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LXV REUNIÓN ANUAL DE LA
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LXVIII REUNIÓN ANUAL DE LA
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ANNUAL MEETING OF BIOSCIENCE SOCIETIES 2020

LXV ANNUAL MEETING OF
SOCIEDAD ARGENTINA DE INVESTIGACIÓN CLÍNICA (SAIC)

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November 10-13, 2020

RESPONSIBLE EDITORS
María Cristina Carrillo
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Maria Cecilia Larocca

LA TAPA

María de Luján Alvarez. Ludueña

Técnica: óleo sobre tela

Medidas: 60 x 40 cm, año 2016

Gentileza de la autora

La obra de tapa refleja un lugar típico rosarino. El arroyo Ludueña nace en los campos de las afueras de Rosario y finaliza en el barrio Arroyito de la ciudad, donde desemboca en el Río Paraná.

María de Luján Alvarez es Bioquímica y Doctora en Ciencias Biológicas. Es investigadora adjunta (CIC-CONICET) en el Instituto de Fisiología Experimental (IFISE-CONICET) y docente en el área Morfología de la Facultad de Ciencias Bioquímicas y Farmacéuticas de la Universidad Nacional de Rosario (UNR). Alumna del taller de arte Tunkeyén, estudió con la pintora rosarina Ana Petrini. Ganó el segundo premio en el 12º Salón de Pintores Nóveles de la Sociedad Argentina de Artistas Plásticos de Rosario (2004), el primer premio en el 2º Salón Pintando Argentina de Rosario (2010), una mención al trabajo realizado en el 2º Encuentro de Pintores de Rosario organizado por la Asociación Cultural Museo Ambrosio Gatti (2018) y el tercer premio en el Concurso de Pinturas 150 años de la Sociedad Filantrópica Suiza (2018). Participa frecuentemente en muestras colectivas de diferentes salones pictóricos rosarinos y sus obras han sido expuestas en espacios de arte organizados por CONICET y la UNR.

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detector coupled gas chromatography (GC-MS). IBD activity in patients was clinically estimated using the Mayo index (UC) or the Harvey-Bradshaw index (CD). Dietary and plasmatic tryptophan levels were comparable in all the study groups. The amount of tryptophan consumed was directly correlated with the excretion values detected for the tryptophan metabolite 1H-indole-2,3-dione ($r = 0.7631$, $p = 0.0168$). In addition, non-tryptophan derived metabolites such as citric acid or 2-hydroxybutyric acid were able to discriminate patients with IBD from the control group. Although the amount of tryptophan consumed was not related to the activity of IBD in patients with UC, we found that the amount of tryptophan consumed was inversely correlated with the stage of IBD in patients with CD ($r = -0.6971$, $p = 0.0251$). Our findings suggest that increasing the amount of tryptophan in the diet may decrease IBD activity in patients with CD and that metabolomic profile of patients with IBD can provide a new precision medicine tool to improve the management and the quality of life of patients with IBD.

362. (581) **MEMORY T-CELLS IN AUTOIMMUNE LIVER DISEASE: A PRELIMINARY STUDY**

Tanno F[2]; Reggiardo MV[2]; Bessone F[2]; Tanno M[2]; Tanno H[2]; Bottasso O[1] and Villar SR[1].
[1]Instituto de Inmunología Clínica y Experimental de Rosario, Facultad de Ciencias Médicas, UNR (CONICET-UNR).
[2] Servicio de Gastroenterología y Hepatología, Hospital Provincial del Centenario.

Autoimmune hepatitis (AIH) is a progressive inflammatory disease involving many T lymphocyte subsets in its development. For instance, T cell subsets engaged in B cell activation and differentiation, as well as memory T cells. Based on their surface markers, memory T $CD4^+$ cells are classified into two subsets: the central memory T (TCM) cells expressing $CD44^+$ and $CD62L^{high}$ which facilitate their homing to the secondary lymphoid organs; and the effector memory T (TEM) cells which are $CD44^+/CD62L^{low}$ and exit into circulation toward peripheral tissues. The aim of this cross-sectional study was to characterize the immunophenotype markers of memory T lymphocytes in the peripheral blood from five patients with type 1 AIH, attending at the Gastroenterology Service of Hospital Provincial del Centenario de Rosario. Five healthy subjects were included as controls (Co). All patients were treated with prednisone and azathioprine at the time of blood collection. Peripheral blood mononuclear cells (PBMCs) were obtained and processed by flow cytometric analysis. AIH patients were positive for anti-ANA or anti-SMA antibodies showing higher levels of serum IgG, IgM, and IgA if compared to Co. The AIH group presented significantly increased and decreased levels of TCM and TEM cells, respectively in comparison from values in the control group ($P \leq 0.05$). Such increase in TCM cells may be reflecting a pathogenetic role in AIH. Specifically, the higher percentage of TCM cells at the peripheral level, may be associated with a Th2 response profile, and hence responsible for elevated gamma globulin fraction (mostly IgG and IgA) as well as the presence of autoantibody levels.

363. (560) E**VALUATION OF HIGH DIMENTIONAL REDUCTION AND CLUSTERING IN THE PHENOTYPIC DICRIMINATION OF CD5+ B-CELL CHRONIC LYMPHOPROLIFERATIVE DISEASES.**

Báez NS[2], Arroyo DS[2]; Mazone-Rodríguez C[1], Wang JM[3], Rodríguez CM[2] and Iribarren P[1].
[1]CIBICI-CONICET, Fac. de Ciencias. Químicas, UNC. Córdoba, Argentina.
[2]Laboratorio de Biología Molecular y Citometría de Flujo del servicio de Oncología y Hematología, Hospital Nacional de Clínicas, Fac. de Medicina, UNC.
[3]Cancer and Inflammation Program, National Cancer Institute at Frederick, NIH, Frederick, MD, United States.

Introduction: Mature (peripheral) B-cell malignancies represent the malignant counterpart of normal mature B-cells that have differentiated into naive B cells or their progeny. Integration of a complex set of immunophenotypic, morphological, clinical, and cytogenetic information is essential for the subclassification of B-cell chronic lymphoproliferative diseases (B-CLPD).

Phenotyping is essential for the diagnostic classification of many B-CLPD cases, but the current immunophenotyping strategies also face several difficulties. In view of these issues, new methods to facilitate the identification of abnormal B-cell populations in routine clinical flow cytometric data would be desirable.

Methods: We used both 12 and 8 colour staining panels and we applied high dimensional reduction (viSNE) and clustering tools to discriminate between $CD5^+$ B-CLPD cases. Samples from already diagnosed CLL and MCL were analyzed (n=6) and healthy patients' cells were used as controls.

Results: High dimensional reduction (viSNE) revealed at least 6 individual clusters that corresponded to each $CD5^+$ B-CLPD sample. In addition, the two dimensions spatial distribution of the populations showed segregation by disease type ($n=6$, $p<0.05$). Conversely, healthy control samples were separated in two clusters, but all the samples showed overlapping (p=NS). Clustering suggested the heterogeneity in markers expression in each disease sample. For instance, we detected clusters with higher expression of Ig-k and CD20, that corresponded to MCL samples, $p<0.05$ and $p<0.01$, respectively. Deeper analysis of these samples is currently under investigation.

Conclusions: These preliminary results suggest that combination of high dimensional reduction and clustering might be an additional tool that can be used, at least, to distinguish between $CD5^+$ B-CLPD. Further research is required to confirm these results and to evaluate the power of these tools in the classification of atypical forms of the B-CLPD.

364. (13) **HYDATID FLUID FROM ECHINOCOCCUS GRANULOSUS INDUCE THE AUTOPHAGY PROCESS IN DENDRITIC CELLS AND PROMOTE ANTIGEN PRESENTATION AND T- CELL PROLIFERATION**

Maia Chop[1], Natalia Plá[1], Julia Loos[2], Celeste Nicolao[2], Andrea Cumino[2], Christian Rodriguez Rodrigues[1]
1. Dto de Química, FCEyN, UNMdP.
2. Laboratorio de Zoonosis Parasitaria, FCEyN, UNMdP.

Background: Autophagy is an important process for the presentation of endogenous and exogenous proteins on MHC I and II molecules, promoting activation of CD8+ and CD4+ T cells respectively. The aim of this work is to analyze if hydatid fluid (HF) from Echinococcus, constituted by a wide range of parasite proteins could trigger autophagy improving antigen presentation and T cell proliferation. Methods: BMDCs were cultured in complete RPMI. Hydatid fluid (HF) was punctured from the hydatid cysts collected of infected cattle slaughtered. Antigen uptake was measured with (FITC-OVA) in BMDCs using a standard method. HF-stimulated BMDCs, were evaluated in autophagy induction and MHC II expression. For it, fixed cells were immunostained with LC3-b (clone H50) and analyzed them by immunofluorescence confocal microscopy. CFSE-stained splenocytes were co-incubated with BMDCs using a DC: splenocyte ratio of 1:4 Cellular proliferation was assayed after 4 days of culture by flow cytometry. Results: First, we evaluated if stimulation of HF during 18 h in BMDCs, induce different rates of antigen uptake. Effectively, the presence of Echinococcus antigens induces a markedly decreased OVA-uptake compared to control (**$p<0.01$, n=3). Next, we studied if stimulation with Eg antigens induces changes in the basal level of autophagy. HF-stimulated BMDCs significantly enhanced the mean fluorescence intensity of MHC II and LC3 and showed a trend in the increment of number and the average size of LC3-positive structures in comparison with unstimulated cells (*$p<0.05$, **$p<0.01$, ***$p<0.001$ HF-stimulated cells vs controls). Finally, we observed that culture splenocytes in the presence of stimulated DC induce their proliferation % CFSE+ cells CTRL:99%, HF:55% (***$p<0.001$, n=3). Conclusions: These data suggest that HF of Echinococcus induces an increase in autophagy processes promoting the presentation of exogenous antigens presented in MHC II molecules to improve T cell proliferation.

365. (14) **MUCINS AND POLYSACCHARIDES FROM ECHINOCOCCUS GRANULOSUS LAMINAR LAYER INDUCE A MILD MATURATION PHENOTYPE IN DENDRITIC CELLS**

AND PROMOTE GENE EXPRESSION OF PRO-INFLAMMATORY CYTOKINES

Natalia Plá[1], Maia Chop[1], Julia Loos[2], Celeste Nicolao[2], Andrea Cumino[2], Christian Rodriguez Rodrigues[1]
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2. Laboratorio de Zoonosis Parasitaria, FCEyN, UNMdP.

Background: The laminar layer is an acellular structure rich in glycans that surrounds the metacestode, creating a mechanical and immunological protective barrier, crucial in the Echinococcus?host interface. The aim of this work is to analyze if purified laminar layer (pLL) could trigger maturation and cytokine production in dendritic cells by activating mTOR pathway, a central regulator of cell metabolism and environmental signals. Methods: BMDCs were cultured in complete RPMI supplemented with 100 ng/ml Flt3-L.
The germinal layer was removed from pLL by washing with 2M NaCl. Flow cytometry: FITC or PE-conjugated mAbs directed to CD11c, CD40, CD80, CD86, MHC I and MHC II were used. Immunoblotting and confocal microscopy: mouse anti-puromycin and rabbit anti-Phospho-mTOR antibodies were used. Gene expression analysis of IL-10, IL-12p35, IL-6, TNF-a, IL-23p19, TGF-b was performed on a Real Time PCR System Results: The pLL of Echinococcus induce a non-statistically significant, but a trend in the up-regulation of CD86 and MHC II and that expression change was diminished by the use of rapamycin (n=5). Conversely, no changes in the expression of CD40, CD80 or MHC I were registered. Further studies were done to analyze whether pLL was also able to stimulate the production of cytokines by BMDCs. When BMDCs were stimulated with pLL induce the expression of IL-6 and TNF-a (n=3 *p<0.05, **p<0.01), but not differences compared to control were observed in IL-12, IL-23, IL-10 and TGF-b. Finally, we evaluated global protein synthesis and phosphorylation of mTOR using confocal microscopy or western blot. pLL (MFI:_979) showed an increase in translation levels compared to its counterpart without stimulation (MFI:_686, *p<0.05 n=3) and also induce an increase in mTOR phosphorylation levels compared to untreated BMCDs (n=3, p<0.01) Conclusions: These data suggest that Echinococcus pLL are recognized by DCs and induce activation of mTOR pathway favoring cell activation.å

366. (88) **HUMAN RARE SEROTYPE ADENOVIRUS AS VACCINE PLATFORM AGAINST *T. cruzi* INFECTION**

Trinitario SN [1;2;3], Delfino MA [1;2;3], Redolfi DM [1;3], Russo M [1;2], Cardoso AC [1;2;3], Cerny N [1;2], Bivona AE [1;2;3], Malchiodi EL[1;3], Sánchez Alberti A [1;2;3].
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3. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Cátedra de Inmunología. Buenos Aires, Argentina.

Trypanosoma cruzi is an obligate intracellular parasite and stealth invader that causes a chronic infection affecting millions of people worldwide. Benznidazole, the first line antiparasitic drug, has been used for 50 years and is effective during the acute phase of the infection. However, its use in chronic phase where most cases are diagnosed, is still controversial. Considering these issues developing prophylactic and/or therapeutic vaccines might contribute to public health.
In this context, our laboratory has developed Traspain, a novel chimeric antigen that displays key domains for humoral and cytotoxic anti-parasite immune response. In order to improve antigen-specific cell-mediated immunity, we designed a low-seroprevalence recombinant adenoviral vector (Ad48) carrying Traspain gene.
METHODS
Traspain gene was fused to mouse immunoglobulin *Kappa* light chain signal peptide DNA sequence (SPTrasp) to facilitate extracellular antigen export upon vaccination. Adenovirus 48 carrying SPTrasp gene (Ad48-SPTrasp) was generated using traditional cloning and homologous recombination in HEK293 cells. Antigen expression was assessed *in-vitro* by RT-PCR and Western blot. Exploratory immunization experiments were carried out in C57/BL6 mice, administering two subcutaneous doses of Ad48-SPTrasp every 15 days.
RESULTS
We were able to rescue the replication deficient virus and detect antigen expression upon 48 hours of *in-vitro* infection. Vaccinated animals developed anti-Traspain antibodies (immunized vs control animals ELISA titers: 1782 and 235 respectively) and isotype determination indicated an IgG1/IgG2a ratio of 3.4. Robust antigen-specific CTL response was detected using tetramer staining (CD8+ VNHRLTVL+ cells, immunized: 3.5 % vs control: 0.6 %, p<0.01).
CONCLUSIONS
Considering these results, Ad48-SPTrasp appears as a high potential approach for improving the current strategies of vaccine-mediated control of *T. cruzi*.

367. (112) **POLYMORPHISM -174 G/C OF THE INTERLEUKIN 6 GENE, AND SUSCEPTIBILITY TO Toxocara canis IN HUMANS**

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2. Facultad de Ciencias Exactas y Naturales y Agrimensura, Universidad Nacional del Nordeste.

Polymorphisms in the IL6 gene promoter region can give rise to interindividual variation in the transcription of IL6. Low levels of IL6 expression have been associated with susceptibility to some parasitic diseases. Human infection by Toxocara canis is a zoonosis transmitted by dogs, with a high prevalence in NE Argentina. OBJECTIVE: To investigate the -174 G/C single nucleotide polymorphism (SNP) in the promoter region of the IL-6 gene, related to the susceptibility to Toxocara canis human infection. MATERIALS AND METHODS: The study included 79 patients from Chaco, Argentina (without distinction of age or sex) with epidemiological history of exposure to Toxocara canis. The serological analysis was performed using an indirect ELISA test employing locally obtained secretory/excretory T. canis antigens and peroxidase-labeled anti-human IgG serum. The IL6 -174 G/C polimorphism was studied by a nested polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay. RESULTS: Of the 79 patients studied, 14 resulted positive and 65 were negative for T. canis antibodies. The study of the polymorphism genotypes yielded three possible results with the following frequencies: GG: 58.2% (46/79), GC: 38.0% (30/79), and CC: 3.8% (3/79). For this sample, no differences between expected and observed genotype distributions were found. Therefore, Hardy-Weinberg equilibrium is assumed. There was a significant difference in the distribution of the CC genotype between the seropositive and seronegative groups (14.3% vs 1.5%, respectively; OR= 5.12; p=0.02), statistical significance level (p <0.05). CONCLUSION: This study suggests a possible association between the IL6 –174 G/C polymorphism and susceptibility to toxokaryosis in humans. Although the number of patients studied is small, the trend indicates that the presence of the CC genotype could be associated with increased susceptibility to infection.

368. (145) **VIRULENCE FACTORS DELIVERED THROUGH OUTER MEMBRANE VESICLES SHAPE THE OUTCOME OF *B. PERTUSSIS*-MACROPHAGE INTERACTION**

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The outer membrane vesicles (OMVs) are bi-layer structures naturally shed by Gram-negative bacteria that usually contain bacterial virulence factors. In previous studies we found that the OMVs of Bordetella pertussis (Bp), the etiological agent of whooping cough, might influence the outcome of Bp interaction with human MΦ. In this study we tried to dissect the bacterial factors involved in this process. As first approach we determined the proteome of spon-