Splenic dendritic cells (DCs) increased by day 18 after injection of B16F0 in C57Bl/6 mice that were treated with BCG, compared to C57Bl/6 injected with B16F0 alone ($p=0.0286$; Mann-Whitney test). Also on day 18, CD8 + T cells were found to be increased (BCG group compared to the other groups of mice) ($p=0.0348$;Kruskal-Wallis test). In the absence of BCG treatment, cells such as NK, NKT, DCs, and CD8, CD4 T lymphocytes have a trend to decrease from day 11 to 18, which may favor tumor development. **Conclusions:** BCG was able to decrease tumor size and significantly increase survival rates. Besides, BCG induced an increased number of dendritic cells and CD8 + T lymphocytes. Additionally, BGC increased survival after B16F0 injection and may induce strong, specific and non-specific immune system activation. Therefore, BCG (or some of their products) may be used to induce protection against tumor cells and to study the mechanisms involved in the control of melanoma.

Support: PAPES (407752/2012-9)-CNPq

Keywords: BCG, experimental melanoma

LINHA 02: Imunologia Aplicada

In vivo ADMINISTRATION OF *Trypanosoma cruzi* DECREASES THE NUMBERS OF SPLENIC MYELOID-DERIVED SUPPRESSOR CELLS AND INTRATUMORAL REGULATORY T CELLS, DURING THE GROWTH OF EXPERIMENTAL MELANOMA.

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Introduction: Infection or the *in vivo* presence of *Trypanosoma cruzi* (*Tc*) triggers a persistent immune response. Melanoma is an aggressive tumor. Evaluate a possible immunomodulatory activity induced by an avirulent *Tc* strain in the experimental melanoma system and whether it could interfere with B16F0 tumor development. **Methods and Results:** C57Bl/6 mice were divided into the following groups: I – Control: received saline; II – *Tc* group received only the specific strain of *Tc* (Y avirulent strain/inoculum of 0.2 mL of $300x10^3$ parasites); III – B16F0: received melanoma cells (B16F0 – 100µL $1x10^5$ cells); IV – *Tc*+B16F0: received *Tc* and later melanoma cells. We have investigated the following parameters: survival of the animals, tumor growth and the phenotypic profile of cells in the spleen and tumor (NK, NKT, Tregs and suppressor myeloid cells-MDSCs). Mann-Whitney test was used for statistical analysis. Results indicated that in the *Tc*+B16F0 group there was a 2-day delay in mortality and that in the B16F0 group there was a faster tumor growth during the analyzed period. At the end of 40 days after melanoma inoculation, we observed that B16F0 melanoma is lethal in both groups tested. On the 5th day, there was a decrease of NK and increase of NKT in the spleen of the animals in the group *Tc*+B16F0 when compared to the *Tc* group ($p=0,02$). However, when comparing the groups *Tc*+B16F0 to B16F0, there is a reduction of NK in*Tc*+B16F0($p=0,05$). Splenic MDSCs were decreased in the*Tc*+B16F0 group was when compared to the B16F0 on the 5th day ($p=0,0128$). Tumor-infiltrated Tregs cells were detected in all the groups with B16F0 melanoma. However, in *Tc*+B16F0, Tregs had a trend to decrease, at the 20th day. **Conclusion:** An important biological significance is due to the delay in mortality and containment of tumor progression in the Tc + B16F0 group, which may be associated with the initial increase of NKT, which is described to present an important tumoricidal function. Also, the increase of Tregs cells late in the tumor microenvironment may prevent an effective response to be established, which probably culminates in the reduction of an effector anti-tumor response. Increased MDSCs from the start may also be interfering with the antitumor activity of effector cells.

Support: PAPES (407752/2012-9)-CNPq.

Keywords: *T.cruzi,* experimental melanoma

LINHA 02: Imunologia Aplicada

IMMUNOMODULATORY POTENTIAL OF MESENCHYMAL STROMAL CELLS IN SICKLE CELL DISEASE

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Introduction: Sickle cell disease (SCD) is associated with a pro-inflammatory state. Inflammatory cytokines, elevated leukocyte, adhesion to vascular endothelium with subsequent endothelial injury, and repeated ischemia-reperfusion injury contribute to disease pathogenesis. Mesenchymal stromal cells (MSC) are multipotent progenitors that promote hematopoiesis and have unique immunoregulatory properties, making them attractive for use as cell-based therapy. The aim of this project is to evaluate the immunomodulation potential of MSCs in SCD. **Methods and Results:** Peripheral blood mononuclear cells (PBMC) were isolated from control and SCD patients using Ficoll Paque density gradient separator . Lymphocyte markers (CD4+/CD8+/CD3+) and viability (7AAD-) were evaluated before and after cryopreservation and assessed by FACS analysis. Expression of lymphocyte markers and cell viability were unchanged after 4 days culture and cryopreservation. MSC were isolated from adipose tissue and characterized. Isolated MSC from adipose tissue showed typical surface markers (CD29+, CD73+, CD90+, CD105) and multilineage potential for chondrogenesis, adipogenesis and osteogenesis. A standard immunopotency assay to measure MSC mediated T cell suppression was performed after PBMC:MSC co-culture with RPMI 1640 for 4 days at 37ºC humidified atmosphere 5% CO_2 . Anti-CD3/anti-CD28 or PHA were incubated with PBMC to stimulate T cell proliferation, in the absence or presence of MSCs. MSC-induced suppression of CD4+ T cell proliferation was monitored with CFSE and analyzed using flow cytometry. In the immunopotency assay, both PHA and CD3/CD28 beads activated CD4+ lymphocyte proliferation in the absence of MSC. CD4+ Lymphocyte proliferation was reduced when PBMC was co-cultured with MSC. **Conclusion:** The standardized immunopotency assay proved to be feasible and easy to perform, allowing future evaluation of development and characterization of immune response of MSC in SCD patients.

Support: FAPESB

Keywords: Mesenchymal stromal cells, Immunomodulation, Sickle cell disease

LINHA 02: Imunologia Aplicada

SUSCEPTIBILITY TO HEPATITIS B OF INDIVIDUALS AGED 30 TO 70 YEARS RESIDENTS IN SALVADOR-BAHIA, BRAZIL

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Introduction: Although there is an effective vaccine, hepatitis B is still a serious public health problem and is considered a sexually transmitted disease. Cultural habits affects the epidemiology of this infection.The *susceptibility* profile is characterized by the absence of serological contact and vaccination markers.In Brazil, introduction of the vaccine in the public health network was gradual and only in 2015 it was made available to individuals over 50 years old. Objectives were to estimate the frequency of the *susceptibility* profile to hepatitis B and identify possible risk factors for infection in a population sample served by the public health service and born between 1945/1985. **Methods and Results:** Cross-sectional study with 650 patients from one UFBA laboratory selected by lots.A questionnaire containing items about habits and health data was applied. Serological tests were performed for HBsAg/Anti-HBcTotal/Anti-HBs(chemiluminescence).Subjects with positive results for the first two markers were referred for medical care and those with all negative results received a recommendation to seek a vaccination station. The *susceptibility* profile was found in 68% of subjects, most of them women(71.5%) and participants aged 51-70(57.7%),both with $p<0.05$. The majority reported low level of education(43%).Family income of 1-3 minimum wages was informed by 46.8%.

Risk factors were: unsafe sex (96.6%), dental procedures (93.7%),previous surgeries(73.1%),sharing of personal hygiene items(53.4%),glass syringes(49,7%),syringe/needle sharing(29%), injectable vitamin complexes(18.6%),and less than 10% tattooing/piercing,illicit drugs and blood transfusion before 1993.The higher frequency of women may have resulted in the high prevalence of *susceptibility* found in females.The gradual supply of the vaccine in the public network and the high cost in the private network may have hindered the acquisition by low-income people.Incomplete vaccination schedule or non-vaccine responders should be considered.Despite unprotected sexual practices there may have been low viral circulation.The medical procedures to which the population submitted complied with the quality and biosafety criteria. **Conclusions:** Despite campaigns to stimulate condom use, the practice of unprotected sex is frequent. Analysis indicate high *susceptibility* to hepatitis B among individuals over 50 years of age. There is a need for greater attention from health services to this population segment.

Support: Laboratório de Imunologia e Biologia Molecular (ICS-UFBA), Serviço de Gastro Hepatologia do Ambulatório Magalhães Neto (AMN-HUPES), FAPESB, CNPq, PIBIC-UFBA, FAPEX

Keywords: hepatitis B, susceptibility, vaccine, HbsAg, Total Anti-HBc, Anti-HBs

LINHA 02: Imunologia Aplicada

PERIODONTAL MICROBIOME EVALUATION, IMMUNOLOGICAL AND IMMUNOGENETIC MARKERS OF PERIODONTITIS IN SEVERE ASTHMA

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Introduction: Asthma is an inflammatory origin chronic disease of the airways, currently considered as a public health problem. Periodontitis, which has also an inflammatory nature, is a multibacterial etiology chronic disease of the protective fabrics and the support of the teeth, which triggers several immunoinflammatory events. Recently, some studies have shown the influence of periodontitis in asthma either by aspiration of pathogenic organisms, either by raising the epithelium reactions triggered by the immune system. These pathogens have been reported as inducers of the expression of matrix metalloproteinases (MMPs). In addition, they induce the production of cytokines, which in turn lead to increased MMP levels in periodontal lesions. This aspect corroborates greater tissue destruction in both oral and respiratory mucosa. This study intend to evaluate the presence of microbiological and immunological markers periodontitis in individuals with severe asthma and subjects without the disease assessed by PROAR-Salvador/BA. **Methods and Results:** It will be tested the frequency of five periodontopathogenic microorganisms in the biofilm of all participants, the metagenomic of the presence microbiome in the oral mucosa of part of the individuals, the serum levels of anti-Porphyromonas gingivalis antibodies (ELISA) and, finally, polymorphisms in the MMP-1 gene (rs1799750), MMP-8 (rs11225395), MMP-9 (rs3918242) with real time PCR. The partial results of the presence of bacteria in the subgingival biofilm revealed no significant differences between the case group and the control group. **Conclusion:** The presence of the bacteria studied in the subgingival biofilm was not relevant for the biological plausibility that involves asthma and periodontitis. However, after the analysis of the final sample, this correlation may be different.

Support: FAPEX

Keywords: Periodontitis; periodontal pathogens; severe asthma

LINHA 02: Imunologia Aplicada

ASSOCIATION BETWEEN INCREASED PRO-INFLAMMATORY CYTOKINES (TNF AND IL-6) IN INDUCED SPUTUM AND WORSENING OF LUNG FUNCTION IN SEVERE ASTHMA PATIENTS

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Introduction: Asthma is a chronic, heterogeneous, multifactorial disease with multiple phenotypes. The aim of this study was to assess airway inflammation by counting induced sputum cells and measuring the cytokine and chemokines concentrations in the sputum fluids and associate them with the phenotypes of asthma in individuals from the city of Salvador – BA. **Methods and Results**: The study was performed in a total of 66 subjects, divided into three asthma groups [severe asthma resistant to treatment (16) severe asthma partially controlled with treatment (22), mild asthma (19)] and a healthy control group (9). The total cellularity of the sputum samples was counted using a hemocytometer and the differential cytology was observed in cytospin preparations. The measurements of cytokines and chemokines were performed by Luminex (Upstate / Millipore system "Flex kit" chemokines). The statistical analysis was performed using Kruskal-Wallis and Mann-Whitney test, with $p \leq 0.05$. **Results**: The sputum of severe asthma cases resistant to treatment presented increased percentage of neutrophils compared with mild asthma ($p = 0.046$) and eosinophils compared with healthy control group ($p = 0.021$). TNF was increased in the severe asthma resistant to treatment group compared to the healthy control group, mild asthma and severe asthma partially controlled ($p=0.001$). Asthmatic patients treated with high doses of corticosteroids presented higher amounts of TNF ($p = 0.021$) and IL-6 ($p = 0.011$). Increased TNF production was associated with poor lung function [reduction of FEV1 ($p = 0.003$; $p= 0.002$) and FEV1/FVC ($p = 0.029$; $p = 0.02$) pre and post bronchodilator respectively]. **Conclusion**: The measurement of TNF and IL-6 levels in induced sputum might be a biomarker for monitoring the response to treatment in patients with severe asthma in research and medical centers.

Support: FAPESB, CNPq, CAPES.

Keywords: severe asthma; total cellularity; inflammatory cytokines; induced sputum.

LINHA 02: Imunologia Aplicada

EVALUATION OF THE IMMUNOMODULATOR EFFECT OF LINALOL IN CHRONIC PERIODONTITIS

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Introduction: Periodontitis is a multifactorial immuno-inflammatory disease whose primary etiological factor consists of a mixed bacterial infection on the dental surface. Porphyromonas gingivalis is a key pathogen in disease progression having a central role in dysbiosis, characterized by an imbalance in microbial development in biofilm. The host response is preponderant in the onset and development of the disease. The treatment is based on the mechanical removal of the biofilm, with or without the use of antibiotics. The use of chemical adjuvants for the control of periodontitis has been advocated in several forms of administration, but the use of herbal remedies for this purpose is very restricted. With the recent search for alternative therapies, several plants have been studied with varied effects on different types of diseases. Linalool as a major component of essential oils of numerous plants has been tested with acaricide, bactericide and fungicide. **Objectives**: The present study aims to evaluate the immunomodulatory effect of linalool on peripheral blood mononuclear cells (PBMC) of volunteers with and without chronic periodontitis, contributing to

disease control. **Materials and Methods:** The PBMCs of 60 volunteers (30 with chronic periodontitis and 30 without periodontitis selected according to the criteria of Gomes Filho 2007) will be cultured in the presence of the sonicated extract of Porphyromonas gingivalis and linalool for 48 h at 37 C °, under a humidified atmosphere Of CO_2. It will then be checked the role of Linalool in lymphoproliferation and cell death by flow cytometry and to evaluate the inhibition or induction of IL-1beta, IL-8, IFN-gamma, IL-10, IL-6, IL-13 and IL – 17 by immunoassay (ELISA). After analysis of the data distribution with the Kolmogorov-Smirnov test, cytokine levels between healthy and diseased subjects will be compared using Student's or Mann-Whitney's T-tests. **Perspectives:** Linalool is expected to have a modulatory effect on the immune-inflammatory process, thus revealing itself as a potential adjunct in the control of the disease.

Support: FAPESB, UFBA and UEFS.

Keyword: Periodontitis; Linalool; cytokines

LINHA 02: Imunologia Aplicada

NEW N-ACYL HYDRAZONE DERIVATIVE (HAH 2) REDUCES INFLAMMATION IN A MURINE MODEL OF ALLERGIC AIRWAY INFLAMMATION

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Introduction: Asthma is a complex and heterogeneous chronic inflammatory disease, characterized by obstruction of the lower airways. It is estimated that about 300 million people have asthma worldwide and these estimates, as well as the severity of their symptoms, have increased in recent decades. Among the new synthetic molecules, a chemical group that has demonstrated a range of beneficial pharmacological effects is that of the hydrazones, which represent a versatile group, exhibiting a wide variety of biological effects. The compound HAH2 belongs to a new family of hydrazones, the N-acyl-hydrazones (HAH). The aim of this study was to investigate the therapeutic effects of HAH2 in BALB/c mice sensitized and challenged with ovalbumin. **Methods and Results:** Groups of 8 male BALB/c mice were immunized by subcutaneous injection of 10 µg of ovalbumin diluted in 2 mg/ml alum, followed by a booster injection at day 14. A nasal challenge was performed by inhalational exposure to aerosolised 1% ovalbumin for 15 min/day, on five consecutive days. Two hours before each aerosol delivery, mice were treated orally with HAH2 (5, 20 or 80 mg/kg), dexamethasone (20 mg/kg) or vehicle solution. Levels of ovalbumin-specific IgE antibodies were analyzed in serum of mice. Bronchoalveolar lavage (BAL) was collected to evaluate total leukocyte count and differential count. The right lobe of the lungs from each animal was removed for histological analysis. Animals presented an intense airway inflammation, evidenced by a high cellularity and eosinophilia in BAL. Administration of HAH2 by oral via caused the reduction of cellularity and eosinophils in the BAL. Treatment with HAH2 also reduced the cytokines IL-4, IL-5 and IL-13, an effect that was similar to that observed in dexamethasone-treated mice. In contrast, IgE production was not significantly altered after treatment with HAH2. HAH2-treated mice had a reduction in leukocyte infiltration in lung tissue compared to the control group. In addition, HAH2-treated mice demonstrated decrease mucus production compared to treated mice. **Conclusion:** The results show that HAH2 reduces the cellularity and eosinophil numbers in BAL, besides reducing levels of Th2-associated cytokines, suggesting the therapeutic potential of this compound.

Support: CAPES and PRONEX-FAPESB.

Keywords: Asthma, N-acyl-hydrazones, murine model, airway inflammation

LINHA 02: Imunologia Aplicada

EVALUATION OF THE PRODUCTION OF CYTOKINES AND CHEMOKINES IN SUPERNATANT OF WHOLE BLOOD CELLS IN RESPONSE TO SEVERAL STIMULI AND ASSOCIATION WITH ATOPY AND ASTHMA PROFILES

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Introduction: The increase in the prevalence of asthma in the last decades, especially in Latin America, has led to the interest of the study of this subject in the recent years. Due to a new sewage sanitary system and improvements in the population's living conditions of Salvador – Bahia has become a suitable place to investigate asthma and its relations with these sanitary improvements. The SCAALA (Social Changes, Asthma and Allergy in Latin America) program investigated the risk factors for asthma and atopy and the immunological profile in a cohort population study in 2005 and 2013. This present project is related to the2013 wave. **Objectives:** To quantify the IL-5, IL-13 and IFN-γ cytokine of mononuclear blood cells supernatant stimulated with different stimuli. **Materials and Methods:** The study population was composed of 1000 individuals from Salvador-Ba, born between 1994 and 2001 and residents in the suburb areas. Blood samples were collected, and whole blood culture cell culture were performed in the presence of RPMI1640, L-glutamine and antibiotics, 120 hours, at 37 ° C and 5% CO 2. The cytokines and chemokines productions in supernatant of cultures stimulated or not by *Ascaris lumbricoides*, Pokeweed and mites (*B. tropicalis, D. pteronyssinus*), BCG, Vit D, Vit D + Pokeweed (PKM),will be measured by Duo sets (BD-Pharmingen,USA) according to the manufacturer's recommendations. **Perspectives:** The project seeks to elucidate the relationship of environmental, genetic and immunological factors for the development of asthma and allergies. Understanding the mechanisms and environmental risks will allow, in the medium term, the adoption of prophylactic measures aiming to improve the quality of life of the population, reducing public expenditures and in, allowing the development of therapeutic intervention based on the molecular pathways here studied.

Support: FAPESB/PRONEX;

Keywords: Asthma, Atopy, Phenotypes.

LINHA 02: Imunologia Aplicada

CROSS-INHIBITION STUDIES OF GROUP-5 MITE ALLERGENS FROM *Blomia tropicalis* AND *Dermatophagoides pteronyssinus*

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Introduction: *Blomia tropicalis* is well recognized as an independent cause of allergic sensitization in countries with subtropical and tropical climate, although reports have been shown the co-exposure with *Dermatophagoides pteronyssinus*. Blo t 5 is known as a major allergen of *B. tropicalis,* whereas Der p 5 is usually considered a minor allergen of *D. pteronyssinus* in tropical regions. We aimed to investigate both the IgE response against these allergens in Brazilian and Austrian donors, as well as the IgE cross-reactivity between Blo t 5 and Der p 5. **Methods and Results:** A shortened version of Blo t 5 was heterologously expressed in *Escherichia coli* BL21 Star (DE3), purified and extensively

characterized by physicochemical experiments. rDer p 5 was obtained in collaboration with Indoor Biotechnologies (Charlottesville, VA, USA). The IgE reactivity to the allergens was verified through ELISA. Dose-response inhibition curves were performed to access the IgE cross-inhibition level between rBlo t 5 and rDer p 5 using 19 representative sera. The primary structure, the correct folding and lack of aggregation behaviour of rBlo t 5 were confirmed by mass spectrometry, amino acid analysis, circular dichroism, Fourier transform infrared spectroscopy measurements, and dynamic light scattering experiments. It was observed that IgE present in 86.7% and 80.0% of the sera from *B. tropicalis*-allergic donors from Brazil and Austria respectively have reacted with rBlo t 5. Meanwhile, 90.7% and 75.0% Brazilian and Austrian sera donors respectively had IgE reaction to rDer p 5. The maximal heterologous inhibition for rBlo t 5 and Der p 5 in the double positive sera was between 34.6% to 75.1% and 13.9% to 97.2%, respectively. The sera donors only sensitized to rBlo t 5 have presented heterologous inhibition above 40%, from 1 to 100 µg/mL of rDer p 5. On the other hand, the sera that were positive to rDer p 5 alone showed negligible inhibition with rBlo t 5. **Conclusion:** The IgE reactivity to rDer p 5 was significantly higher than previously observed in tropical areas. Moreover, while rBlo t 5 has presented low inhibitory capacity, rDer p 5 inhibitory capacity was considered moderate; thus, further studies, with a higher number of donors and a well-characterized cohort, will be required to identify the IgE epitopes that would be involved in this moderate cross-reactivity, as well as confirm Der p 5 as a major allergen in our region.

Support: FAPESB, CNPq – Science without Borders Program (grant 200307/2015-0).

Keywords: IgE reactivity, cross-reactivity, Blo t 5, Der p 5

LINHA 02: Imunologia Aplicada

EVALUATION OF IMMUNORREACTIVITY OF DOMICILIARY CONTACTS OF TUBERCULOSIS PATIENTS BY THE INTERFERON-GAMA RELEASE TEST (IGRA).

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Introduction: Quantiferon® (QFT, Cellestis) is a test used to diagnose infection caused by *Mycobacterium tuberculosis*. Its performance is superior to that of the currently used tuberculin skin test because its result is not influenced by previous vaccination with *M. bovis* Bacillus of Calmette-Guérin (BCG). We evaluated the QFT performance in detecting tuberculosis infection in newly diagnosed patients with smear-positive pulmonary tuberculosis (TB), as well as in detecting infection among their household contacts. **Methods and Results:** Patients older than 18 years of age who were newly diagnosed with pulmonary TB (index cases) and their respective contacts within 7 to 24 years of age were enrolled in health care units with the TB control program in Salvador-Bahia. The contacts should have lived with the index case for at least seven consecutive days during the three months preceding the diagnosis of tuberculosis in the index case. Volunteers with negative QFT were followed longitudinally and were reevaluated after two, six and twelve months or until conversion to a positive test in the same interval. 100 volunteers were recruited (42 index cases and 58 contacts). A positive QFT was obtained in 38 (91%) of the index cases, while 3 (7%) were negative and 1 (2%) had an indeterminate result. Among the contacts, 35 (60%) had negative QFT and were included in the cohort. To date, 27 of these contacts have already been submitted to the second evaluation (two months after recruitment). After six months, 19 volunteers that were QFT-negative at the two-month interval were re-evaluated, among whom 15 (79%) remained negative in this third evaluation. Follow-up was completed for seven volunteers (at 12 months after recruitment): 4 remained negative and 3 are on-going. Test conversion was observed for six volunteers between time zero and two months (17%), as well as for one volunteer between 2 and 6 months (5%). These results suggest infection from the index case or late detection of individuals who were already infected at time zero due to insufficient QFT sensitivity. **Conclusion:** Our results are in agreement with a good QFT sensitivity to identify TB infection in a sample of patients in whom comorbidities are not frequent, as well as immunosuppressive conditions are not expected.

Support: FAPESB, PIBIC-FIOCRUZ.

Keywords: Latent tuberculosis; Interferon-gamma release assay (IGRA); household; Performance.

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

ASSESSMENT OF ANTI-INFLAMMATORY ACTIVITY OF NEW INHIBITORS OF $mPGES_1$ IN ARTHRITIS MODEL IN MICE

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Introduction Rheumatoid arthritis (RA) is an autoimmune pathology of progressive inflammatory trait, in which genetic and environmental factors contribute to the loss of tolerance to its own antigens. This pathology affects about 0,5-1,0% of the world's adult population. The known undesirable gastric and cardiovascular effects of analgesics, and the toxic effects of immunosuppressant and monoclonal antibodies, are preponderant in the non-adherence to RA treatment. In this perspective, the researches for drugs for inflammatory diseases have grown significantly. The mPGES1 enzyme has been reported in the literature as a promising new therapeutic target for this therapy. **Objectives:** The objective of this project is to assessment the anti-inflammatory activity of new inhibitors of $mPGES_1$ in an experimental model of zimosan-induced arthritis in mice. **Materials and Methods:** The experiments will be performed using male mice of the Swiss lineage. The drugs were initially identified by virtual screening through a pharmacophoric model and obtained from commercial providers by the LABIMM research group. The animals will undergo treatment before and after induction of arthritis with zimozan (intra-articular injection). The swelling of the knee joint will be assessment by measuring the transverse diameter of the left knee using a digital caliper, two, four and six hours after zymosan injection. The leukocyte migratory profile and the cytokine and PGE_2 dosage will be evaluated by cellular lavage with counting in the Neubauer chamber and ELISA method, respectively. In the experimental standardization, the increase of the proliferative profile of neutrophils and joint diameter was verified in the animals submitted to zymosan. **Perspectives:** Considering the previous work by Froes et al. (2015), with studies of the antipyretic profile of molecules with *in silica, in vitro* and *in vivo* research linked with an understanding of the pathophysiology of arthritis and the mechanism of action of $mPGES_1$ in the induction of inflammation, it is expected that these selective inhibitors also have an anti-inflammatory joint profile through inhibition of prostaglandin E_2 production.

Support: CNPq e FAPESB.

Keywords: Inflames; PGE_2; Rheumatoid arthritis

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

NEGATIVE ASSOCIATION OF TNF BLOOD LEVELS WITH OXYGEN SATURATION IN PATIENTS WITH COPD FALTAM SUPPORT E KEY WORDS

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Introduction: Chronic Obstructive Pulmonary Disease (COPD) is characterized by airflow limitation, eventually caused by exposure to inhalation of noxious particles or gases. Chronic inflammation has been observed in patient with COPD, which exhibit high levels of inflammatory cytokines in peripheral blood. Studies indicate that this systemic inflammation play a role in the pathogenesis of COPD. The aim of this study was to evaluate whether TNF blood level were associate with disease severity markers in patients with COPD. **Methods and Results**: Twenty-one patients (9 females and 12 males) were evaluated. The disease severity markers evaluated were spirometry, six-minute walk test, peripheral oxygen saturation (SpO_2) and dyspnea index. TNF was determinate in peripheral blood by ELISA technique. There was an negative association between TNF blood concentration and SpO2 levels ($r = – 0.5$ and $p < 0.05$). Female patients (mean ± SD = 4.5 ± 2) showed a tendency in higher levels of TNF in relation to males (mean ± SD= 2.5 ± 1.8, p=0.0512). **Conclusions:** These results indicate that systemic inflammation observed in COPD could be associated with worse pulmonary function.

Support: FAPESB.

Keywords: COPD, TNF, SpO2.

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

LUPEOL PRESENTS *IN VITRO* NEUROPROTECTIVE AND GLIAL MODULATORY FUNCTION IN CEREBELLUM CULTURES

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Introduction: Neuroinflammation is mainly based on astrocyte and microglial activity in the presence of some chemicals, pathogens and central nervous system (CNS) dysregulations, this inflammatory mechanism is primordial for the progression of neurodegenerative diseases (DNG's) such as Multiple Sclerosis and Alzheimer's disease. Lupeol is a triterpene found in plants such as *Betula alnoides.* It has several activities already described by the scientific community among them: anti-inflammatory, anticancer, and by some actors anti-inflammatory activity *in-vivo* models of DNG's like Allzheimer. **Methods and Results:** Cerebellar primary cultures of wistar rats with eight days of birth (p8), cultured for three days in a CO^2 oven at 5%, and treated with 0.1uM Lupeol and modulated with 1µg / mL LPS. The cultures were evaluated by MTT to measure viability of cells, Fluoro Jade B observed the percentage of viable neurons, nitric oxide dosage observing the anti-inflammatory capacity of Lupeol, and Immunocytochemistry techniques where the morphology of astrocytes and neurons was observed It is possible to observe lupeol's ability to increase cell viability in cerebellum cultures using the MTT assay. Levels in pg / mL of nitric oxide were reduced in the treatments with Lupeol, and percentage of FJB + neurons was reduced to levels lower than that of baseline death of the control. In this work we can observe in which mechanisms Lupeol is acting in the inflammatory modulation as the increase of astrocytes with Bergmann profile, also reducing the percentage of astrocytes with reactive morphology. Population of astrocytes from the Tyocites profile, another modulating activity observed was the ability to increase the percentage with polygonal profile. **Conclusion:** Lupeol has been shown to protect neurons from neuroinflammation generated by LPS, probably acting as a neurogenic drug, suggesting to Lupeol an important protective activity to neurons and glial modulation in neuroinflammation models in cerebellum cultures. Suggesting lupeol, as drug, with therapeutic potential in neurodegenerative disorders.

Support: FAPESB e CAPES.

Keywords: Neuroinflammation, immunomodulatory, Glial modulatory, Lupeol.

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

STANDARDIZATION OF THE IN VIVO EXPERIMENTAL MODEL OF INDUCTION OF DAMAGE BY AMINOCROTIC WISTAR RATS AT THE LABORATORY OF NEUROCHEMISTRY AND CELL BIOLOGY

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Introduction: The Parkinson's disease (PD) is mainly characterized by the loss of dopaminergic neurons containing neuromelanin in substantia nigra pars compacta. The mechanisms responsible for this neurodegeneration remain unknown, however, some cellular and molecular disorders are considered involved in this process, α-synuclein accumulation, oxidative stress, mitochondrial damage, proteosomal dysfunction, autophagic dysfunction and neuroinflammation. Many of the effects mentioned above, among them, neuroinflammation plays a crucial role in the aggravation of the neurodegenerative process, capable of generating an unhealthy environment for the neurons, as a consequence of the exacerbated release of inflammatory components. In this sense, this work has as main focus the study of the anti-inflammatory effects of in vivo model of Parkinsonism induced by aminochome. **Methods and Results:** For the in vivo experiments we used Wistar (machos, 200-250 g). The aminochrome was applied by stereotactic in the striatum region located in the forebrain, the animals were divided into four groups, (saline control, 200 µM aminochrome, 1000 µM aminochrome and 200 µM aminochrome + Dicumarol 100 µM), all experimental procedures were sanctioned by the animal research ethics committee under protocol no. 011/2017. At 14 days after injection of the toxin, the animals were submitted to behavioral tests of the Open-field and cylinder tests. In the open field test it was observed that the animals that received aminochrome 200 µM and 200 + DIC µM increased the number of peripheral crossings and 1000 µM aminochrome reduced the peripheral crossings in relation to the control group. Aminochrome 200 and 1000 µM and 200 µM + DIC increased the grooming time in relation to the control. In the cylinder test it was observed that animals treated with 200 and 1000 µM aminochrome increased the number of contralateral touches. **Conclusions:** These results suggest that aminochrome at the concentration of 1,000 µM may be a good candidate as concentration of choice for future experiments in vivo to evaluate neuroprotective effects of flavonoids or other potential drug in perspective.

Support: FAPESB, CNPq and CAPES.

Keywords: Aminochrome, Behavioral Testing, Parkinson's Disease.

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

AGATHISFLAVONE PROTECS SH-SY5Y CELLS AGAINST MITOCHONDRIAL DAMAGE AND LYSOSOMAL DYSFUNCTION INDUCED BY AMINOCHROME

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Introduction: Parkinson's disease (PD) is one of the most prevalent neurodegenerative diseases. There are several hypotheses to explain the cause of dopaminergic degeneration in this pathology, such as alpha synuclein accumulation; dysfunction of altered protein degradation, mitochondrial dysfunction; oxidative stress; and neuroinflammation. Aminochrome has been suggested as a more physiological preclinical model capable to inducing five of the six mechanisms of neurodegeneration in PD. **Methods and Results:** In this study, SH-SY5Y cells were cultured in DMEM-HAMF12 medium and maintained under 5% CO2, 37° C. Cells were treated with agathisflavone at concentrations of 0.1-50 µM, for 24 h and / or exposed to 10 µM aminochrome, for 24 h. The neuroprotective activity was performed by the calcein AM and propidium iodide test; the analysis of mitochondrial damage was performed by JC1 and the analysis of lysosomal dysfunction was performed by acridine orange and lysosensor dyes. We have shown that the agathisflavone does not present a cytotoxic profile in SH-SY5Y cells exposed to concentrations of 0.1-50 **µM**, for 24 h. In addition, the flavonoid at concentrations 0.1 and 1 **µM** protected the cells against aminochrome (10 **µM**) induced damage, for 24 h exposition. Moreover, we have shown that agathisflavone (0.1 and 1 **µM**, for 24 h) did not cause lysosomal dysfunction, characterized by increased red fluorescence when compared to control. Aminochrome (10 **µM**, for 24 h) induced loss of lysosomal acidity and agathisflavones (0.1 and 1 **µM** for 24 h) restored the acidification of this organelle. In addition, agathisflavone (0.1 and 1 µM, for 24 h) was able to maintain normal mitochondrial membrane potential in cells submitted to neurotoxin damage. **Conclusions:** These results demonstrate the neuroprotective ability of agathisflavone to reestablish the acidity of organelles that are essential for the maintenance of cell viability, pointing to this flavonoid has a potential as a possible therapeutic agent for the treatment of Parkinson's Disease.

Support: CAPES/PVE.

Keywords: aminochrome, flavonoids, Neuroprotection.

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

EFFECTS OF RUTIN ON EXPRESSION OF MICROTUBULE-ASSOCIATED PROTEIN 1A/1B-LIGHT CHAIN 3 (LC3) UP-REGULATED BY MICROGLIA CONDITIONED MEDIUM IN PC12 CELLS

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Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disorder in developed countries. Its incidence has increased exponentially since the 1960s and there are predictions that will increase dramatically with the increase in life expectancy, since it is strongly associated with aging. Studies have been shown the involvement of soluble molecules derived from microglia, such as TNF and NO, in the dopaminergic neurodegeneration. Actually, one of the main therapeutic strategies for development of new therapies for PD is the look for anti-inflammatory and neuroprotective agents. **Methods and Results:** Primary microglial cultures from P8 rats (ICS/CEUS 0027/2012) were treated with LPS and/or rutin and the conditioned medium (CM) with or without SFB was collected after 24 h. Following, the MC (with or without SFB) was used to treated PC12 cells. The expression of autophagy markers in PC12 cells was evaluated by Western Blot for LC3 and P62, after 24 h exposure to MC. It was observed that the use of CM without FBS, from microglia exposed to LPS, induced a higher expression of LC3-II and P62 on PC12 lineage cells. Furthermore, it was also possible to observe the reduction of LC3-II and P62 expression on the groups treated with the MC from microglia exposed to LPS and rutin concomitantly. **Conclusions:** We suggest that the anti-inflammatory effect of rutin may interfere in neuroprotective mechanisms associated to release of microglial molecules that inhibits the autophagy. More research needs to be done to clarify the neuroprotective mechanisms of rutin on experimental models of Parkinson's disease.

Support: FAPESB, CAPES

Key-words: Parkinson's disease, autophagy, TNFα, neuroprotection, flavonoid.

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

INVESTIGATION OF THE EFFECT OF FLAVONOIDS ON THE MODULATION OF ENTERIC GLIA ASSOCIATED WITH THE INTESTINAL MICROBIOTA IN MODELS OF PARKINSON'S DISEASE

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Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disease in developed countries. It is estimated that around 1.5% of the world population over 65 years is affected by PD and that its prevalence is increasing due to the progressive aging of the population. The mechanisms responsible for the loss of dopaminergic neurons that contain neuromelanin in substantia nigra pars compacta remain unknown, however it is already well established that as lesions are multicentric and affect neuronal structures outside the CNS with involvement of the enteric nervous system. Damage associated with the development of PD may start in the gut, so there is a possibility that the CNS may be affected by the modification of the intestinal environment. Therefore, alteration of the intestinal microbiota should be considered in the onset of PD. The intestinal microbiota influence neurodevelopment, modulate behavior, and contribute to neurological disorders. However, a functional link between gut bacteria and neurodegenerative diseases remains unexplored. Another interesting fact is that natural substances, like the flavonoids, can lower the risk for the development of PD. **Objectives:** To investigate the effect of modulator of flavonoids on enteric glial associated with intestinal microbiota in experimental models of PD. **Materials and Methods:** We will perform Induction of experimental model of Parkinson's disease in adult Wistar rats by administration of aminocromo that will be divided into groups treated or not by flavonoid (Rutin). We will determine the profile of the intestinal microbiota by the qPCR technique and quantify 2 families of bacterium: Prevotellacea and Enterobacteriacea, using group-specific primers to amplify the gene encoding the 16S rRNA. In addition, glial cells will be cultured for immunoblotting of GFAP, SOX10 and S100b and we will perform immunohistochemistry of gut sections from the mice with PD. **Perspectives:** Given these projections, it is expected that at the end of this project it will be possible to clarify neuromodulator mechanisms of flavonoids against the enteric glial associated with the intestinal microbiota. We wish to observe if the response of the Enteric Nervous System will be altered in experimental models of PD in this modulation.

Support: FAPESB and CAPES

Keywords: Parkinson's disease, Enteric Glia, intestinal microbiota, flavonoids.

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

INVESTIGATION OF NEUROPROTECTIVE AND ANTI-INFLAMMATORY ACTIVITY OF APIGENIN *IN VITRO* MODELS OF NEUROINFLAMMATION TODOS OS NOMES ABREVIADOS

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Introduction: Alzheimer's Disease (AD) is characterized by accumulation of the β amyloid protein (Aβ) and increase of inflammatory response mediated by microglia and astrocytes, which once activated, release pro-inflammatory cytokines such as IL1β, resulting in neurodegeneration. This study evaluated the neuroprotective and anti-inflammatory potential of flavonoid apigenin *in vitro* models of neuroinflammation induced by LPS, IL1β or Aβ. **Methods and Results:** Co-cultures of neurons and glial cells were cultivated from the cortex of Wistar rats. Cells were exposed for 24 h to LPS (1µg/mL) or IL1β (10ng/mL) or for 4 h to o*ligomers* Aβ (500 nM) and then treated with apigenin (1µM) for more 24 h. It was observed by Fluoro Jade B and caspase 3 immunostaining that apigenin was not neurotoxic and has a neuroprotector effect against inflammatory damage. The immunofluorescence analysis revealed that apigenin reduced microglial inflammatory activation and proliferation through decrease of staining for CD68 and BrdU markers, respectively, and preserved neuronal and astrocytic of cellular integrity, also modulating the microglial morphological pattern, determined by staining for βtubulin III, GFAP and Iba1 proteins, respectively. The immunomodulatory effect of apigenin, evaluated by qPCR demonstrated that apigenin did not induce changes on expression of IL-6, IL-1β and CCL5 and induced increase the expression of BDNF. IL-1β treatment induced increase in the levels of IL-1β, IL-6, and CCL5, and decrease the expression the IL10 and BDNF. However, association of apigenin to IL-β induced decrease in the expression of IL-6 and CCL5 and increase the expression of IL-10 and BDNF. **Conclusions:** These data suggest that apigenin presents neuroprotective and anti-inflammatory potential.

Support: CNPq, CAPES

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

LINHA 03: Imunofarmacologia e Neuroimunoendocrinologia

A NEW MODEL OF GESTATIONAL DIABETES MELLITUS IN MICE AND ITS CONSEQUENCES TO THE CENTRAL NERVOUS SYSTEM OF THE OFFSPRING

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Introduction: Gestational diabetes mellitus (GDM) is the glucose intolerance that occurs during pregnancy. Propensity to obesity and cognitive decline in offspring born to diabetic mothers has been suggested, but the mechanisms involved are unknown. The aim of this study was to establish a new model of GDM in mice and evaluate effects on the cognition of the offspring in adulthood. **Methods and Results:** Swiss mice (12 weeks, 25 to 40g) were mated. Females received either saline or S961 (30nmol/kg/day,s.c.) starting on the 7th gestational day until delivery. Fasting glycemia and glucose tolerance test (GTT) were performed 7 days after starting the treatment, and dams which received S961 presented higher values. S961 group showed elevated water consumption. S961 treatment did not cause differences in maternal behavior, physical and reflex development of the pups, and neither in locomotion or the anxious profile. Offspring received a high-fat diet (HFD) or standard diet between P60 and P90 and locomotion and anxious profile were revaluated, but did not present statistical differences. Males and females offspring submitted to intrauterine hyperglycemia and fed with HFD presented higher body mass values, but just males revealed cognitive impairment at hippocampal memory task. Hippocampus were collected from the males for western blot and analyzed. Results indicate an increased inflammatory profile, and a greater activation of GSK3β pathway. Student's *t* test, area under the curve (AUC), one and two-way ANOVA and Tukey's post-test were used to statistical analysis at Graph Pad Prism 6.0. **Conclusions;** A new model of GDM was described. Offspring had normal behavior when evaluated in adulthood, but responded exaggeratedly when exposed to HFD, developing obesity and early cognitive impairment.

Support: Capes, CNPQ, Faperj.

Key words: *gestational diabetes, memory, S96,1 obesity, high-fat diet.*

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

INSULIN RESISTANCE AND RISK OF CARDIOVASCULAR DISEASES IN HEPATITIS C

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Introduction Insulin resistance (IR) has frequently been described in patients chronically infected with hepatitis C virus (HCV). However, the association between type 2 diabetes mellitus and cardiovascular diseases (CVD in hepatitis C still is controversial. Objective: We investigated the presence of IR, CVD risk factors, and dyslipidemia in Brazilian patients with chronic hepatitis C living in Bahia. **Methods and Results:** Twenty-five patients chronically infected with HCV, of both genders and age ranging from 41 to 78 years were evaluated. Production of atherogenic and anti-atherogenic cytokines by peripheral blood mononuclear cells (PBMC) stimulated with phytohemagglutinin (PHA) was also investigated in these individuals. Thirty-five dyslipidemic subjects with atherosclerosis (age range = 45-75 years) and 27 healthy individuals (age range = 37-65 years) formed the control groups. The median of HCV viremia in the patients was 6,26 x 10^5 IU/mL, predominating the infection by HCV genotype 1, which was followed by HCV gen 3 and 2. Mild to moderate stages of fibrosis and liver necroinflammatory activity was found in 77% and 56% patients, respectively. Insulin resistance, corresponding a HOMA-IR ≥2,5 was observed in 48% of them. However, IR was not associated with CVD risk factors as hypertension, diabetes mellitus, metabolic syndrome or obesity. The median apo B/apo A ratio in HCV subjects (0.64) and healthy controls (0.66) was similar but differed from that presented by atherosclerosis individuals (0.91, P=0,065). PCR levels were also increased only in the group with atherosclerosis (P=0,0099). The CMSP from these three groups differed in their production of IL-6 and IL-10 after PHA stimulation (P < 0.0001 and P = 0.0095, respectively). **Conclusion:** Insulin resistance is a clinical condition commonly associated with chronic HCV infection in Brazilian patients. However, these individuals do not present risk factors for cardiovascular diseases or alteration in CVD serum biomarkers related to dyslipidemia and atherosclerosis.

Support: CAPES and FAPESB (PPSUS).

Keywords: chronic hepatitis C; inflammatory biomarkers; cardiovascular risk; insulin resistance

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

CROSS-ANTIGENICITY OF *CORYNEBACTERIUM PSEUDOTUBERCULOSIS* MOLECULES IN IMMUNE CELLULAR RESPONSE IN VITRO OF INDIVIDUALS INFECTED WITH *MYCOBACTERIUM TUBERCULOSIS*

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Introduction: Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*M. tuberculosis*), is an infectious disease that mainly affects the lungs. Although TB is a millennial disease, it remains a serious public health problem in several regions of the world. *M. tuberculosis* and *Corynebacterium pseudotuberculosis* (*C. pseudotuberculosis*) share some virulence/pathogenicity factors which was confirmed by bioinformatics analysis. Proteins must be analyzed for cross-reactivity studies, by the evaluation of cellular immune response. The aim of this study was to evaluate *in vitro* immunoractivity of semi-purified soluble extract of *C. pseudotuberculosis* strains in a proposed model with samples of patients with diagnosis of active pulmonary tuberculosis. **Methods and Results**: This study was approved by the Research Ethics Committee ICS-UFBA (CAAE 57662016.8.1001.5662) and all participants signed the Informed Consent Term. Voluntary participants of the Hospital of the Specialized Hospital of pulmonary diseases of Bahia, with diagnosis of TB and without treatment (n=35) and participants adults, without complains, no history or symptomatology of TB or of *M. tuberculosis* infection (n=35). With heparinized blood, after white blood cell count, the plate stimulation was carried out using mitogen (PWM) and *C. pseudotuberculosis* secreted protein extract (strains A, B and C). The cytokines were measured by BD Cytometric Bead Array (CBA) Th1/Th2/Th17 Cytokine Kit and the BD ™ CBA Human IP-10 Flex kit. Analyzes were performed with FCAPArray™ software. Secreted Extract of *C. pseudotuberculosis* induced the production of the cytokines in the blood samples in the studied groups. In addition, they differentiated the study groups when compared to IFN-γ and IP-10, under stimulation with Strain A; IFN-γ, IL-2 and IL-6, under stimulation with B Strain and IP-10 and IL-4, under stimulation with C Strain. **Conclusion**: The extracts from A, B and C Strains of *C. pseudotuberculosis* induce

the production of IFN-γ, IP-10, TNF, IL-2, IL-6 and IL-10 in blood samples from individuals infected with *M. tuberculosis*. Under the stimulus of the extracts used, the detection of IFN-γ and IP-10 differentiates the control and active TB groups.

Support: CAPES, CNPq, LABIMUNO, PPGIm, PIBIC-UFBA.

Keywords: *Corynebacterium pseudotuberculosis*; immunoractivity; *Mycobacterium tuberculosis*

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

REVERSE VACCINOLOGY IN MURINE AND CANINE MODEL FOR THE CONTROL OF *Toxocara canis* INFECTION

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Introduction: toxocariasis is a zoonosis of global importance, toxocariasis has recently been named one of the five neglected parasitic infections in the USA by the CDC; *Toxocara* infection in pets and fecal egg shedding are of great public health importance, up to now there is no program to control this infection, and vaccination may provide a good tool to achieve this goal. **Objective:** this research will be applied the methodology of reverse vaccinology in the murine and canine models with the aim of contributing to the control of toxocariasis in canines through immunoprophylaxis. **Materials and methods:** from the genome and proteome of *Toxocara canis*, an *in-silico* analysis, it was select 8 proteins of immunogenic interest. These proteins were expressed in bacterial vectors, purified, and are been tested in murine model, in a project already in course in the Laboratory. For the present project, the best proteins will be pooled and used to immunize C57Black mice in a using different adjuvants (N-Glycolyl-MDP VacciGrade™ and Gardiquimod VacciGrade™ Th1 profile; and Quil-A® and Chitosan VacciGrade™ Th1/Th2 profile). RNA from PBMC will be purified and the expression of the cytokines IL-4, IL-5, IL-10, IL-12, TNFα, INFɣ and TGF-β will be carried out through PCR; the immunoglobulin profile will be investigated using indirect ELISA commercially available (IgG, IgM, IgA, IgE); also histopathological analysis will be carried out. The best adjuvant will be selected for further immunization of dogs with the proteins. The experiments in dogs will be carried out in dogs cells and in *in-vivo* immunization using animals from a private dog kennel. These studies will be done in collaboration with Prof. Stella Barroiun, researcher from the Medical Veterinary School of UFBA. **Perspectives:** It is expected that this project will have as a product a vaccine for toxocariasis which might be used for dogs, therefore decreasing the environmental contamination with this parasite eggs and possibly will have an impact in the control of human toxocariasis.

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

Keywords: Human toxocariasis, immunoprophylaxis, vaccine, zoonosis.

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

EXPRESSION AND CHARACTERIZATION OF IMMUNODOMINANT PROTEINS FOR THE IMMUNODIAGNOSIS OF TOXOCARIASIS, SELECTED THROUGH IMMUNOPROTEOMIC ANALYSIS OF *TOXOCARA CANIS* LARVAE EXCRETORY/SECRETORY PRODUCTS AND EXTRACT

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Introduction: Toxocariasis is an important zoonosis caused by the parasitic nematodes *Toxocara canis* or *T. cati*. In humans, when *Toxocara* spp. Eggs containing infective larvae are accidentally ingested, the eggs hatch in the small intestine and larvae migrate through somatic organs and systems, preferably liver, eyes and brain. The most common method available for serodiagnosis of toxocariasis is an enzyme-linked immunosorbent assay (ELISA) using *Toxocara canis* excretory-secretory antigens (TES). However, it has been shown that ES antigens are cross-reactive against serum samples from patients with a variety of helminth infections and environmental allergens. Therefore, the aim of this study was to identify immunodominant antigens of *Toxocara canis* recognised by sera of *Toxocara* spp infected donors for the development of more specific immunodiagnosis to toxocariasis**. Methods and Results:** An immunoproteomics of *T. canis* larval TES and total extracts was used to identify potential molecules useful for the immunodiagnosis of toxocariasis. Four proteins were identified that immunoreacted with sera from *Toxocara* spp –infected hosts (Mucin, CTL-4, TES-32, and TES-26). The gene sequences of the identified proteins were optimized for expression in *Escherichia coli* system, synthesized and cloned in the plasmid pET-28 a (+) by a commercial company (Genscript, Piscataway, NJ, USA). The plasmid was transformed into *E. coli* BL21 (DE3), and the induction was done with IPTG at 37°C overnight. Proteins were expressed with polyhistidine-tag, purified by immobilized metal affinity chromatography (IMAC) and analyzed in 12% SDS-PAGE Results: The recombinant proteins were successfully expressed, purified and their expressions were confirmed by Western blotting using anti-His antibody. **Conclusions:** Four proteins of *Toxocara canis* were identified by immunoproteomics using sera of positive

donors. The recombinant versions of these proteins were expressed in *E. coli* and purified by IMAC.*Toxocara* spp-positive serum pool will be tested with the recombinant proteins rMucin, rCTL-4, rTES-32, and rTES-26 using an enzyme-linked immunosorbent assay (ELISA) and Western bloting using sera from donors with different helminth infections to test the specificities of these molecules. These molecules can be used in future to develop a highly specific, sensitive and low cost assay for the diagnosis of human toxocariasis.

Support: CNPq and UFBA

Keywords: immunodiagnostics, recombinant protein, toxocariasis

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

IMMUNOMODULATORY EVALUATION OF LEAVES EXTRACTS OF *L. insiginis* AND *L. origanoides* PERIPHERAL BLOOD OF PATIENTS WITH CHRONIC PERIODONTITIS

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Introduction: Periodontitis is an inflammatory, infectious and multifactorial disease resulting from mixed bacterial inflammation (primary factor) of tissues supporting the teeth and progressive loss of conjunctive insertion.Thus, studies demonstrate that resistance to conventional antibiotic therapy and oral antiseptics demand the search for new methods to support the clinical treatment of periodontitis. For this reason, the use of medicinal plants such as *Lippia origanoides* and *Lippia insiginis* are important therapeutic resources for the prevention and treatment of periodontal diseases. **Methods and Results:** The leaves *of Lippia origanoides* and *Lippia insiginis* were collected and processed to obtain the crude extract made by LAPRON. After obtaining the crude extracts of these plants, dilution with DMSO/Methanol at 3% was carried out, with this dilution the protein dosage was performed by the Lowry technique. Subsequently, some concentrations (10 µg / mL, 100 µg / mL in 1000 µg / mL) of the extract diluted with both DMSO/Methanol 3% and ethanol were used for the cytotoxicity test with *Artemias salinas*. The participants were invited and chosen using exclusion criteria. From this, a periogram for the identification and classification of periodontitis was performed using the Gomes-Filho criterion (2012). In addition, a volume of 30mL of peripheral blood was collected from the participants to perform the culture of whole blood cells stimulated by *Porphiromonas gingivalis* antigens, *Pokeweed* and extracts from L. insiginis and L.origanoides with the objective of studying the inhibition or induction of IL-1β, IL-8, IFN-γ, IL-10 and IL-6 cytokine production by the ELISA technique. According to the results already obtained, a low cytotoxicity at concentrations of 10 µg / mL, 100 µg / mL for the *L. origanoides* extract at 24, 48 and 72 h was observed for both dilutions; for the *L. insiginis* extract the concentrations of 1000 µg/mL, 100 µg/mL and 100 µg /mL were lower at the DMSO/Methanol 3% dilution than Ethanol at the same time. **Conclusion:** Preliminary results indicate that the extracts do not present a high cytotoxicity for extracts of *L. origanoides* and *L. insiginis*. Despite this the continuation of the studies are necessary for the understanding of extracts in periodontitis.

Support: CAPES, NUPPIM-UEFS, LAPRON-UEFS, LABIMUNO-UFBA.

Keywords: Citoxidade,Periodontite, *Lippia, Porphiromonas gingivalis*

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EVALUATION OF IMMUNOMODULATORY EFFECTS OF RECOMBINANT *TRICHURIS TRICHIURA* (rTtMIF AND rTtFBPA) AND *TOXOCARA CANIS* (rTcCis) PROTEINS *IN VITRO* AND IN EXPERIMENTAL MODEL OF RESPIRATORY ALLERGY

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Introduction: The prevalence of allergic diseases has been growing steadily throughout the world, among them asthma is noticed for affecting a large part of the world population. The "hygiene hypothesis" suggests that reducing exposure to infections as parasites during childhood generates an imbalance in the immune system, resulting in more frequently development of allergic and autoimmune diseases. Therefore, parasitic infections can act as a protective factor against these disorders. Currently, the hygiene hypothesis has been referenced in relation to several immunological diseases, including asthma. The use of helminth infections in therapy is not feasible, but biologically active parasitic products may become a promising alternative, using its immunomodulatory activity and it is not necessary to subject individuals to the pathogenic effects of infections. **Objectives** This project aims to evaluate the immunomodulatory potential of two recombinant *Trichuris trichiura* proteins, homologous to

macrophage migration inhibitory factor (rTtMIF) and Fructose Biphosphate Aldolase (rTtFBPA) and *Toxocara canis*, Cystatin (rTcCis), proteins that have already been described in literature because they have immunomodulatory effects. **Materials and Methods:** For this, these proteins will be tested in culture of peripheral blood mononuclear cells (PBMC) of allergic and non-allergic subjects and in an experimental model of respiratory allergy induced by *Blomia tropicalis*.. **Perspectives:** By getting confirmation of immunomodulatory effects, these proteins could be an alternative to the current therapies for allergic respiratory diseases.

Support: FAPESB, CNPq and PIBIC-UFBA.

Keywords: asthma, down regulation, allergy, recombinant proteins

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FUNCTIONAL ASSESSMENT OF TAX AND HBZ GENES IN THE HIV-1/HTLV-1 COINFECTION.

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Introduction: HIV and HTLV share the same shape and tropism for T CD4+ cells, however the viral cycle are different. Studies have shown that HIV-1 patients are more susceptible to HTLV-1 infection. Tax is a HTLV-1 protein essential for viral replication and to initiate the malignant transformation of cells. HBZ protein has a major role in the HTLV-1 pathogenesis. The HIV-1/HTLV-1 co-infection occurs by mechanisms that demonstrate they are complex. **Objectives:** General objective: To evaluate Tax and HBZ expressions and genes polymorphisms in the HIV/HTLV coinfection. Specifics objectives: To compare Tax and HBZ genes polymorphisms between HTLV monoinfection and HIV/HTLV coinfection; To evaluate the cytokines expression of HIV-1 / HTLV-1 in coinfected patients. **Materials and Methods:** The present study refers to a cross-sectional where the activation indexes of the Tax and HBZ genes and their products will be evaluated to HIV-1 and HTLV-1 coinfected patients. Initially, a selection of patients will be performed by HIV viral load and TCD4+ lymphocyte quantification and positive results for HIV-1 and HTLV-1 serological tests,. All the procedures will be realized in the Laboratory of Infectology of the University Hospital Professor Edgar Santos located in Salvador, Bahia, Brazil, according to the following flow: Volunteers will be recruited by the researcher => Patients sign the inform consense to participate in the study = > Collection of the samples => Flow cytometry procedures => Evaluation of the results. The idetification of Tax and HBZ proteins and cytokines expression. Will be determinated by flow cytometry. **Perspectives:** Its expected that Tax and HBZ genes polymorphisms and expression of this proteins can to presente new functions in the HIV/HTLV coinfection.

Support: CAPES, PPGIm and HUPES-UFBA.

Keywords: Co-infection, HIV-1 and HTLV-1.

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

EVALUATION OF ANTI-*PORPHYROMONAS GINGIVALIS* ANTIBODY PRODUCTION IN INDIVIDUALS WITH CHRONIC GRAFT-VERSUS-HOST DISEASE

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Introduction: Graft versus host disease (GVHD) is one of the main complications following halogen transplantation of hematopoietic progenitor cells (HTHPC) that occurs when immunocompetent donor cells attack recipient tissues. Represents a cause of high morbidity and mortality observed in transplanted individuals. The oral cavity may be the main or the only site of chronic GVHD and may have persistent lesions even after resolution in other areas. Approximately 80% of patients with extensive chronic GVHD have some type of oral involvement, including oral pain, oral lesions and xerostomia, which, in turn, may lead to modifications of the oral microbiota, with a consequent increase in the index of oral infectious diseases, such as periodontitis. **Objectives:** The present study aims to investigate the production of serum antibodies specific for *Porphyromonas gingivalis*, a key pathogen in periodontal biofilm dysbiosis, involved in the onset and progression of periodontitis, in individuals who received allogeneic transplantation of hematopoietic progenitor cells and developed chronic GVHD. **Materials and Methods**: In this case-control study, 42 volunteers will be enrolled. 21 participants who have received HTHPC but haven't developed GVHD will compose the control group, while those who have developed the GVHD will compose the case group. Blood samples will be collected from individuals assisted at the dental service of University Hospital Complex Professor Edgard Santos. The diagnosis of the presence and severity of chronic GVHD will be performed by an oncologist. Clinical periodontal examination will be performed by a single dentist trained by the research team. Serum levels of IgG (total and subclasses) against *Porphyromonas gingivalis* antigens will be semi-quantified by indirect enzyme-linked immunosorbent assay (ELISA). Descriptive analysis will be conducted for all variables considered in the study in relation to GVHD. Depending on the distribution of the data, IgG levels between case and

control groups will be compared using the parametric Student T or the non-parametric Mann-Whitney test. The data analysis will be performed using SPSS 21.0 software. **Perspectives:** To find association between GVHD and periodontitis and to generate knowledge about the immunopathogenesis of these diseases and propose new therapeutic approaches.

Support: CAPES, CNPq and PIBIC-UFBA.

Keywords: Graft versus host disease; ELISA; Chronic periodontitis, *Porphyromonas gingivalis*.

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PHENOTYPIC AND FUNCTIONAL CHARACTERIZATION OF B CELLS IN TEGUMENTARY LEISHMANIASIS

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Introduction: Leishmaniasis is an infectious disease, considered by WHO as neglected, caused by different species of *Leishmania* protozoa of the genus, which affects the skin and mucous membranes. It is a zoonotic infection, which can affect animals other than humans. The whole emphasis regarding the pathogenesis of leishmaniasis has been given to the participation of CD4 + or CD8 + cells. However, different B cell subpopulations are often found in leishmaniotic ulcer and peripheral blood of patients. Similar to T cells, B cells express regulatory molecules involved in apoptosis and are capable of regulating the innate and adaptive immune response. Furthermore, effectors B cells secrete different profiles of cytokines that stimulate other cells of the immune system. **Objectives:** This study aims to characterize phenotypically the B cell subpopulations in peripheral blood of patients, to evaluate the functional activity of effector and regulatory B cells. In addition, characterize the profile of autoantibodies in leishmaniasis and associate the phenotypic profile and the production of cytokines with the clinical forms of patients with cutaneous leishmaniasis. **Materials and Methods:** Will be include 20 patients, resident of Corte de Pedra, Presidente Tancredo Neves, Bahia, with tegumentary leishmaniasis, 10 patients with cutaneous leishmaniasis and 10 with mucosa, without previous treatment, of both genders and varied age. The control group will consist of 10 healthy individuals living in the same region. Peripheral blood mononuclear cells will be separated, cryopreserved and stimulated with phytohemagglutinin (PHA), LPS, recombinant antigens LbSM, denatured LbSM and LbSOD, recombinant antigen preparation buffer and SLA standard antigen. The subpopulations of B lymphocytes in peripheral blood will be identified by multiparametric flow cytometry using rhodamine R123 and fluorescent monoclonal antibodies IgM / APC, IgD / FITC, CD10 / FITC, CD19 / BIOTIN, CD24 / FITC, CD27 / PE and CD38 / APC. Functional identification of these effector and regulatory B cells will be performed by the analysis of the intracellular cytokines IFN-gama/APC, TNF-alfa/PE, IL-6/FITC e IL-10/APC. P values < 0.05 will be considered statistically significant. **Perspectives:** Expected to get a better understanding of the involvement of B cells in the immunopathogenesis of cutaneous leishmaniasis and generate relevant information to carry out an increasingly effective treatment.

Support: INCT

Keywords: leishmaniasis, lymphocytes, flow cytometry, B cells

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EFFECT ON THE PRODUCTION OF IL-6, INF-Γ, IL-17 AND IL-10 IN THP-1 CELLS INHIBITED FOR ERK1 / 2, JNK AND P38 AFTER ANTIGENIC STIMULI OF PORPHYROMONAS GINGIVALIS

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Introduction: Periodontal disease result a infectious process that promotes the destruction of protective tissues and dental support. The process of beginning and establishment of the disease occurs due to imbalance between bacteria and host factors, resulting from the change in the absolute or relative number of certain microorganisms that change the pathogenic potential or modulate particular factors of the host. Among the existing microorganisms, many studies point to *Porphyromonas gingivalis* (Pg) as a key pathogen in inducing the rapid progression of the disease and aggravation of the process. It has been described in several reviews that Pg produces a wide range of potent virulence factors involved in colonization and tissue destruction as well as modulation of host response, such as gingipains and HmuY. Both HmuY and gingipains serve for nutrient uptake and survival of the microorganism, but also have the capacity to influence the inflammatory process by multiple mechanisms. These virulence

factors activate signaling pathways, which result in the production of mediators and cytokines, responsible for the aggravation of the inflammatory process in the periodontal microenvironment, studies have pointed out that LPS Pg was able to activate via TLR2 the JNK pathway. **Objectives:** To evaluate the interaction between HmuY and Kgp (K17 and K18) gingipains antigenic peptides of Pg and human HSp60 with inhibited THP-1 lineage cells for ERK 1/2, JNK and p38 in the production of IL-6, IFN-γ and IL-10 cytokines. **Materials and Methods:** Expansion of THP-1 tumor monocytic lineage cells in culture medium with RPMI, 10% SFB and 1% antibiotic will be performed after the expansion will be induced to differentiate these cells into macrophages by treating for 24 hours with PMA 80 nM/ ml. These macrophages will be exposed to the following inhibitors of MAPK, p38, ERK 1/2 and JNK at a concentration of 40 nM for one hour prior to stimulation with secreted antigens (sonic extract, HmuY, K17, K18 Pg and human HSP60). Cultivation will be carried out at 37ºC, under a humidified atmosphere and in the presence of CO_2 for 48 h. When the ELISA Immunoassay for the determination of IL-6, IL-10, IFN-**γ** and IL-17 will be performed in the culture supernatant. **Perspectives:** Expected that these MAPK signaling pathways are of fundamental importance for Pg antigens to induce the inflammatory process and consequent tissue destruction observed in the disease.

Support: CAPES UFBA e UEFS

Keywords: MAPK, *Porphyromonas gingivalis*, Gingipains

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ASSOCIATIONS BETWEEN MICROBIOLOGICAL AND IMMUNOLOGICAL BIOMARKERS RELATED TO CHRONIC PERIODONTITIS AND LEPROSY REACTION

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Introduction: the leprosy reaction is an immunological phenomenon that is not well-understood. As chronic periodontitis is an inflammatory disease of infectious etiology that is characterized by the production of inflammatory and immunological mediators, it may be associated with the development of leprosy reaction. **Objectives:** to investigate associations between microbiological and immunological markers of chronic periodontitis, both in saliva and peripheral blood, and the occurrence of leprosy reactions in individuals with leprosy seen at the HUPES university hospital complex. **Materials and Methods:** this epidemiological case control study, will estimate the association between periodontitis and leprosy reactions. The sample will consist of 244 individuals. Genotyping for the presence of periodontalpathogens in the subgingival biofilm will be performed via qPCR. To evaluate cellular immune response, peripheral mononuclear blood cells will be cultured with antigens crude extract antigens of *Porphyromonas gingivalis.* Cytokine levels of IFN-γ, IL1 – β, IL-12, IL-13, IL-5, IL-10, IL-23, IL 17, IL – 6, IL-22, IL-9, TGF-β, TNFα will be quantified in the supernatants by Enzyme Linked Immunosorbent Assay. Humoral immune response will be evaluated by measuring serum levels of anti-*Porphyromonas gingivalis* IgG and salivary levels of anti-*Porphyromonas gingivalis* IgA by indirect ELISA. The data analysis will be performed using Stata, v.9.0 and SPSS 17.0 softwares. **Perspectives:** the relationship between chronic periodontitis and leprosy reaction can be better understood by the elucidation of the role of periodontal biomarkers, and thus to improve the leprosy reaction management.

Support: FAPESB and CNPq

Keywords: leprosy, periodontitis, immunoglobulin, cytokines

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SYNTHETIC PEPTIDES FROM *PORPHYROMONAS GINGIVALIS* LYS-GINGIPAIN TO STUDY IMMUNE RESPONSE IN CHRONIC PERIODONTITIS

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Introduction: *Porphyromonas gingivalis* (Pg) is a keystone pathogen in Chronic Periodontitis (CP). Works on the immunogenicity of its virulence factors may contribute in the understanding of host response to infection. The present study aimed to identify immunogenic peptides from Lys-gingipain (Kgp) virulence factor of Pg ATCC 33277 (NCBI Taxonomy ID: 431947), which was selected based on previously performed immunogenicity experiments using chromatografic fractions of Pg extract. **Methods and Results:** Kgp sequence (1723aa) was obtained from the NCBI Protein Database (YP_001929844) and it was scanned for amino acid patterns indicative of MHCII binding using the *MHC-II Binding Predictions* tool from IEDB (http://tools.immuneepitope.org/mhcii/). This analysis considered 9 HLA alleles (loci DQ and DR), which were observed in previous studies involving subjects with CP from Salvador (BA), Brazil. T-cell epitope prediction resulted in 16 peptide sequences (15-mer) from Kgp. 9 Kgp peptides were selected within different regions of the protein (UniProt B2RLK2), they were chemically synthesized and they were tested by indirect ELISA method to verify presence of specific IgG in serum of subjects with CP and without Periodontitis (WP). 41 subjects from Feira de Santana (BA), Brazil, were evaluated. They had no systemic disease and they were clinically classified into CP (20 subjects) and WP (21 subjects) according to periodontal parameters. Serum samples were pooled into CP and WP pools based on clinical periodontal parameters of the subjects in addition to IgG anti-Pg level of each serum sample tested by indirect ELISA method using Pg extract antigen; such as CP pool (6 samples: O.D. 0,53 – 1,10) and WP pool (5 samples: O.D. 0,22 – 0,38). Optimal coefficient between CP pool and WP pool was determined for each analysed peptide by checkerboard ELISA. Pg extract (5μg/mL) was used as positive control in the screening of these Kgp synthetic peptides (10μg/mL). All of them were recognized by specific IgG in both sera pools, but K12 (within the catalytic subunit) presented the best coefficient between CP and WP pools, so it was selected to later *in vitro* experiments. **Conclusion:** K12 from the Kgp virulence factor seems to be an epitope candidate for *in vitro* experiments to analyse Pg immunogenicity. CAAE 32535914.4.0000.0053

Support: FAPESB, FAPEX, LABIMUNO (ICS – UFBA), PPGIm (ICS – UFBA), NUPPIIM (UEFS) and NECBAO (EBMSP).

Keywords: *Porphyromonas gingivalis*, Chronic Periodontitis, gingipain.

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ASSOCIATION BETWEEN RESISTENCE TO LEISHMANICIDAL DRUGS AND THE CYTOKINE PRODUCTION PROFILE OF PATIENTS WITH THERAPEUTIC FAILURE IN CUTANEOUS LEISHMANIASIS.

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Introduction: The Cutaneous leishmaniasis (CL) refers to a chronic skin lesions with different clinical forms, courses of disease, and tissue reactions. For over five decades, first line treatment has been antimonial drugs, the treatment success with these drugs can be as low as 25%. The identification of determinants of treatment response in cutaneous leishmaniasis provides the basis to orient the selection of treatment, and to design interventions for those factors that are modifiable. The objective of this study was to investigate whether the therapeutic failure in cutaneous leishmaniasis has an association between the resistance of Leishmania strains and the patient's immunological profile. **Methods and Results:** Ten strains of *Leishmania braziliensis* were isolated from patients with therapeutic failure against cutaneous leishmaniasis were selected from Corte Pedra region (Bahia, Brazil). These strains were conserved and expanded in contact with the drugs (Amphotericin B, Glucantime, Pentamidine or nitric oxide) for further assessment of cell viability by MTT assay. We also performed a test of associations between the viability of the strains to the drugs and the cytokine production of patients which strains were isolated. Cytokine production TNF, IL-10, CXCL9, CXCL10 and IFN-γ were obtained from PBMC, stimulated with SLA and antibody (IgG, IgG1 and IgG2) were accessed by ELISA. Statistical analysis was done on the GraphPad Prism and R software. There was a association between the therapeutic failure and resistance to Glucantime, as well as with CXCL10. It was found with a negative correlations between Glucantime resistance with CXCL10 (R= – 0.8197, p= 0.05), as well as between Glucantime and IgG1 resistance (R= – 0.7748, p <0.05). Amphotericin showed an negative correlation with TNF (R= – 0.8235, p= 0.0444). **Conclusion:** The low production of CXCL10, IgG1 and TNF may be one of the factors that contribute to the therapeutic failure in cutaneous leishmaniasis.

Support: CAPES, PPGIM

Keywords: *Leishmania braziliensis*, drug resistance and therapeutic failure

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

THE ROLE OF METHALOPROTEINASES (MMP) – 3 AND MMP-9 IN THE PATHOGENESIS OF HTLV-1 INFECTION

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Introduction: The HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TPS), one of the most important diseases associated to HTLV-1 infection, is characterized by central nervous system (CNS) demyelination. Infected cells, mostly T lymphocytes, migrate into the CNS due to high production of the cytokine (IFN-γ and TNF) and chemokines (CXCL9 and CXCL10). These cells are also responsible for the metalloproteinases (MMPs) productions. The MMPs are enzymes that affect blood-brain barrier (BBB) integrity, degrading the basal lamina and protein complexes, which would facilitate the migration of cells present in the blood into the CNS. The aim of this study is to evaluate the importance of metalloproteinases (MMP) in the pathogenesis of HTLV-1 infection. **Methods and Results:** The MMP-3 and MMP-9 were measured by ELISA in serum and cerebral spinal fluid (CSF) of the HTLV-1 carrier, HTLV-1 infected individuals with manifestation of overactive bladder (HTLV-OAB) and HAM/TSP. In the serum, the levels of the MMP-3 in patients with HAM/TSP (median 4478pg/mL, n=45) were significantly lower when compared with HTLV-1 carrier (median 4962pg/mL, n=38), p=0.01. The concentrations of MMP-9 in HTLV-OAB (median 1098pg/mL, n=44) were lower when compared to HAM/TSP (median 1966pg/mL, n=45), p=0.0002, and HTLV-1 carrier (median 1681pg/mL n=38), p=0.007. In CSF, there was no difference in MMP-3 production between the groups (HTLV-OAB, n=14 and HAM/TSP, n=17), regarding MMP-9 production, it was not detected by the method used. **Conclusion:** The involvement of MMPs in the process of destruction of the BBB is not yet clear. It is necessary to analyze the inhibitors of metalloproteinases (TIMP-3 and TIMP-4). The possible explanation for the low MMP-3 levels observed in serum from HAM/TSP patients is the probable consumption of this protein leading to BBB destruction of these individuals.

Support: FAPESB, CNPq and INCT-DT

Keywords: HTLV-1, HAM/TPS and Metalloproteinases (MMPs)

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

OVINE EXPERIMENTAL INFECTION WITH CORYNEBACTERIUM PSEUDOTUBERCULOSIS: CLINICAL EVALUATION AND IMMUNE RESPONSE

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Introduction: Caseous Lymphadenitis (LC) is a disease that mainly affects goats and *sheep, caused by the* intracellular pathogen, *Corynebacterium pseudotuberculosis (*Cp*)*. The widespread occurrence and economic importance of this pathogen reinforce the need to expand studies on its pathogenesis (Micro Rese.165: 312-320, 2010). Cellular immunity is more important than humoral immunity against Cp, and enlargement of the pre-scapular lymph node is the most common clinical sign in CL (Comp Clin Pathol.21: 667-671,2012). This work proposed to evaluate the clinical, anatomopathological and immune responses of sheep during 190 days of experimental infection with Cp. CEUA-ICS no082 / 2015. **Methods and Results:** 15 SRD sheep divided in control group (G1; n = 4) and infected (G2; n = 11). The G2 received $1x10^7$ of Cp strain VD57 and G1 received saline solution. On 13 occasions, throughout the experiment, blood was collected for clinical and immunological follow-up. IgG response by ELISA and in vitro assay of IFN-γ with Bovigam® kit after incubation with protein extract of VD57 and PAT10 strains were analyzed. At the end of 190 days, euthanasia was proceeded, according to legal guidelines. Data were analyzed using Microsoft Excel® and GraphPad Prism 6. In G1 no clinical changes were observed over time. In G2, 2 days after infection, 40% of the animals developed fever and an increase of the pre-scapular lymph node (55%). All animals formed papule, edema and presented temperature increase at the inoculation spot, which evolved into the formation of caseous abscess. There was leukocytosis due to neutrophilia with emergence of rods, after 2 days of infection, which was maintained in some animals until the 7th day with mild lymphocytosis. In G1 no anatomopathological changes were found and in G2 an increase of the right pre-scapular lymph node with lesion formation compatible with granuloma (55%) was observed. 7 days after infection, G2 already had positive serology, which remained during the 190 days. This group had higher IFN-γ production during the chronic phase, especially in the antigenic extract of PAT10. G1 remained with negative serology over time and low production of IFN-γ against in vitro stimulus. **Conclusion:** Clinical and anatomopathological findings are compatible with actinomycetic infections, and extracts from both strains can be used in immunological tests to evaluate infection in sheep.

Support: CAPES, CNPq, LABIMUNO, PPGIm,UFBA

Keywords: caseous lymphadenitis; C.pseudotuberculosis; small Ruminants

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SENSITIVITY OF *Leishmania (V.) braziliensis* TO FLUCONAZOL IN CORTE DE PEDRA-BAHIA

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Introdution: Leishmaniasis is caused by protozoa of the genus Leishmania, considered an endemic disease with wide distribution, and is one of the six major infectious diseases worldwide. In Brazil, *Leishmania (V.) braziliensis* has a high refractory index to pentavalent antimony. This is observed in the endemic area of Corte de Pedra, Bahia, where the localized cutaneous form (CL) is the most common presentation of leishmaniasis. In Corte de Pedra, about 60% of patients require two or more series of intravenous treatment with antimony, increasing the chance of toxicity and resulting in elevated costs. Moreover, parenteral administration has lower effectiveness in the countryside, due to difficult access to health facilities. Thus, the use of drugs administered orally has the potential to increase the adherence and healing rate in CL patients. **Methods and Results:** The following methodology was performed: (1) randomized phase III clinical trial, which compared the treatment of patients with ATL employing Fluconazole and pentavalent antimony, and the cure was defined as complete reepithelialization of the ulcer evaluated six months after the last dose treatment; (2) resistance in vitro test of *L. (V.) braziliensis* promastigotes due to pentavalent antimony, Fluconazole and Miltefosine. 53 subjects were included. According to the randomization list, 26 of CL patients underwent treatment with pentavalent antimony (Glucantime®), as recommended by the Ministry of Health, and 27 underwent treatment with fluconazole orally, in 28 days, with a daily dose of 6.5-8.0 mg / kg. In the six-month evaluation, the cure rate in the fluconazole group was 22,2% (6/27) and in the group using Glucantime® was 53,8% (14/26). These data were corroborated by in vitro experiments, which showed greater sensitivity of promastigotes to Glucantime® and Miltefosine compared to fluconazole. **Conclusion:** The Fluconazole is not effective in the treatment of *L. (V.) braziliensis* in Corte de Pedra, Bahia.

Support: CNPq

Keywords: Fluconazole*, Leishmania (Viannia) braziliensis*, Clinical Trial.

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ANALYSIS OF HUMORAL IMMUNE RESPONSE AGAINST *PORPHYROMONAS GINGIVALIS* IN SEVERE ASTHMA.

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Introduction: Chronic Periodontitis is a multifactorial disease. Its pathogenesis is related to the host immune inflammatory factors and to the oral microbiota. *Porphyromonas gingivalis* is a keystone pathogen on its etiology. Asthma is a chronic disease of the airways with an inflammatory origin and it is considered a public health problem in Brazil. Works have suggested an influence of periodontitis on asthma, especially in severe asthma form. It may be due to aspiration of pathogenic microrganisms or to epithelial reactions triggered by the immune response. Thus, there is a biological plausibility of the association between chronic periodontitis and severe asthma. It seems to be related to the presence of common immunological factors for both diseases. It is known that individuals with chronic periodontitis produce higher serum levels of IgG and subclasses specific to *Porphyromonas gingivalis.* Thus, this case-control study aims to evaluate the humoral immune response against *Porphyromonas gingivalis* antigens in individuals with severe asthma and individuals without the disease. **Methods and Results:** Serum levels of IgG and subclasses anti – *Porphyromonas gingivalis* in subjects (n = 220) with severe asthma and subjects without asthma from the Program for the control of asthma and allergic rhinitis in Bahia – PROAR will be evaluated by indirect ELISA. Twenty-four (243) were instructed, which conduct or control-case study. The case group (severe asthma) was composed of 117 individuals (48.2%), while the control group (without asthma) was composed of 126 individuals (51.8%). An average age without group case was 43 years. It is already a mean age of the control group of 45.2 years. Regarding the sex of the individuals, in the case group 95 (39.1%) were female and 22 (9.1%) were male. In the control group, 107 (44%) were female and 19 (7.8%) were male. It was then observed that those with and without severe asthma had levels of anti-Porphyromonas gingivalis IgG in serum. **Conclusion:** It is expected that the subclasses of IgG may better differentiate the case and control groups, thus contributing to the understanding of the association between chronic periodontitis and severe asthma.

Support: CAPES,FAPESB,LABIMUNO(ICS-UFBA),PPGIm(ICS-UFBA),PROAR

Keywords: Asthma, Periodontitis Chronic, Immunoglobulin G

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PLASMATIC IFN-γ AND IP-10 IN INDIVIDUALS WITH ACTIVE PULMONARY TUBERCULOSIS: PRELIMINARY RESULTS

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Introduction: Pulmonary tuberculosis (TB) is an infectious disease, transmissible, caused mainly by *Mycobacterium tuberculosis* (*M. tuberculosis*) and curable in most new cases. Current studies have demonstrated promising results of interferon-gamma (IFN-γ) and IP-10 as alternative biomarkers with potential for the development of new TB testing platforms (Expert Rev Mol Diagn.12:175-87, 2012; PLoS One. 5(2): e9051, 2010). With the incorporation of real-time PCR technology into the laboratory routine and its use as an automated platform for bacillus DNA research and Rifampin resistance mutations (TRM, XPERT®MTB / RIF, Cepheid, USA), it is necessary the interpretation of the result in the clinical-epidemiological context. The purpose of this study was to analyze the clinical and laboratory profiles of individuals diagnosed with tuberculosis (TRM positive), both sensitive and resistant to rifampicin. **Methods and Results:** After approval by the Research Ethics Committee – CEP ICS (CAAE nº 57662016.8.1001.5662), this descriptive study included volunteer participants attending a reference laboratory in TB in Bahia, diagnostic information was collected at the institution's bank and in the SINAN and SITE TB Systems. With TRM positive and/or smear microscopy data, culture with sensitivity test was classified into three groups: TB without treatment (n = 35), TB with treatment and Rifampicin sensitive (n= 35), and TB MDR (multidrug resistant) (n=35). The control group (n=35) was composed of healthy adults with no history or symptoms of TB. A venous blood sample was collected for leukogram and for IFN-γ production (IGRA QTF TB Gold) and IP-10 (BD ™ CBA Human IP-10 Flex kit). They will be characterized as to the number of previous treatments, body mass index (BMI) and resistance or not to Rifampicin, the main drug of the therapeutic regimen. The analysis are ongoing. It was found that the concentration of IP-10 in the group with TB (without treatment) was higher than in the control group. Male advantage was observed (63%) and age of the study population was between 36 and 43 years old. In the three groups with TB (63-67%) the BMI was normal or eutrophic (18.5 to <25) with three being the mean number of tuberculosis retreatments among MDR-TB. **Conclusion**: Data analysis may contribute to the knowledge and characterization of the biomarkers profile in order to facilitate the diagnosis, and in monitoring the response to anti-TB treatment, in a translational approach.

Support: INCT-DT e LABIMUNO

Keywords: Tuberculosis, resistant TB, diagnosis, XPERT®MTB/RIF, IFN-Gamma, IP-10, IGRA.

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EXPRESSION OF TYPE-2/REGULATORY CYTOKINES BY TCD4⁺ LYMPHOCYTES FROM INDIVIDUALS WITH PERIPORTAL FIBROSIS SECONDARY TO SCHISTOSOMIASIS

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Introduction: *Schistosomiasis is one of the most important parasitic diseases in terms of the importance of public health. In developing countries, 200 million people are infected. The aim of this study was to evaluate the frequency of CD4⁺ T lymphocytes and the intracellular expression of cytokines IL-4, IL-5, IL-13, TGF-β and IL-10 in mononuclear cells of individuals with periportal fibrosis secondary to shistosomiasis.* **Methods and Results***: Ultrasonographic evaluation of 122 patients aged 13-70 years was performed to diagnose the degree of periportal fibrosis, being 53% classified as "without fibrosis", 18% with "periportal fibrosis not excluded", 10% with "possible / probable periportal fibrosis", 16% with "periportal fibrosis" and 3% with "advanced fibrosis". The frequency of different molecules in the CD4⁺ T lymphocytes from patients with periportal fibrosis was performed using flow cytometry technique. The results were expressed as median (min-max) and statistical analyzes were performed on Graphpad prism, version 6.0. The e frequency of CD4⁺ T lymphocytes were similar between non-stimulated [24.6 (9.3-37.5)] or SEA-stimulated cultures [25.9 (12.6-41.7)]. Regarding the intracellular expression of the IL-4 cytokine, we observed that it was higher in the SEA stimulated cultures [23.7 (16.6-28.3)] compared to cultures without stimulus [20.5 (18.0-31.9)]. We did not observe statistical differences regarding the expression of IL-5, IL-13 or TGF-β cytokines in both non-stimulated cultures [IL-5: 24 (16-55.9); IL-13: 65.15 (60.6-105) and TGF-β: 6.36 (4.51-7.55)] compared*

to the cultures stimulated with SEA [IL-5: 32.2 (17, 6-52,3); IL-13: 73.6 (60.0-102) and TGF-β: 6.84 (6.3-7.25)]. Regarding the mean fluorescence intensity of CD4⁺T cells expressing the regulatory cytokine IL-10 we observed that the cultures stimulated with SEA showed an increase in the expression of IL-10 [MFI: 8,225 (6,08-9,5)], compared to non-stimulating cultures [MFI: .705 (7.05-8.66)]. **Conclusion:** *These results suggest that other cellular subpopulations may be involved in periportal fibrosis and, therefore, further studies will needed to clarify the role of cytokines in the pathogenesis of schistosomiasis.*

Support: FAPESB (APP 0051/2016) and CAPES.

Keywords: CD4⁺ T lymphocytes, Fibrosis, Cytokines, Schistosomiasis

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NOTCH SIGNING AND INFLAMMATORY RESPONSE IN PATIENTS INFECTED BY HTLV-1

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Introduction: The human T-lymphotropic virus type1(HTLV-1) is a retrovirus that infects about 10-20 million people worldwide. The most infected individuals remains asymptomatic(AS) and about 3% develop a chronic neuroinflammatory disease called myelopathy/tropical spastic paraparesis associated with HTLV-1(HAM/TSP). The Notch pathway can act as a regulator of proliferation and cell survival through the Notch intracellular domain(NICD), which is released after intracellular cleavage carried out by γ-secretase protein. Believed to deregulate activation of Notch signaling can result in excessive lymphoproliferation in HTLV-1. **Methods and Results:** For analysis by ELISA of IL-1β, IL-6, TNF, IFN-γ, CXCL-9 and CXCL-10 levels, peripheral blood mononuclear cells(PBMC) from patients with HAM/TSP and AS were cultured for 72h in the presence or absence of DAPT, JLK6, anti-Notch1 and anti-Notch3. The pro-viral load will be analyzed by RT-PCR. By using JLK-6 decreased significantly of TNF, CXCL-9 and CXCL-10 levels in AS PBMC cultures when compared to the medium. By using the DAPT decreased significantly of IFN-γ levels in AS PBMC cultures when compared to the medium. It was not possible to observe statistically significant differences in other conditions tested using the JLK-6 and DAPT. There was no significant difference when using anti-Notch 1 and anti-Notch 3 compared to middle. **Conclusion:** The γ-secretase blockers act on reducing TNF, CXCL-9 and CXCL-10(JLK6); and IFN-γ(DAPT) PA, suggesting that the Notch pathway might be participating in the inflammatory response in the HTLV-1 carriers.

Support: Capes, PPGIM, SIM and NIH.

Keywords: HTLV-1, HAM / TSP, Notch, γ-secretase, anti-Notch1, anti-Notch3, γ-secretase.

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EXPRESSION AND CHARACTERIZATION OF MEMBRANE PROTEINS FROM *TOXOCARA CANIS* AS THERAPEUTIC TARGETS

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Introduction: *Toxocara canis* is a nematode parasite of canines, which can be accidentally transmitted to humans by accidental ingestion of embryonated eggs. This zoonotic disease has a significant relevance because the symptomatology is analogous to another illness. The clinical forms of the disease are classified as visceral or ocular larva migrans and the treatment is based on the drugs administration. The aim of this study was to use an approach using bioinformatics software to identify therapeutic targets that can be used in the development of a vaccine for the control of helminth infection in their native host. **Methods and Results:** In this work; to select the proteins that will be used to develop the vaccine formulation against T. canis, was made a literature investigation. After this research was selected 30 sequences, all these sequences were analyzed in silico using different bioinformatic programs, to select some potential targets. Four sequences were selected and optimized to be cloned in the

plasmid pET-21 and expressed in *E. coli*, the proteins were purified by affinity chromatography. Four sequences were selected and optimized using bioinformatic tools; Tc_03886 G-protein-couple receptors (GPCRs), Tc_014421 (Two pore potassium channel protein sup-9), Tcan_06969 (Cadherins), Tc_18226 (Cystatin). The synthesis and cloning of the four genes were performed by the company GeneScript in the plasmid pET-21 with His-Tag. All expression and purification condition were standardized using different IPTG concentrations and *E. coli* strains. Until now the proteins Tc_014421, Tcan_06969, and Tc_18226 were successfully expressed and purified. The recombinant proteins were tested in an immunoblotting assay with pool serum samples of infected dogs. The result of this test showed that these proteins are immuno-recognized by the IgG antibodies present in the serum of the dogs. **Conclusion:** These proteins are shown as a potential immunological target for the development of immunoprophylaxis therapies.

Support: FAPESB, CNPq and PIBIC-UFBA.

Keywords: *T. canis, vaccine, recombinant proteins, zoonotic disease.*

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SECRETED PROTEIN PROFILE OF THREE DIFFERENT *CORYNEBACTERIUM PSEUDOTUBERCULOSIS* STRAINS USING SODIUM DODECYL SULFATE – POLYACRYLAMIDE GEL ELECTROPHORESIS

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Introduction: *Corynebacterium pseudotuberculosis (C. pseudotuberculosis) is the agent of caseous lymphadenitis that mainly affects goats and sheep (Journal of medical microbiology, v. 56, n. 4, p. 480-486, 2007). The bacteria can infrequently infect humans, being difficult to diagnose (BMC genomics, v. 11, n. 1, p. 728, 2010). There are various strains of the bacteria collected from different geographic areas and isolated from caprine, ovine and also from humans. They have been used in antigens production for ELISA and western blotting to identify reactive animals in different preparations (Revista de Ciências Médicas e Biológicas, Salvador, v. 3, n. 1, p. 44-52, jan./jun. 2004). The objective of this study is to analyze the main similarities and differences among secreted proteins from three strains of C. pseudotuberculosis used by the LABIMUNO research group.*
Methods and Results: *C. pseudotuberculosis (strains A, B and C) were grown in Brain Heart Infusion (BHI) broth and the culture supernatants were treated by Three-Phase Partitioning (TPP) according to Paule et al (Protein expression and purification, v. 34, n. 2, p. 311-316, 2004). Strains were also grown in Chemically Defined Medium (CDM) according to Moura-Costa et al (Revista Brasileira de Saúde e Produção Animal, v. 3, n. 1, 2005). Protein concentration of each supernatant was performed by Lowry kit (R&D-USA). Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) were made using linear gels (stacking 4% and running 12%). Samples in loading buffer were added into wells, considering 31-48 µg proteins/well of each sample from strains A, B and C grown in both media and 2 µL of the Prestained Protein Ladder (Size Range 10-180 KD – Thermo Fisher). After silver staining, it was analyzed using GelAnalyzer 2010 software. There was observed in gels that the TPP-treated BHI supernatant showed bands of 72, 45 and 28-26 kD, with different supernatants profiles for the C. psudotuberculosis strains grown in that medium, and also more protein bands were found, with low variation between their molecular weights. When compared, the samples of the three strains in the two media secreted protein profiles, there were found few differences, mainly between the mid molecular weight (between 25-150kD) and high molecular weight (>150kD) bands when was used CDM.* **Conclusions***: The secreted proteins obtained from the different strains studied showed little difference between their molecular weights.*

Support: FAPESB, CAPES, LABIMUNO and PIBIC-UFBA.

Keywords: Corynebacterium pseudotuberculosis, TPP, MQD. SDS PAGE, Protein Profile, Molecular Weight protein profile.

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

TOLEROGENIC DENDRITIC CELLS REDUCE CARDIAC INFLAMMATION IN CHRONIC CHAGASIC DISEASE

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Introduction: Chronic chagasic cardiomyopathy (CCC) is present in 30% of *Trypanosoma cruzi*-infected people who are in the chronic phase of the infection. We have demonstrated that infected mice in which cardiac immune tolerance to myosin was induced developed a milder myocarditis than control mice, suggesting that autoimmune phenomena participate in the pathogenesis of CCC. Dendritic cells (DCs) have the potential to reprogram an immune response in an antigen-specific manner being an interesting target for immunotherapeutic strategies to controlling inflammatory and autoimmune diseases. **Objective:** The aim of the study was to evaluate if myosin-sensitized tolerogenic DC could interfere with the development of chronic cardiomyopathy in an experimental model of Chagas disease. **Methods and Results:** DC were produced from bone marrow of C57Bl/6 mice. The cells were cultured in medium supplemented with 30% supernatant from a culture of cells x-63 containing GM-CSF. Tolerogenic DC were obtained by the addition of dexamethasone on days 3 and 6 culture and activated with 1 ug/ml of bacterial lipopolysaccharide for 24 hours. Groups of C57Bl/6 mice, infected by *T. cruzi* Colombian strain, received four intraperitoneal injections of tolerogenic DC 3 months after infection at 30 days intervals between them. Naive and *T. cruzi*-infected control groups received injections of saline. Six months after infection, mice were euthanized for evaluation of cardiac inflammation, cardiac function and cytokines quantification. GFP tolerogenic DC were generated to evaluate cell migration after 6, 24 and 48h of injection. Morphometric analysis show decrease in inflammation in the hearts of DC treated mice, corroborated by reduction in expression of CD45, analysed by qPCR. Maybe the results observed with un pulsed DC group is due to the uptake of expose myosin after cardiac lesion. No difference were observed in the exercise capacity among the groups. **Conclusions:** Our preliminary results indicate that tolerogenic DC could reduce CCC. To confirme those data cell migration and cytokines analyses are ongoing.

Support: Fiocruz, CAPES and CNPq

Keywords: *Trypanosoma cruzi*, Cardiomyopathy, Dendritic cells, Immune tolerance.

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

EVALUATE OF T NATURAL KILLER CELLS CYTOTOXIC POTENTIAL FROM HTLV-1-INFECTED PATIENTS WITH HTLV-1 ASSOCIATED MYELOPATHY (HAM/TSP)

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Introduction: Brazil represents one of the largest endemic areas for human T-lymphotropic virus cells type 1 (HTLV-1) infection and associated diseases like HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). HAM/TSP is a chronic and progressive inflammatory disease of the central nervous system and your immunopathogenic mechanisms are not completely understood. In this study we evaluated the cytotoxic potential of T natural killer cells ($TCD56^+$) from HTLV-1-infected patients with HAM/TSP. **Methods and Results:** Assays immunophenotyping by flow cytometry were conducted to assess NKT granzyme B^+ ($GrzB^+$) or $perforin^+$ ($Perf^+$). We analyzed 12 uninfected subjects (controls) and 10 HTLV-1-infected patients – 5 without myelopathy (asymptomatic-ASS) and 5 with HAM/TSP. Infected patients showed a decreased proportion of T natural killer cells. The proportion $TCD56^+GrzB^+$ cells was two times higher in HTLV-1-infected patients compared to uninfected volunteers (P=0.003). The frequency of cells expressing perforin presented similar between groups (P=0.36). However, the percentage of $TCD56^+$ cells containing granzyme B and perforin was six times higher in infected individuals (P=0.025), suggesting an increased cytotoxic potential. The ASS and HAM/TSP groups showed similar frequencies of $TCD56^+GrzB^+$ and/or $Perf^+$. No significant differences were observed in these cytotoxic mediators expression between the two infected groups studied. **Conclusion:**These preliminary findings suggest that cytotoxic potential of T natural killer cells is not different between AAS and HAM/TSP HTLV-1-infected groups. Further studies will be conducted in an attempt to clarify these questions.

Support: FAPESB.

Keywords: HTLV-1, HAM/TSP, NKT.

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

DETERMINATION OF IL-1β PRODUCTION PATHWAYS IN PATIENTS WITH CUTANEOUS LEISHMANIASIS

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Introduction: The activation of inflammasomes components leading to production of IL-1β is associated with the pathogenesis of a variety of inflammatory diseases. Recent work has shown the importance of the inflammasome activation for IL-1β production in murine leishmaniasis and a role for NLRP3 in IL-1β production was reported. CL due to *Leishmania braziliensis* infection is an inflammatory disease where skin ulcer development is associated with mononuclear cells infiltrate and high levels of inflammatory cytokines. Therefore, our hypothesis is that CL patients have increased expression of NLRP3 and produce high levels of IL-1β. **Methods and Results:** Serum, lesion biopsies and peripheral blood mononuclear cells (PBMC) were obtained from healthy subjects or individuals infected with *L. braziliensis*. Biopsies and PBMCs were stimulated or not with soluble *Leishmania* antigen (SLA) for 72 hours. IL-1β concentrations were determined by ELISA. We also identified the source of IL-1β by flow cytometry by stimulating PBMC with SLA for 8 hours and staining for CD14, CD16 and IL-1β. Bone marrow-derived macrophages (BMDMs) were obtained from C57BL/6 wild type and mice deficient for CASPASE-1, ASC, NLRP3, AIM2 and IL-1R. BMDMs were treated with LPS for 6 hours, infected with *L. braziliensis* or stimulated with monosodium urate for 42 hours. IL-1β was detected by ELISA. In addition, PBMCs from patients were differentiated into macrophages, infected with *L. braziliensis* or stimulated with SLA for 2 hours. Gene expression of NLRP3 was determined by real-time PCR and intracellular expression of NLRP3 by flow cytometry. Our results showed high production of IL-1β in serum, supernatants of biopsies and PBMCs stimulated with SLA in patients infected with *L. braziliensis* from the early to the late stage of the disease and reduction after the cure. The main source of this cytokine was intermediate monocytes (CD14+CD16+). In our murine experiments we found that IL-1β production in response to *L. braziliensis* was dependent on NLRP3, CASPASE-1 and ASC. Additionally, we observe an increased expression of NLRP3 genes in macrophages and protein in intermediate monocytes from CL patients. **Conclusion:** Human intermediate monocytes from CL patients produce high levels of IL-1β, probably, through NLRP3 activation.

Support: INCT-DT, CAPES, FAPESB and NIH (AI088650-ICIDR)

Keywords: Inflammasome, IL-1β, NLRP3, Leishmaniasis

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

INCREASED FREQUENCY OF CD4+ AND CD8+ T CELLS ACTIVATED IN KERATOCONJUNCTIVITIS SICCA ASSOCIATED WITH HTLV-1

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Introduction: HTLV-1 is the causative agent of leukemia/lymphoma adult T-cell (ATLL), tropical spastic paraparesis / myelopathy associated with HTLV-1 (HAM / TSP) and uveitis. In addition, keratoconjunctivitis sicca (KCS), a multifactorial disease of the tear and of the ocular surface, has been more frequently reported in patients infected with HTLV-1. As for other HTLV-1-associated diseases, KCS has been related to a high proviral load. This study aimed to evaluate the frequency of CD4+ and CD8+ T cells activated (HLA-DR +) of patients with KCS associated with HTLV-1 **Methods and Results:** Assays immunophenotyping by flow cytometry were conducted to assess the frequency of CD4+HLADR+ e CD8+HLADR+. Thirty-seven HTLV-1 individuals were included (27 asymptomatic for HAM/TSP with positive diagnosis of ocular manifestation (KCS), 10 with negative diagnosis (ASS – asymptomatic). Seventeen non-infected individuals were included as controls (NI). There was an increased frequency of CD4+ and CD8+ T lymphocytes expressing HLA-DR in the ASS and KCS groups in relation to the NI control group ($p < 0.0001$ and $p < 0.0001$, respectively). Through the analysis of the fluorescence intensity, it was not observed among the three groups significant differences in the expression of this activation molecule in CD4+ T lymphocytes ($p = 0.14$) and CD8+ ($p = 0.57$). **Conclusion:** The HLA-DR molecule has been described as a marker of cellular activation in HTLV-1. Our study shows that you are concerned ASS and HATM / TSP, the KCS there is an increased activation of CD4+ T cells and CD8+.

Support: FAPESB, CNPq.

Keywords: HTLV-1, KCS, HLA-DR

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

MICROGLIAL EVALUATION IN MIXED CULTURE OF RATS INFECTED WITH *NEOSPORA CANINUM*

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Introduction: The involvement of cellular components of the CNS, mainly microglia, reveals a diversity of morphofunctional alterations capable of ensuring neuroprotection in the presence of infectious agents, such as *Neospora caninum*. The aim of this paper was to describe the microglial activity in response to the stimulation of live tachyzoites of *Neospora caninum*, without addition of inflammatory stimuli, in order to contribute towards the understanding of immunopathogenesis. **Methods and Results**: Primary cultures of glial cells were obtained from the cerebral cortex of newborn Wistar rats (0 to 48 hours). These cells were grown in 24-well plates at a density of $2x10^5$ cells per well and infected with *N.caninum* in a 1:1 ratio, then maintained in a biological oven for a period of 18 day. There was a significant reduction of microglia in cultures infected with *N. caninum* 48 hours post infection. **Conclusion**: The morphological diversity in the mixed culture infected by *N. caninum*, without addition of proinflammatory factors, suggests the presence of parasite proliferation in microglia, however this cell does not modulate the parasitic control.

Support: FAPESB.

Keywords: Primary cultures, microglia, cell morphology, *Neospora caninum.*

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

SCHISTOSOMA MANSONI SM29 ANTIGEN MODULATES MONOCYTES IN SEVERE ASTHMA.

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Introduction: *Studies have reported the ability of Schistosoma mansoni infection to reduce the severity of asthma and prevent atopy. The aim of this study was to evaluate the ability of S. mansoni Sm29 antigen to modulate in vitro activation of monocytes from asthmatics in response to allergen from the mite Dermatophagoides pteronyssinus (Der p1).* **Methods and Results:** *Five patients with severe asthma were enrolled in this study. Peripheral blood mononuclear cells (PBMCs) were stimulated with Sm29 in the presence or absence of Der p1. The expression of surface markers and cytokines on monocytes were evaluated by flow cytometry. Monocytes were classified into classical ($CD14^{++}CD16^{-}$), intermediate ($CD14^{++}CD16^{+}$), and nonclassical ($CD14^{+}CD16^{++}$). It was observed that cultures stimulated with Sm29 [65% (58.2% – 85.3%)] led to an increase in the frequency of CD80 expression in classical monocytes compared with Der p1 cultures [22.9% (8.3% – 37.3%; p<0.01)]. Similarly, there was an increase in the frequency of intermediate monocytes expressing CD80 in cultures stimulated with Sm29 [93.6% (73.8% – 98%)] compared with cultures stimulated with Der p1 [60.9% (39.7% – 81%); p<0.05] and non-stimulated cultures [59.1% (16.1% – 95.1%); p<0.05]. Cultures stimulated with Sm29 [13.9% (2.8% – 72.9%)] and Der p1+Sm9 [14.8% (3.2% – 59.2%)] had a reduced frequency of $CD86^{+}$ intermediate monocytes compared to cultures without stimulation [77.9% (54.1% – 84%); p<0.05]. This reduction was also observed in the subpopulation of nonclassical monocytes in cultures stimulated only with Sm29 [2.2% (1.0% – 7.9%)] and Der p1+Sm29 [3.7% (1.6% – 14,5%)] compared with Der p1 [22.8% (17.1% – 48.8%); p<0.05)] and cultures without stimulation [22.5% (5.0% – 51%); p<0.05)]. In addition, there was an increase in the frequency of classical monocytes expressing IL-10 in cultures stimulated with Sm29 [32% (4.5% – 40.9%)] compared with cultures without stimulation [2.5% (0.06% – 3.4%); p<0.05]. We also observed a higher frequency of nonclassical monocytes expressing IL-10 in cultures stimulated with Sm29 [13.8% (10% – 50%)] compared to cultures stimulated with Der p1 [4.2% (0,4% – 23.5%); p<0.05].* **Conclusion:** *These results suggest that the addition of Sm29 to cell cultures from subjects with severe asthma reduced cell activation and induced significant regulatory mechanisms to control the inflammatory response in asthma.*

Support: PRONEX/CNPq; INCT-DT/CNPq

Keywords: Monocytes, asthma, Sm29, *Schistosoma mansoni* antigen

LINHA 04: Imunologia das Doenças Infecciosas e Parasitárias

THE PREVALENCE OF TOXOPLASMOSIS AND ITS ASSOCIATION WITH THE LEVELS OF ALLERGEN SPECIFIC IgE IN TEENARGERS

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Introduction: Toxoplasmosis is a worldwide parasitic disease caused by *Toxoplasma gondii* an obligate intracellular protozoan that infect most species of warm-blooded animals, including humans. These are infected by the ingestion of tissue cysts present in meat or by the ingestion of soil, water, or food contaminated with sporulated oocysts and vertically by taquizoites from infected mothers. Based on the serological studies, it is known that 25-30% of world's population is infected by *T.gondii*. Atopy can be defined by either a positive skin prick test (SPT) or the presence of allergen-specific IgE in serum (sIgE) and this condition is considered a risk factor for the development of asthma. Our research's group has found a negative association between the seropositivity for anti-*T.gondii* IgG and a higher prevalence of sIgE in children 4 – 11 years old. The present study, aimed at analyzing this population, now 12 – 19, and associate data from the prevalence of this with circulating sIgE. **Methods and Results:** A total of 990 teenagers enrolled in SCAALA (Social Change, Asthma and Allergy in Latin America) Program, a cohort, originally recruited early in infancy, living in many poor neighbourhoods in the city of Salvador, Northeast Brazil, was included. The serum was prepared and used for measurement of following four sIgE: *D.pteronyssinus*, *B.tropicalis*, *B.germanica*, *P.americana* using the Immunocap System. Sera with ≥0.70 kU IgE to any of the four allergens were considered positive. For the measurement of serum anti-*T.gondii* IgG, an Indirect Enzyme Linked ImmunonoSorbent Assay (ELISA) was performed, using as antigen the soluble antigen extract of *T. gondii* tachyzoites (STAg). The data was analyzed performing the Mann-Whitney test, in the software GraphPad Prism 5. The preliminary analysis of 353 adolescents demonstrated a prevalence of *T.gondii* infection of 26, 6% and an difference of the amount of sIgE between the two groups, those that was positive or negative for the presence of antibodies IgG anti-*T.gondii*, with a P value < 0, 05 in every test performed. **Conclusion:** These preliminary results revealed the incidence of the seropositivity and a significant association between the presence of IgG anti-*T.gondii* and lowest levels of sIgE in sera of the teenagers studded. Therefore, we expect to perform soon further analyses of the association of this infection with atopy and asthma, in the whole studied population, and compare these data from the two surveys.

Support: CNPq and PIBIC-UFBA.

Keywords: *Toxoplasma gondii*, sIgE, teenagers.

LINHA 5: Imunogenética/Genômina/Proteômica

IMPACTO DA ANCESTRALIDADE BIOGEOGRÁFICA SOBRE O DESENVOLVIMENTO DE ASMA, ATOPIA E INFECÇÕES HELMÍNTICAS EM UMA POPULAÇÃO BRASILEIRA: UM ESTUDO DE MAPEAMENTO POR MISCIGENAÇÃO

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Introduction: Asthma is a disorder of the lower airways, which represents a serious public health problem affecting approximately 334 million people worldwide. According to the "old friends" hypothesis, this increase in the prevalence of asthma and allergies may be related to decreased exposures to certain organisms including bacteria and helminths. Studies of biogeographic ancestry point out differences in the prevalence of asthma between distinct racial and ethnic groups within the same country. Some of these studies in North America found a higher prevalence of asthma and IgE levels in individuals with African ancestry when compared to those with European ancestry. **Objective**: In the present study we intend to use custom panels with ancestral markers (AIMs) to perform a mapping by miscegenation identifying loci associated with asthma, atopy and helminth infections in the population of Salvador, seeking to evaluate the pro-inflammatory and regulatory immunological profiles associated with biological routes of these outcomes, as well as metabolic pathways associated with cellular function itself**. Materials and methods:** DNA of 1.253 subjects were genotyped using Illumina 2.5 Human Omni Beadchip. Estimation of local ancestry will be done through PCAdmix and RFmix programs. Logistical and linear regressions will be performed through software R. **Perspectives:** In Brazil, there are no studies describing the prevalence variations for these diseases according to global and local biogeographic ancestry. In addition, studies using informational markers of ancestry have been very scarce in the population of Bahia, less information is still available about the structuring of genetic diversity for the population of Salvador. Understanding how biogeographical ancestry influences immunological routes and is associated with the occurrence of asthma and infections in our population may contribute not only to the understanding of biological causal mechanisms, but also to support the development of interventions for this disease.

Support: Capes, CNPq

Keywords: Asthma, Atopy, Helminth infections, Biogeographical ancestry, Miscegenation.

LINHA 5: Imunogenética/Genômina/Proteômica

GENETIC MARKERS LINKED TO ZIKA VIRUS INFECTION AND ITS OUTCOMES

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Introduction: The Zika virus (ZIKV) is spreading worldwide. It is estimated that a large proportion (up to 80%) of the Zika virus infections may present in a mild or asymptomatic manner. In addition, the most common symptoms are not specific, which makes it difficult to quickly and conclusively diagnose suspected infection. The relevance of specific detection of ZIKV infection is evidenced by the increasing number of cases with neurological complications associated with this infection. For this reason, ZIKV infection and its transmission have acquired a state of public health emergency of international interest, mainly in relation to the infection in pregnant women, associated to the development of microcephaly and other neurological disorders. In Brazil, approximately 5,000 cases of microcephaly and / or CNS disorders suggestive of congenital infection have been reported in the last two years. Genetic polymorphisms may be responsible for the imbalance of the inflammatory process, being potential markers of susceptibility to ZIKV as well as responsible for the associated symptoms and their outcomes, such as congenital zika syndrome. **Objectives:** Is evaluate if there is a genetic susceptibility favoring or protecting the appearance of microcephaly in infants exposed to the ZIKV during pregnancy and evaluate the contribution of the genetic makeup to the outcomes of the infection. **Materials and Methods**: This project will be conducted in accordance with the norms of the Resolution No. 466/2012 of the Ethics National Council. Blood sample from previously selected patients collected and we will separate serum, plasma and buffy coat and stored at – 80 ° C until use. Genomic DNA extraction will be performed according to the protocol of the Gentra® Puregene® Blood Kit (Qiagen). Genotyping will be performed with the Illumina HTS Custom Genotyping BeadChips trade panel. Logistic regression will be used to examine the association between genetic variants and infection, assuming an additive model for the outcome. The Principal Component analysis will be performed to control the ancestral confounding, in addition to the calculation of the lambda genomic inflation factor. **Perspectives:** Genetic studies provide indications about possible genetic variants associated with increased susceptibility to the development of congenital Zika syndrome, and characterize new molecules as potential therapeutic targets, diagnoses and prognoses of clinical forms of the disease.

Support: CAPES, FAPESB

Keywords: Zika, microcephaly, genetic susceptibility.

LINHA 5: Imunogenética/Genômina/Proteômica

GENETIC VARIANT (RS6587666) IN THE *FILAGGRIN* (*FLG*) MAY PROTECTS AGAINST ECZEMA ACCORDING TO THE AFRICAN GLOBAL ANCESTRY

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Introduction: Eczema is the most common skin disease worldwide that have diverse trigger factors, including interactions between skin barrier defect and immunological factors. In several studies, mutations in the *Filaggrin* (*FLG*) were reported for the risk of eczema. *FLG* codes a key protein to the formation of the stratum corneum of the skin. Besides, some previous works have observed ethnic differences in *FLG* mutations. Up to 50% of Europeans with eczema bear certain *FLG* mutation. Meanwhile, in African populations *FLG* mutations are not common. The Brazilian population is characterized by an admixture between Africans, Europeans and Native Americans, with different proportions of ancestral populations according to the region of the Brazil. African ancestry component had the greater contribution in Salvador, Bahia, Brazil. Until now, there are no studies evaluating global ancestry, genetic variants in *FLG* with eczema. In this way, the objective of this work was to evaluate the association between *FLG* mutations and eczema according to the African global ancestry contribution. **Methods and Results:** DNA was extracted from peripheral blood of 1,246 participants residents in Salvador, Brazil from a longitudinal cohort study on the Social Changes, Asthma and Allergy in Latin América (SCAALA). The samples were genotyped using Illumina 2.5 Human Omni Beadchip. Eczema was defined according to the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. We have stratified the studied population according to the African global ancestry by tertiles (1^{th}, 2^{th} and 3^{th}). Logistics regressions were performed using PLINK 1.9. The analyses were adjusted for sex, age and helminth infection. P<0.05 was considered significant. Our results have shown that among the participants from the 3th tercile, a negative association of rs6587666 *FLG* was found for eczema (OR: 0.38; CI 95%: 0.18-0.79; P: 0.01). In population with 1th and 2th tertiles of African ancestry, the association was not significant. **Conclusion:** Although variants in *FLG* have been already described associated with eczema, here, we have shown the rs6587666 protecting against eczema in individuals with high African global ancestry. Further studies are needed to better explain such association.

Support: FAPESB and CAPES.

Keywords: eczema, African ancestry, genetic variant.

LINHA 5: Imunogenética/Genômina/Proteômica

GENETIC VARIANTS IN *OXA1L* ARE ASSOCIATED WITH ASTHMA AND ATOPY IN A BRAZILIAN POPULATION.

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Introduction: Atopy and Asthma are considered complex diseases resulting from genetic and environmental factors. The *OXA1L*is involved in the biogenesis of proteins from mitochondria membrane. Changes in oxidative stress and calcium homeostasis in bronchial smooth muscle cells increase mitochondrial biogenesis, cell proliferation, and remodeling of the airways. Thus, we hypothesize that genetic variants in *OXA1L* are associated with asthma and atopy in an admixture population from Brazil. **Methods and Results:** DNA from 1,307 individuals was genotyped using Illumina Human 2.5-8 Omni Bead chip. Logistic regression analyses were performed to verify the association of polymorphisms in *OXA1L* with asthma and allergy markers using PLINK 1.9 software adjusted for sex, age, helminth infections and ancestry markers using an additive model. *In silico* gene expression analysis was performed in whole blood tissue using GTEx browser. The C allele of rs4981436 in *OXA1L* was positively associated with asthma (OR: 1.41; CI: 1.08-1.84; p: 0.012). Additionally, the G allele of rs8572 was positively associated with skin prick test to *Dermatophagoides pteronyssinus* (OR: 1.33; CI: 1.05-1.70; p: 0.020), *Periplaneta americana* (OR: 1.32; CI: 1.03-1.70; p: 0.029) and dog epithelium (OR: 2.21; CI: 1.02-4.82; p: 0.045). The same allele (G for rs8572) was also positively associated with anti-*D. pteronyssinus* specific IgE (OR: 1.27; CI: 1.10-1.56; p: 0.027). In relation to the *in silico* gene expression analysis, the G allele of rs8572 led to a higher *OXA1L* expression in whole blood. **Conclusion:** Variants in *OXA1L* were positively associated with asthma and allergymarkers in our population. At least in part, this association can be explainedby the increased expression of this gene observed herein.

Keywords: Asthma, Atopy, Polymorphisms, OXA1L.

Support: CNPq, CAPES, FAPESB.

LINHA 5: Imunogenética/Genômina/Proteômica

A GENOME-WIDE ASSOCIATION STUDY (GWAS) FOR SUSCEPTIBILITY TO TRICHURIS TRICHIURA INFECTION IN BRAZILIANS.

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Introduction: Geohelminthiases are associated to chronic infections able to impair the physical growth, the cognitive development and deficiencies of micronutrients and there is Strong epidemiological evidence that host genetic factors are important determinants of the outcome of host-pathogen interactions. Progress in genomics and bioinformatics advances have facilitated the successful implementation of genome-wide association studies (GWAS) to understand the genetic basis of infectious diseases. To evaluate genetic determinants involved in the protection or susceptibility of the host to *Trichuris trichiura* infection using a genome-wideassociation study approach. **Methods and Results:** This study was conducted with 1,248 children / adolescents participating between 2005 and 2013, the Social Change, Asthma and Allergy in Latin America (SCAALA) program. The SCAALA subjects were previously genotyped for 2.3 million SNPs distributed along the 23 chromosomes of the human genome, using standardized commercial panels currently available from Illumina (2.5 Omini beadchip[CF1]). Genetic associations were made in the PLINK program and RStudio (StataCorp LP, College Station, TX, USA). We report here a genome-wide association study for host susceptibility to Trichuris trichiura infection using 130 individuals with T. trichiura (cases) and 1.090 population controls samples from SCAALA. Primary analysis identified 4 top SNPs with significance (rs9450204 / P = 1.9 × 10-7 / odds ratio = 0.95); (rs12948860 / P = 4.8 x 10-7 / odds ratio = 0.003); (rs74796379 / P = 4.9 x 10-7 / odds ratio = 0.01) and (rs12620585 / P = 4.5 x 10-7 / odds ratio = 0.002). **Conclusions:** In summary, to our knowledge, we report the first GWAS for Trichuris trichiura infection resulted in a description of the main genetic determinants related to a pathogenic or protective response in Trichuris trichiura infection, thus contributing to a better understanding of the parasite-host interaction biology. Further studies should be conducted to elucidate the causal variant within the associated region and to identifying the functional effects of the associated variant.

Support: CNPq and UFBA

Keywords: Gwas, *Trichuris trichiura*, SCAALA.

LINHA 5: Imunogenética/Genômina/Proteômica

POLYMORPHISM IN FOXP3 GENE IS ASSOCIATED WITH THE EXPRESSION OF FOXP3 BUT NOT TGF-β AND IL-10 IN T LYMPHOCYTES FROM ASTHMATICS.

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Introduction: Asthma affects about 334 million people worldwide, and genetic and environmental factors can influence the development of this disease. FOXP3 is a transcription factor responsible for the function and development of regulatory T cells (Treg), which are responsible for suppressing immune responses in allergic disorders especially through cell-cell interactions and / or the production of TGF-b and IL-10. This study evaluated the associations between FOXP3 genetic variantswith FOXP3, IL-10 e TGF-β expression in T lymphocytes. **Methods and Results**: Individuals were recruited from ProAR (Program for Asthma and Allergic Rhinitis Control in Bahia). DNA was extracted from peripheral blood and the SNPs in FOXP3 (rs2280883, rs2294021, rs2294021, rs2232365) were genotyped using TaqMan probe. The expression of FOXP3, TGF-b e IL-10 in T lymphocytes was determined in a subsample of 73 individuals and the peripheral blood monoclonal cells (PBMC) were obtained through the Ficoll-Hypaque gradient. PBMCs were labeled with monoclonal antibodies to the surface markers and to intracellular cytokines, and anti-cytokine monoclonal antibody conjugated to the fluorochromes phycoerythrin (PE) and APC ("Allophycocyanin"). Next, they were acquired by cytometry (FACSCanto – Becton Dickinson). The expression was evaluated according to the genotypes of the variants in Graphpad software. Expression of FOXP3 in T lymphocytes was significant only for rs3761548 in TT individuals when compared with GG (* p <0.05) and GT (* p <0.05). On the other hand, no association was found with the different genotypes for FOXP3 variants and TGF-β and IL-10 producing-lymphocytes. **Conclusion:** Higher expression of FOXP3 was observed in TT for rs3761548 however none of the polymorphisms studied in FOXP3 gene were able to affect TGF-β and IL-10. Further studies are being carried out to better understand how such polymorphisms affect the expression of these molecules in asthmatic patients.

Support: CAPES

Keywords: asthma; FOXP3; T lymphocytes

LINHA 5: Imunogenética/Genômina/Proteômica

EXPRESSION OF M2 MACROPHAGES-RELATED MICRORNAS IN RELATION TO TUMOR-ASSOCIATED MACROPHAGES IN ORAL SQUAMOUS CELL CARCINOMA

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Introduction: The squamous cell carcinoma (OSCC) is a malignant neoplasm with high degree of locally aggressive and metastasis. The lesion grows with proliferation of malignant cells associated to an inflammatory component present in the tumor microenvironment, including macrophages. M2 macrophages play a crucial protumoral role in solid tumor development, however the approach of microRNAs (miRNAs) regulators of macrophages polarization/activation in OSCC is almost completely unexplored. The purpose of this study was to investigate in OSCC the expression pattern of miRNAs related to M2 macrophages functions in relation to tumoral distribution of these cells and histopathological grading of tumors. **Methods and Results:** This study was approved by Ethics Committees of Aristides Maltez Hospital – Salvador, Bahia, Brazil (267/10). After microdissection, expression of miRNAs was investigated by qRT-PCR in 35 paraffin embedded OSCC samples. Additionally, localization and semi-quantification of total (CD68+) and M2 (CD163+ and CD204+) macrophages in periparenchymal stroma and intraparenchymal compartment were performed in corresponding samples by immunohistochemistry. The investigated samples showed deregulated expression of miR-511-5p (84.85%), miR-511-3p (81.25%), miR-143-3p (60%) and let-7c-5p (60%). Particularly, miR-511-5p exhibited overexpression in 72.73% of the cases. In addition, miRNAs levels were positively correlated ($p < 0.05$). No association between miRNAs expression and histopathological grading of tumors was demonstrated. All cases exhibited presence CD68+, CD163+ and CD204+ macrophages, with massive infiltration in the periparenquimal stroma. The subpopulations of macrophages were positively correlated in both microlocalizations ($p < 0.05$), with no differences between the CD68+, CD163+ and CD204+ macrophages counting. The number of CD68+ macrophages in the periparenquimal stroma was elevated in moderately/poorly differentiated tumors ($p = 0.017$). However, no correlation was observed between number of macrophages and miRNAs expression. **Conclusion:** Our data suggest that overexpression of miRNA-511-5p presents involvement in OSCC tumorigenesis. Moreover, similarities observed in infiltration of investigated subpopulations corroborates to the current evidence that in OSCC microenvironment the macrophages predominantly express alternative activation.

Support: FAPESB, CNPq and PIBIC-UFBA

Keywords: oral squamous cell carcinoma, miRNAs, macrophages

LINHA 5: Imunogenética/Genômina/Proteômica

VARIANTS IN THE *NPS* GENE IS ASSOCIATED WITH CHILDHOOD ASTHMA AND ATOPY IN A BRAZILIAN POPULATION

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Introduction: The neuropeptide S (NPS) sequence is a conserved 20-amino-acid peptide, with few variations located in the center and C-terminus of the peptide. NPS and its receptor affect multiple neuroendocrine, behavioral, and inflammatory responses. NPS selectively binds and activates a NPS receptor inducing intracellular signalling via mobilization of calcium, increase in cAMP levels, and the mitogen activated protein kinase pathway. NPS–NPSR complex may play a role in modulating innate immunity and chronic inflammation, such as macrophage adherence, migration and phagocytosis of bacteria, chemotaxis, and induction of proinflammatory cytokines, this mainly implicated in susceptibility to asthma and inflammatory disorders in humans. The aim of this study was to investigate whether single nucleotide variants (SNVs) in the *NPS* are associated with asthma and allergic markers. **Methods and Results:** The study comprised 1,246 children from the SCAALA (Social Changes Asthma and Allergy in Latin America) program. The genetic variants in *NPS* were associated to different phenotypes such as asthma; and IgE and skin prick test for at least one allergen. The genetic information location between 129347613 and 129350935 from chromosome 10 was accomplished using the Illumina 2.5 Human Omni bead chip. Logistic regression was used to assess the association between asthma, allergy markers and *NPS* variants performed in PLINK 1.07 software with adjustments for sex, age, helminth infection and ancestry markers. Also, the haplotype analysis was made using the SNPSTATs. In additive model, three SNVS were associated with asthma: the rs11018195 (OR 0.43; IC 0.26-0.71; p 0.001), rs11018194 (OR 1.39; IC 1.01-1.90; p 0.04), rs990310 (OR 0.60; IC 0.42-0.87; p 0.008). The rs35729370 was associated with allergy markers, IgE (OR 0.80; IC 0.64-0.99; p 0.04)

and SPT (OR 0.77; CI 0.61-0.98; p 0.03) for at least one allergen. The rs990310 variant is missense, with change from Serine to Leucine at position 14. The haplotype was only significant for rs11018195 and rs990310 (OR 0.43; IC 0.26-0.71; p 0.001) with its polymorphic variants. **Conclusion:** The variants in the *NPS* gene are significantly associated with asthma and/or allergy markers. We believe that this missense variant may change the signal peptide decreasing the susceptibility for asthma, affecting the subcellular location. Therefore, these SNVs may offer an impact on the occurrence of the asthma and atopy in this population.

Support: CAPES, CNPQ, FAPESB.

Keywords: Asthma, Atopy, Polymorphism, *NPS*, Genetic Association.

LINHA 5: Imunogenética/Genômina/Proteômica

POLYMORPHISMS IN THE 5 – LIPOXYGENASE ENZYME ARE ASSOCIATED WITH ATOPIC ASTHMA AND ATOPY IN BRAZILIAN POPULATION

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Introduction: Asthma is a chronic inflammatory disease of the lower airways, characterized by bronchial hyperreactivity, mucus hyperproduction and variable airflow limitation. Atopic asthma is the most common phenotype, which is characterized by the production of IgE and Th2-type cytokines in response to aeroallergens. 5-Lipoxygenase (5-LO) is an enzyme that catalyzes the biosynthesis of leukotrienes (LTs) from arachidonic acid (AA). LTs play key roles in the pathology of allergic asthma, rhinitis and arthritis but also contribute to the pathogenesis of cardiovascular disease and cancer. The 5-LO is an important therapeutic target and there are already licensed drugs to inhibit its action. This is the first genetic study in this gene performed in the Brazilian population where the prevalence of asthma is one of the largest in the world. **Methods and Results:** Genotyping was performed using a commercial panel (Illumina), and carried out in 1,245 participants of SCAALA program (Social Change, Asthma, Allergy in Latin American). Logistic regressions for phenotypes such as asthma, atopic asthma, asthma severity were performed using PLINK 1.9 software adjusted for sex, age, helminth infections and ancestry markers. In our study the SNVs rs11239524, rs11239500, rs61854092 and rs10900213 located on intron region in *5-LO* were negatively associated with atopy in two genetic models of association (additive and dominant). The SNVs rs11239524, rs10900213, rs11239505, rs7919239, rs6593484 and rs61854092 were all negatively associated with atopic asthma in both genetic models as well. **Conclusion:** Polymorphisms in *5-LO* are associated with allergic asthma phenotype and atopy in a Brazilian population. Functional studies must be carried out in other to explore the impact of such alterations in this protein that could, at least in part, explain the observed associations.

Support: CNPQ, FAPESB

Key words: polymorphisms, asthma, allergy

LINHA 5: Imunogenética/Genômina/Proteômica

NLRP3 VARIANTS ARE ASSOCIATED WITH ASTHMA AND *BLOMIA TROPICALIS*-INDUCED IL-13 PRODUCTION IN A BRAZILIAN POPULATION

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Introduction: *Blomia tropicalis* mite is the main asthma-induced allergen in tropical and subtropical regions such as Brazil. Atopic asthma is a chronic inflammatory disease in airways characterized by the production of Th2-type cytokines such as Interleukin (IL)-4, IL-5 and IL-13. IL-33 exacerbates antigen-driven features of allergic asthma. This cytokine active several immune cells through its membrane receptor (ST2L) and induces release of Th2-type cytokines, polarizing the Th2-inflammation. NLRP3 is located in the nucleus of Th2 cells and regulates the transcriptional Th2 program acting like a transcription factor in these cells. On the other hand, activation of NLRP3 inflammasome culminates in inactivation of functional free IL-33 by activation of caspase-1. Therefore, it becomes of great importance to study the influence of *NLRP3* variants on asthma and allergic diseases and the aim of this study was to associate single nucleotide variants (SNVs) in the *NLRP3* with asthma and allergy markers, never explored before in a Brazilian population. **Methods and Results:** DNA was extracted from peripheral blood from 1,244 subjects and the samples were genotyped using Illumina 2.5 Human Omni Beadchip. Logistics regressions were carried out for asthma and IL-13 production using PLINK software 1.07 adjusted for sex, age, helminth infection and ancestry markers, using the additive model. In addition, haplotype and genetic risk score analysis were performed using SNPStats program. The SNVs rs72553860 and rs12137901, respectively were positively associated with asthma (OR 1.38; p=0.004) and (OR 1.28; p=0.016). On the other hand, rs36021952 and rs74154644, respectively, were negatively associated with asthma (OR 0.69; p=0.038) and

(OR 0.69; p=0.038). The polymorphisms rs4378247, rs12565738, rs45624634, and rs7525979, respectively, were negatively associated with IL-13 production (OR 0.39; P=4e-04), (OR 0.24; P=0.004), (OR 0.41; P=0.001) and (OR 0.38; P=0.006) when peripheral blood cells were stimulated with *Blomia tropicalis*. In addition, haplotype and genetic risk score analysis also showed a statistically significant difference between the two studied phenotypes (asthma and IL-13). **Conclusion:** Variants in *NLRP3* were associated with asthma and IL-13 production in our population. However, additional studies should be conducted to investigate the functional role of these variants that could explain the development of complex diseases such as asthma.

Support: CNPq, CAPES, FAPESB, SCAALA.

Keywords: *NLRP3*; variants; asthma; *Blomia tropicalis*.

LINHA 5: Imunogenética/Genômina/Proteômica

THE AIRWAYS MICROBIOME AND ASTHMA: A REVIEW.

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Introduction: Over the past few years the scientific community widely assumed that asthma was an allergic/atopic disease caused by allergen exposure only. Recently new evidences suggesting changes in airways microbiome play important roles on asthma development. Here, we review the results of such studies on the composition of microbial communities in the airways of individuals with asthma and not asthmatics. The main goal was to identify relevant studies describing the relationship between airways microbiome on development of asthma. **Methods and Results:** We searched scientific articles in the PubMed electronic database using the following search terms: "airways AND microbiome AND asthma AND human" within title words or MeSH (Medical Subject Headings) terms. Studies that met the following criteria were selected: original article employing 16S rRNA gene sequence analysis, English language and published between 2014 and 2017. Review articles, commentary, editorials, duplicate articles or studies with murine model were excluded. The literature search described above yielded 29 studies. A total of 6 articles were included in this review. Two articles reported an inverse association of asthma with bacterial diversity. In asthma patients the respiratory tract microbiota undergoes a qualitative transformation: as compared to healthy individuals the relative abundance of the phyla Proteobacteria and Firmicutes increases. *Moraxella* and *Streptococcus* were the most frequently associated with asthma in the included articles. It remains unclear whether alterations on microbiome would be cause or consequence of asthma. **Conclusion:** It is of considerable interest to determine the role of the microbiome in the development of asthma, and to understand how distinct microbial communities from the airways are established in asthmatics individuals and influences the different phenotypes of disease.

Support: ERC, FAPESB.

Keywords: Asthma, Microbiome, Airway.

LINHA 5: Imunogenética/Genômina/Proteômica

ASSOCIATIONS OF GENETIC VARIANTS IN *TGF-B1* GENE WITH SEVERE ASTHMA

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Introduction: Asthma is a chronic respiratory disease caused by a combination of genetic and environmental factors. Transforming Growth Factor beta 1 (TGF-β1) plays a key role in airway remodeling and asthma through its immune regulatory activity. Polymorphisms in the TGF-B1 gene have been implicated in susceptibility to asthma, however results are controversial. The aim of the present study was to explore the associations between genetic variants in the TGF-β1 gene with the risk for severe asthma in a case-control study in Salvador, Bahia, Brazil**. Methods and Results:** This study included 1,418 patients with asthma (465 mild and 510 severe) and 443 control subjects recruited from ProAR (Program for Asthma and Allergic Rhinitis Control in Bahia). Four SNPs (rs1800469, rs1800469, rs2241712, rs2241715) in *TGFB1* were genotyped using TaqMan assay. This study evaluated the role and frequency of genetic polymorphisms of the TGF-β1 gene in the different study groups. Genotypic associations between theses SNPs and asthma were evaluated using logistic regression analysis adjusted for sex, age and skin color. For the four polymorphisms analyzed, no significant differences were observed for allele or genotype frequencies between the asthmatics patients and controls ($p > 0.05$). No significant difference was observed in genotype between patients with refractory asthma and controls ($p > 0.05$). However, the SNPs rs2241715 and rs1800469 was positively with severe asthma when compared to mild asthma (OR= 1.45; CI 1.07 – 1.97 and OR= 1.38; CI 1.02 – 1.87, respectively). **Conclusion:** These results indicate that the polymorphisms in TGF-β1 gene may play an important role in the modulation of asthma severity.

Support: FAPESB

Keywords: asthma, polymorphisms, TGF-β1

LINHA 5: Imunogenética/Genômina/Proteômica

VARIANTS IN *CRISPLD2* ARE ASSOCIATED WITH ASTHMA AND ASTHMA SEVERITY IN SALVADOR/BA

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Introduction: Asthma is a disease multifactorial and its development depends of genetic and environmental factors. The glucocorticoids response interferes in the expression of some genes such as cysteine rich secretory protein LCCL domain containing 2 (*CRISPLD2)* that codifies a protein with the same name related with the increases of glucocorticoids response. Functional experiments showed that in airway smooth muscle cells, *CRISPLD2* mRNA and protein levels changed in response to treatment with a glucocorticoid or proinflammatory cytokine, and that knockdown of *CRISPLD2* resulted in increased levels of IL1b-induced IL6 and IL8 mRNA expression. The objective of this study is to evaluate the association of genetic variants in *CRISPLD2* with asthma and severity of asthma. **Methods and Results:** The study comprised 1,245 children from SCAALA (Social Changes, Asthma and Allergy in Latin America) Program. The children were classified with asthma through the ISAAC phase II questionnaire. DNA was extracted from whole blood samples and genotyped using Illumina 2.5 Human Omni Bead chip panel. Logistic regression was used to assess the association between asthma and asthma severity and *CRISPLD2* variants in PLINK 1.07 software adjusted for sex, age, helminth infection and ancestry markers. The study included 111 SNPs in *CRISPLD2*. The allele G of rs4261526 was positively associated with asthma (OR = 1.45; 95% CI: 1.18-1.80 and P value: 0.000547) and asthma severity (OR = 1.43; 95% CI: 1.10-1.87 and P value: 0.00807) in the additive model. The allele T of rs56290224 was negatively associated with asthma (OR = 0.64; 95% CI: 0.48-0.87 and P value: 0.00437) and asthma severity (OR = 0.63; 95% CI: 0.42-0.95 and P value: 0.026) in the additive model. These SNVs is located in introns and have never been associated with asthma or other diseases in other populations. **Conclusion:** The rs4261526 may be a risk factor and the rs56290224 may be a protective factor for asthma and the severity of this disease. Being in introns, these SNVs can alter gene expression and the level of proteins production. Further studies are necessary to show how variants in this gene may influence in the levels and function of this protein and how these affect asthma.

Support: CAPES.

Keywords: Asthma; variant; CRISPLD2.

LINHA 5: Imunogenética/Genômina/Proteômica

VARIANTS IN *STAT1* AND *IL6* ARE ASSOCIATED WITH ASTHMA AND ASTHMA SEVERITY IN A LATIN AMERICAN POPULATION

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Introduction: Asthma is a chronic inflammatory disease in which environmental and genetic factors are major risk factors. Studies have associated Interleukine-6 (*IL6)* with the developing of severe asthma. *IL6* encodes a cytokine with the same name that acts in inflammation. This cytokines can be produced by primary lung epithelial cells in response to dangers. IL-6 has emerged as an important regulator of effector CD4 T cell fate, because when it is secreted into the serum IL-6 induces a transcriptional inflammatory response, in part because *STAT1 (signal transducer and activator of transcription 1)* activation. The protein encoded by this gene act as transcription activators, and mediates the expression of a variety of genes involving in asthma. Single nucleotide Variants (SNVs) are the most common variations in the genome and are responsible for phenotypic differences among individuals. Many SNVs in the *IL6* and *STAT1* were identified. Our aim was to investigate the potential association between variants in *IL6* and *STAT1* with asthma and asthma severity. **Methods and Results:** Genotyping was performed using a commercial panel Illumina 2.5 Ominichip in 1,245 participants of Social Change, Asthma, Allergy in Latin American program. This study included the analysis of 7 SNVs in *IL6* and 28 SNVs in *STAT1*. The phenotypes of Asthma symptoms and severity were defined according to ISAAC-II. Logistic regressions for asthma symptoms and asthma severity were performed using PLINK 1.9, using the three genetic models, adjusted for sex, age, helminth infections and ancestry markers. *In silico* regulation function of SNVs was analyzed using rSNPbase and RegulomeDb databases. Also, gene tissue expression was performed by Gtex and Genetic score with SNPSTATs. In *STAT1* the allele C of rs11305 was positively associated with asthma (OR: 2.7;95%CI: 2.74-2.82) in recessive model, and positively associated with asthma severity (OR:1.7; 95%CI: 1.6-1.9) in the same model. In *IL6* the allele A of rs41511150 was negatively associated with asthma (OR:0.80 and 95%CI: 0.69-0.90) and positively associated with IFN levels (OR:1.78 and 95% CI: 1.80-1.95), both in additive model. The two SNVs are involving in proximal and distal regulation of DNA. **Conclusion:** Genetics variants in *IL6* and *STAT1* may influence the developing of asthma and severity of asthma. Additional studies may clarify the function of the *IL6* and *STAT1* SNVs and its correlation with asthma severity.

Support: FAPESB, CNPq.

Keywords: Variants, asthma, IL-6, STAT-1

LINHA 5: Imunogenética/Genômina/Proteômica

BIOGEOGRAPHIC ANCESTRY AS ASTHMA AND ATOPY IN A BRAZILIAN POPULATION

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Introduction: Allergic asthma is a chronic inflammatory disease of the lower airways characterized by eosinophilic inflammation, increased IgE levels, and bronchial remodeling with reversible obstruction in response to common environmental allergens. It is a multifactorial disease influenced by environmental, socioeconomic and genetic factors affecting more than 300 million people in the world. However, studies have shown differences in the prevalence of this disease between distinct racial and ethnic groups, and a greater risk for individuals with African ancestry, suggesting an important role of biogeographic ancestry in the development of allergic diseases such as asthma. In Brazil, the asthma is one of the major causes of hospitalization and considering the strong African ancestral component in the city of Salvador, it is necessary to establish the role of biogeographic ancestry on the occurrence of asthma and atopy in our population. **Objectives:** To analyze the association between the physiological measures associated with the diagnosis of asthma and atopy with global ancestry, considering the inflammatory (Th2 response) and regulatory (IL-10 and TGF-β) cytokines involved in the pathophysiology of such diseases. **Materials and Methods:** For this project we will genotype 1,253 children recruited from the SCAALA (Social Change in Asthma and Allergies in Latin America) cohort through an Illumina chip, containing informational ancestral markers. For the association between cytokines and asthma/ atopy will be performed logistic and linear regressions using R software. **Perspectives:** Identify markers in African ancestry related to inflammatory (Th2 response) and regulatory (IL-10 and TGF-β) cytokines and its role on asthma and atopy.

Support: FAPESB, CNPq and PIBIC-UFBA.

Keywords: asthma, ancestrality, markers.

LINHA 5: Imunogenética/Genômina/Proteômica

VARIANTS IN *IL25* GENE ARE ASSOCIATED WITH ASTHMA AND ATOPY MARKERS IN A LATIN AMERICAN POPULATION

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Introduction: IL-25, also known as IL-17E, is a member of the IL-17 cytokine family encoded by a gene localized in the chromosome 14q11.2. It was first identified in 2001 and found to induce a Th2-type immune response, by stimulating IL-4, IL-5 and IL-13 gene expression, via the interaction with IL17 receptor beta (IL-17RB) and the induction of nuclear factor kappa-B. Because of its interaction with cellular targets directly involved with the pathogenesis of atopic asthma, such as Th2, Th9, monocytes and eosinophils, and its capacity of inducing eosinophilic airway inflammation, mucous metaplasia and airway hyperresponsiveness, IL-25 has been considered one of the various candidate genes for asthma and allergy susceptibility. **Methods and Results:** Genotyping was performed in 1.245 participants of SCAALA program (Social Change, Asthma, Allergy in Latin American) using Illumina 2.5 Omini chip. We then analyzed three single nucleotide variants (SNVs) on *IL25*. Logistic regressions for asthma and allergy markers (skin tests and IgE production) were performed using PLINK software 1.9, in the three genetic models, adjusted for sex, age, helminth infections and ancestry markers. Asthma was defined accordingly with The International Study of Asthma and Allergies in Childhood (ISAAC). The pairwise linkage disequilibrium (LD) was created using Haploview 4.2. We found that the allele C of the rs3811178 was positively associated with asthma (OR: 1.51; CI:1.00-2.10; p: 0.01) in a recessive model, also positively associated with asthma severity in an additive (OR: 1.35; CI: 1.05-1.74; p: 0.01) and recessive (OR: 1.87; CI: 1.25-2.78; p: 0.002) model, and negatively associated with skin test (OR:0.71; CI:0.52-0.96; p: 0.02) and specific IgE production (OR: 0.76; CI: 0.60-0.97; p: 0.03) for *Blatela germanica* in an additive model. And both of the other two SNVs, the allele C of rs8014568 (OR: 0.71; CI: 0.53-0.97; p: 0.03) and the allele C of rs7145551 (OR: 0.68; CI: 0.50-0.93; p: 0.01) were negatively associated with the specific skin test for *B. germanica,* in an additive model. These SNVs are in high LD.. **Conclusion:** Therefore, in this work, *IL25* SNVs were inversely associated with asthma and atopy, playing suggestively a protective role for atopy but acting as a risk factor for the development of non-atopic asthma. More studies are essential to clarify the function of role of IL-25 and its correlation with atopy and asthma.

Support: FAPESB and CNPq.

Keywords: single nucleotide variant, IL25, asthma.

LINHA 5: Imunogenética/Genômina/Proteômica

VARIANTS IN *IL17RB* ARE ASSOCIATED WITH ASTHMA AND ATOPIC MARKERS IN A BRAZILIAN POPULATION

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Introduction: Asthma is a chronic inflammatory disease of the airways. Classically the asthma is atopic, orchestrated by molecules and cytokines produced by T-helper-2 cells profile. Genetic variants have an important role in the course of asthma and represent a risk factor. Many studies have associated the *Interleukin 17 Receptor B* (IL17RB) with atopic asthma and cytokines of Th2 profile. This gene encodes a protein named IL-17RB, which is a receptor that binds to IL-17B and IL-17E, through this bind NF-kappaB is activated and start the pro-inflammatory cytokines production. Single Nucleotide Variants (SNVs) are responsible for the multiples endophenotypes in asthma. Many SNVs in the *IL17RB* were identified as a risk factor to develop atopic asthma. Thus, our aim was to investigate the potential association between variants in *IL17RB* with asthma and atopic makers. **Methods and Results:** Genotyping was performed using a commercial panel Illumina 2.5 Ominichip in 1,245 participants of Social Change, Asthma, Allergy in Latin American program. This study included the analysis of 12 SNVs in *IL17RB*. Logistic regressions for asthma and atopic markers were performed using PLINK 1.9, using the dominant model, adjusted for sex, age, helminth infections and ancestry markers. Gene tissue expression *in silico* was performed by Gtex databank. The analysis of case-control associations showed that the C allele of rs3017 was positively associated with asthma (OR: 1.72; 95%CI: 1.10-1.91) and skin test for *Blatela germanica* (OR: 1.41; 95%CI 1.10-192). The T allele of rs999514 was negative associated with IgE production (OR:0.71; 95%CI: 0.52-0.97) and asthma (OR: 0.43; 95%CI 0.42-0.95) . The first variants increase the levels of IL17RB expression in the lung**. Conclusion:** Variants in *IL17RB* may influence the developing of atopy and asthma, maybe because this receptor acts in Th2 pathway. More studies are necessary to clarify the function of the *IL17RB* and its correlation with atopy and asthma.

Support: FAPESB, CNPq.

Keywords: Variants, asthma, IL17RB

Fundada em 2002, a **Revista de Ciências Médicas e Biológicas** é editada pelo Instituto de Ciências da Saúde da Universidade Federal da Bahia e tem por objetivo publicar, quadrimestralmente, os resultados de pesquisas originais que venham a contribuir para o desenvolvimento do conhecimento científico e tecnológico nas áreas médica, bioética e biológica.

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ISSN 1677509-0