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Diagramación y Diseño: Andrés Esteban Zapata - aez.sgi@gmail.com

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Clostridioides difficile infection (CDI) is the major cause of hospital-acquired diarrhea associated to antibiotics treatment in developed countries. CDI has become a health security threat and a considerable challenge to public health worldwide. The increased incidence and the severity of disease have been linked to the emergence and fast spread of hypervirulent epidemic strains. Moreover, a further increase in community-acquired infections and the zoonotic potential of *C. difficile* lead to a highly dynamic epidemiology of CDI. Enzyme immunoassay (EIA), a technique with high specificity but low sensitivity, is widely used as a diagnostic tool for *C. difficile* nowadays. To optimize the diagnosis and provide information for epidemiological surveillance strategies, the expression of glutamate dehydrogenase and toxin B (TcdB) of *C. difficile* was determined by EIA, direct PCR of stool samples and colony PCR of anaerobic culture. We also conducted comparative analysis to determine the performance of the direct PCR for *C. difficile*.
Faecal samples from 81 hospitalized individuals with diarrhea were collected. Clinical and demographic data were analyzed. We found a frequency of 18.5% for toxigenic strains. Treatment with antibiotics or proton-pump inhibitors were the main risk factors for CDI present in our cohort. No differences were observed between CDI^+ and CDI^- individuals for the aforementioned risk factors, nor comorbidities or age distribution. However, we did detect an increase in leukocytes, lymphocytes and monocytes counts in CDI patients ($p<0.05$).
To validate our direct PCR method we used the EIA as the reference test. Our results showed a sensitivity of 1.0 and a Negative Predictive Value of 0.85 compared to EIA. Although a larger number of samples is needed to validate the method and determine specificity, this technique could be a useful method for *C. difficile* infection screening.

288. (546) **EFFECT OF TOFACITINIB ON THE ACTIVATION OF T LYMPHOCYTES IN PATIENTS WITH RHEUMATOID ARTHRITIS**

*Onofrio Luisina[1,2], *Alamino Vanina Alejandra[1,2], Zacca Estefanía[1], Ferrero Paola[1], Acosta Cristina[1], Álvarez Ferreira María Clara[1], García Oro Agustina[1], Reta Arbó Lucas[1], Werner Marina[1], Onetti Laura Beatriz[1], Cadile, Isaac Ignacio[1], Mussano, Eduardo Daniel[1], Carolina Montes[2], Gruppi Adriana[2], Acosta-Rodriguez Eva Virginia[2].
[1]Hospital Nacional de Clínicas (HNC). Facultad de Ciencias Químicas, UNC - CIBICI, CONICET

Tofacitinib (Tofa) is a Jak1/3 inhibitor that blocks the intracellular signaling of inflammatory cytokines and is used as 3rd line of treatment in Rheumatoid Arthritis (RA). Tofa is very effective to achieve disease remission but it is associated to higher incidence of herpes zoster reactivation likely due to alterations in cellular immunity. While several studies have evaluated on the effects of Tofa on the immune system in the context of RA, knowledge about its impact on the activation and differentiation of T lymphocytes (TL) is scarce. We aimed to study this aspect in vivo and in vitro by determining the functional status of TL in different groups of treated RA patients (Tx RA) and the effect of Tofa in the activation of T cells from healthy donors (HD), respectively. Thirty-one HD and 106 RA patients were recruited in the Rheumatology Service (HNC) to evaluate numerous biochemical and immunological parameters. Principal component analysis showed that 82 of these variables explain around 70% of the variance, with variables related to the activation and differentiation of TL as the main difference between HD and different groups of Tx RA. Compared to HD, Tofa Tx RA patients presented a significant increase in the % of populations with terminal differentiation characteristics including CD27-CD28- of CD4+ TL ($p<0.01$) and KLRG1+CD57+ CD4+ and CD8+ TL ($p<0,05$). In addition, in vitro studies showed that Tofa reduced the activation of purified CD4+ and CD8+ TL as evidenced by a decrease in the upregulation of CD25, T-bet and the frequency of Ki-67+ cells. These effect were a dose-dependent and observed in total, naïve and, mainly, memory TL. Interestingly, Tofa increased the expression of senescent marker p21 in memory CD8+ TL. Altogether, our findings suggest that Tofa-induced replicative immunosenescence could underlie the biological effects of this drug in RA and be also involved in side effects, restraining the activity of memory TL involved in viral control.

289. (558) **CHEDIAK HIGASHI SYNDROME: CASE REPORT**

Introduction: Chediak Higashi Syndrome (CHS) is a rare autosomal recessive disorder, characterized by partial oculocutaneous albinism, prolonged bleeding, immune and neurologic dysfunction, and risk for the development of hemophagocytic lympohistiocytosis. The presence of giant secretory granules in leukocytes is the classical diagnostic feature, which distinguishes CHS from closely related Griscelli and Hermansky Pudlak syndromes.
The accelerated phase or HLH, is the primary cause of mortality in CHS and can occur at any age
Objective: Present patient with late diagnosis without development of accelerated phase
Clinical case: 5 year old male referred by Hematology due to the presence of intracytoplasmic granulations in neutrophils and gray hair
First child of healthy parents, not consanguineous. Recurrent obstructive bronchitis treated with budesonide with good response. No relevant infections. Difficult management of epistaxis and mild neurocognitive delay. Physical examination only shows gray hair and nystagnmus.
In laboratory, moderate neutropenia and mild anemia. Negative EBV and CMV serologies
Hair´s microscopic evaluation detects dispersal of pigment clumps throughout the hair shaft.
Normal abdominal ultrasound.
Conclusions: CHS is a rare disease. The diagnosis is suggested by characteristic findings on hair microscopy and pathognomonic giant cytoplasmic granules in leukocytes on a peripheral smear. Confirmation is made by the identification of a pathogenic variant in the CHS1/LYST gene The prognosis of the HLH phase is poor and hence early diagnosis on the basis of characteristic clinical findings and diagnostic laboratory examinations is critical to facilitate timely bone marrow transplantation before the development of accelerated phase.

290. (567) **DETECTION OF INTESTINAL MICROBIOTA COMPONENTS IN THE SYNOVIAL MICROENVIRONMENT OF PERIPHERAL SPONDYLOARHRITIS AND ITS ASSOCIATION TO IMMUNOPATHOGENIC MECHANISMS**

José Luis Arias[1], Eduardo Callegari[2], Daniela Paez[2], Blas Rodrigo[3], Alicia Munarriz[4], Rodolfo Pardo-Hidalgo[5], Héctor Tamashiro[6]. María Silvia Di Genaro[1].
[1]Universidad Nacional de San Luis-IMIBIO-SL (CONICET-UNSL), San Luis, Argentina; [2]SD Biomedical Research Infrastructure Network (SD BRIN) Sanford School of Medicine, University of South Dakota, Vermillion, SD, USA; [3]Centro Médico MEDICI, San Luis, Argentina; [4]Centro Médico CENYR, San Luis, Argentina; [5]Centro de Rehabilitación Médica CER, San Juan, Argentina; [6]Centro Médico Bolívar, San Luis, Argentina.

A role for intestinal microbes in arthritis is being considered. We analyzed intra-articular microbiota components and their association with immunopathogenic mechanisms of Spondyloarthritis (SpA). Synovial fluid (SF) of peripheral SpA patients were pooled (n=9): 6 psoriatic arthritis, 2 reactive arthritis, 1 undifferentiated SpA (Protocol approved CE002-2017). IL-17, IL-6, IL-23 and TGF-β levels were quantified in each SF sample by ELISA and compared with SF from osteoarthritis (OA). Moreover, SW982 cells (human synovial fibroblasts) were incubated with the SpA SF pool in absence or presence of polymyxin B (LPS inhibitor) and 48 h later the IL-6

levels in the supernatant were measured by ELISA. Furthermore, intestinal microbiota proteins were analyzed in the SpA SF pool through a Gel-LC bottom-up mass spectrometry-based proteomic study. Higher levels of IL-17, IL-6, IL-23 and TGF-β were detected in SpA compared with OA SF ($p<0.001$, $p<0.01$, $p<0.001$, and $p<0.01$, respectively). Since segmented filamentous bacteria (SFB) have a cardinal feature to induce Th17 cell differentiation in gut immunity, we searched for SFB peptides in the SF of SpA. We found 54 peptides of SFB with abundance estimated with an exponentially modified Protein Abundance Index (emPAI) from 0.01 to 0.28. In addition, LPS is present in synovial microenvironment of SpA since polymyxin B treatment significantly reduced IL-6 secretion by synovial fibroblasts stimulated with SpA SF ($p<0.05$). Therefore, we explored the synovial presence of peptides of microbiota Gram-negative bacteria, particularly genus *Dialister* because it was described as a potential intestinal microbial marker of disease activity in SpA. Accordingly, we found 55 peptides of genus *Dialister* (emPAI 0.02-0.33). Our findings show the presence of LPS and microbiota bacterial proteins in the synovial microenvironment of peripheral SpA and suggest their potential association with immunopathogenic mechanisms of this inflammatory arthropathy.

291. (570) **YAO SYNDROME (YAOS). FIRST REPORT OF A CASE IN ARGENTINA**

Gabriela F. Mora MD, MSc, PhD[1]; Rita Valdez MD, MSc[2]; Vanesa Lotersztein MD[3].
1. Clinical Immunology Service – Hospital Militar Central, Buenos Aires, Argentina.
2. Medical Genetics Service - Hospital Militar Central, Buenos Aires, Argentina.
3. Medical Genetics Service - Hospital Militar Central, Buenos Aires, Argentina.

Autoinflammatory syndromes (AIS) are characterized by apparently unprovoked episodes of inflammation, in the absence of autoantibodies or antigen-specific T cells, and result from genetic variants of the innate immune system.
Yao syndrome (YAOS), a NOD2-associated autoinflammatory disease, (first described in 2011) appears as episodic attacks of fever, dermatitis, polyarthritis, gastrointestinal and sometimes sicca symptoms associated with specific NOD2 sequence variants.
A 20 years-old previously healthy female, started 6 months previous to first visit, with **urticaria, angioedema, high grade fever, arthralgia, abdominal pain and diarrhea**. She was treated as chronic urticaria, **with poor response to anti-histaminics and NSAIDS.** Ambulatory evaluation by rheumatology and internal medicine showed no association to autoimmune nor infectious disease. Laboratory evaluation depicted **elevated acute phase reactants: ESR, CRP, fibrinogen, platelets, ferritin, together with granulocyte predominant leukocytosis.** MRI showed a mild splenomegaly with small scattered lymph nodes in abdomen and mediastine, which were metabolically active in a PET-CT.
Bone marrow aspiration and biopsy were hypercellular, with normal phenotype. Lymph node biopsy depicted chronic lymphadenitis with follicular hyperplasia, negative for neoplasia. Screening for PIDs was negative. Upper endoscopy and colonoscopy showed normal findings.
Inflammatory episodes continued lasting a few days to a week, with response to high dose steroids. Next generation sequencing for AIS and PID target genes was run (saliva sample, Illumina© sequencing and Sanger, MLPA, MLPA-seq, Array CGH confirmation) and detected the **NOD2 variant c.2104C>T (p.Arg702Trp).**
YAOS was diagnosed according to 2015 criteria, with the patient fulfilling 2 major, three minor and the molecular criteria. She is on moderate dose meprednisone regimen with good response to date.
This is the first description of a case of YAOS in Argentina.

292. (603) **PHENOTYPIC AND FUNCTIONAL CHARACTERIZATION OF PERIPHERAL T CELL POPULATIONS FROM COVID-19 PATIENTS HOSPITALIZED IN HOSPITAL PRIVADO UNIVERSITARIO CÓRDOBA- ARGENTINA.**

Luisina Onofrio*, Jeremías Dutto*, Sabrina Bossio*, Ruth E. Baigorri*, María Belén Brugo*, Laura Almada**, Constanza Marín**, Federico Ruiz Moreno**, Ximena Volpini**, Mariel Almeida, Carolina Olivera, Nicolás Ponce, Juan Nahuel Quiroz, Silene Silvera Ruiz, Lucia Bofelli, Eva Acosta Rodríguez, Carolina Amezcua Vesely, Daniela Arroyo, Fabio Cerbán, Laura Cervi, Laura Fozzatti, Paula Icely, Pablo Iribarren, Belkys Maletto, Gabriel Morón, Cecilia Rodríguez Galán, Cinthia Stempin, Claudio Abiega#, Daina Escudero#, Adrian Kahn#, Juan Pablo Caeiro#, Mariana Maccioni, Cristina Motrán, Laura Chiapello, Carolina Montes, Adriana Gruppi, Claudia E Sotomayor. **Grupo ImmunoCovidCBA**
*All these authors contributed equally. **All these authors contributed equally
Departamento de Bioquímica Clínica, CIBICI-CONICET, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba. #Hospital Privado Universitario de Córdoba, IUCBC.

SARS-CoV-2 infection results in asymptomatic, mild or severe disease. T cells could contribute to these different outcomes, but it remains unclear whether T cell response is dysfunctional or excessive. Here, we evaluated the phenotypic and functional features of circulating T cells from a cohort of 40 COVID-19 patients (Cpts) with moderate (MOD) and severe (SEV) clinical disease (aged 21-80 years) and 14 aged matched healthy controls (HC) by FACS. All Cpts exhibited a reduced frequency of CD3+T and Tregs cells compare to HC ($p< 0.05$). When exhaustion was evaluated, SEV Cpts showed higher % of PD-1+ and CD39+ in T conv cells ($p<0.05$), whereas no differences were found in BTLA or TIGIT expression. Even though, no differences in cytokine production (INF-γ, IL-2 and TNF) were observed, T conv cells from SEV Cpts showed a higher % of GZMB+ and CD107+ cells than MOD Cpts or HC ($p<0.05$). Circulating CD8+ T cells express different levels of CD8, where CD8lo cells represent highly activated cytotoxic T cells. COVID-19 patients presented a higher % of CD8lo T cells than controls and this increment was even more pronounced in SEV Cpts ($p=0.04$, MD vs HD; $p=0.0012$, SD vs HD). CD8lo T cells exhibited impaired cytokine production and CD107a expression compared to CD8hi T cells, although GZMB levels were similar among both CD8+ subsets. CD8lo population from HC showed higher % of naïve T cells than effector memory (EM)($p=0.04$) or EMRA ($p=0.008$) subsets, but this distribution was not seen in MOD or SEV Cpts. Indeed, MOD or SEV Cpts showed higher % of EM cells than HC.
Conclusion: the disease severity impacts on the phenotype and functional features of CD4+ and CD8+ T cells, with a pronounced increment in the % of CD8lo T cells as the disease worsens. These cells appear to have dysfunctional phenotype with an impairment of effector cytokines production but maintaining cytotoxic potential. The CD8hi/CD8lo ratio might be a useful parameter to predict the disease outcome.

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293. (145) **EXTRACELLULAR DNA TRAPS: NEW POTENTIAL BIOMARKERS AND THERAPEUTIC TARGETS FOR CHRONIC HEMOPHILIC SYNOVITIS IN PATIENTS TREATED WITH PRP**

Paula Oneto[1], María Eulalia Landro[2], Carla Daffunchio[2], Ana Laura Douglas-Price[2], Mirta Schattner[1], Horacio Caviglia[2], Eugenio Antonio Carrera Silva[1], Julia Etulain[1]
1.Laboratorio de Trombosis Experimental. IMEX-CONICET, Academia Nacional de Medicina. CABA. Argentina, 2.Hospital Juan A. Fernández. CABA, Argentina.

Introduction & aims: Hemarthroses in hemophilia cause chronic hemophilic synovitis (CHS) and the role of neutrophils infiltration on the pathophysiology of CHS is unknown. Neutrophils release extracellular DNA traps (ETs), structures containing DNA fibers and Elastase, which are associated with chronic inflammation. We aim to evaluate the association of ETs with join damage in CHS, the protective effect of platelet rich plasma (PRP) against ETs formation and after intraarticular injections in patients with CHS. **Methods:** Synovial Fluid (SF), PRP and platelet-poor plasma were