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gle-dose of OVA and CpG-ODN nanoformulated with Coa-ASC16 (OCC), with OVA and CpG-ODN in solution (OC) prepared to room temperature (RT), with OVA and CpG-ODN solution heated and then cooled down to RT (OCø), with OVA solution heated and then cooled down to RT plus CpG-ODN solution at RT (Oø/C), with OVA solution at RT plus CpG-ODN solution heated and then cooled down to RT (O/Cø). Heating and cooling processes recreated the conditions of the nanoformulation preparation. On the 160th day of post-immunization (pi), mice were intraperitoneally challenged with OVA/CpG-ODN and sacrificed 7 days later. OVA-anti IgG titers (ELISA) and splenocytes by flow cytometry were evaluated. When antigens at the injection site were measured, the formulations were prepared using fluorescent-dye labeled OVA and in vivo scanning of mice was performed on Odyssey®CLx. OCC induced IgG titers higher than OCø and Oø/C at 145 day pi ($p<0.001$). Post challenged (day 167), OCC IgG titers were comparable to OCø group and higher to Oø/C group ($p<0.01$). O/Cø failed to generate OVA-specific IgG. At 167 days pi, OCC generated higher OVA-specific ($CD3^-F480^-CD19^+IgM^-IgD^-IgG^+GL7^-CD38^+OVA^+$) memory and germinal center ($CD3^-F480^-CD19^+IgM^-IgD^-IgG^+GL7^+CD38^-OVA^+$) B cells ($p<0.05$) than the other formulations. In OCC group, the OVA fluorescence signal in the injection site was higher than in the other groups since 0.3 ($p<0.0001$) until 12 days pi ($p<0.01$). Our results show that the nanostructure improve the memory response and induce antigen depot at the injection site.

382. (300) **EXPRESSION AND MODULATION OF PROLACTIN RECEPTOR IN IMMUNE CELLS: INDUCTION OF mRNA AND PROTEINS BY DEXAMETHASONE**

Moreno-Sosa MT[1,2,3], Sánchez MB[1,2], Neira FJ[1,2], Soaje M[1,2], Pietrobon EO[1,2], Valdez SR[1,2], Rivero VE[3,4], Jahn GA[1,2], Mackern-Oberti, JP[1,2].

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It is known that there is a relationship between hyperprolactinemia and autoimmunity. However, the role of prolactin receptor (PRL-R) in autoimmune development is still controversial. The aim of this work is to analyze the expression of PRL-R in murine immune cells, and determine whether PRL-R are modulated during activation with Concanavalin A (conA) and suppression with Dexamethasone (dexa) in healthy mice and three mice models for Lupus. For this end, splenocytes from C57BL/6 (C57), and lupic FcgRIIb KO (RIIb), NZM, and MRL/MpJ-Faslpr (FAS) mice were stimulated with 1 μg/ml of conA or 1 μg/ml dexa and kept in culture for 24 hours. RNA from splenocytes was isolated using Trizol and retrotranscribed to cDNA to detect PRL-RL by qPCR. Protein determination was carried out by flow cytometry using Anti-CD4, Anti-CD19, and Anti-PRL-R. We found that splenocytes from RIIb mice have higher mRNA of PRL-RL expression than other strains. In CD4+ T cells from C57 mice PRL-R increased by suppression with dexa and did no changes when stimulated with conA. In contrast, in CD4+ T cells from FAS mice, PRL-R increased after conA and decreased with dexa, while the CD4+ T cells from RIIb and NZM mice displayed no changes. In CD19+ B cells from C57 and FAS mice, we observed an increase of total PRL-R when we stimulated with dexa and no changes with conA, while in CD19+ from RIIb and NZM mice, did not display changes. These results show a differential behavior of PRL-R expression in C57 mice compared with the lupic mice after stimulation with conA and dexa. The fact that C57 displayed low levels of PRL-R during activation but high in suppression gives us the notion that PRL-R may contribute to maintaining a cellular immune balance by limiting PRL trophic effects. By contrast, the high levels of PRL-R during activation in FAS mice suggest an exacerbated trophic effect of PRL. Our data show that differential PRL-R expression in immune cells may contribute to regulate the immune response.

383. (313) **ORAL ADMINISTRATION OF MINTHOSTACHYS VERTICILLATA ESSENTIAL OIL ACTIVATES CD4+ AND CD8+ T CELLS IN MICE**

Noelia Anahí Campra *(INBIAS-CONICET-UNRC)*, Ivana Dalila Montironi *(Facultad de Agronomía y Veterinaria-UNRC)*, José María Raviolo *(Facultad de Agronomía y Veterinaria-UNRC),* María Carolina Grosso *(Facultad de Agronomía y Veterinaria-UNRC)*, Fernando Mañas *(Facultad de Agronomía y Veterinaria-UNRC)*, Romina Valeria Bellingeri *(IITEMA-CONICET-UNRC), Laura Noelia Cariddi (INBIAS-CONICET-UNRC)*

Minthostachys verticillata essential oil (EO) has demonstrated antimicrobial, antioxidant and immunomodulatory activity. The aim of this study was to evaluate the immunomodulatory effect of oral administration of *M. verticillata* EO in a murine model. Male Balb/c mice (n=9) were divided in three groups and administered orally by gavage once a day for 10 consecutive days as follows: Control group 100 μl of saline solution (ClNa 0.9%), Treatment 1 (T1) group 100 μl of EO (5 mg/kg/day) and Treatment 2 (T2) group 100 μl of EO (10 mg/kg/day). Body weight, fecal consistency and fecal occult blood were evaluated as important indicators of intestinal health. The blood parameters were evaluated trough total and differential leukocyte count in peripheral blood. At the end of the assay mice were sacrificed by cervical dislocation and spleens were collected for $CD4^+$ and $CD8^+$ T cells quantification by flow cytometry. An increase in the body weight gain was observed in T1 group compared to the control and T2 groups ($p<0.05$). No difference was observed in diarrhea scores among treatments neither damage in the digestive system evidenced by the absence of fecal occult blood in all groups. T1 and T2 groups showed an increase in *total leukocyte count* compared to the control group ($p<0.05$). The leukocyte formula revealed that lymphocytes percentage were significantly higher in T2 group compared to control group ($p<0.05$). The number of $CD4^+$ T cells in splenic tissue were significantly higher in T1 and T2 groups compared to control group ($p<0.05$). The number of $CD8^+$ T cells was not altered in mice treated with EO. These results indicated that oral administration of *M. verticillata* EO was safe and modulates the systemic adaptive cellular immunity in mice *through positive regulation of T cells subsets.* Further studies will need to be carried out to elucidate whether this natural product could be used as an immunomodulatory food additive.

384. (319) **MINTHOSTACHYS VERTICILLATA ESSENTIAL OIL ALONE OR MICROENCAPSULATED ACTIVATES TH1 CELLS AND INDUCES THE PRODUCTION OF OPSONIZING ANTIBODIES**

Noelia Anahí Campra *(INBIAS-CONICET-UNRC)*, Melina Vanesa Moliva *(INBIAS-CONICET-UNRC)*, Sofía Arsaute *(INBIAS-CONICET-UNRC)*, José María Raviolo *(Facultad de Agronomía y Veterinaria-UNRC)*, Nahuel Matías Camacho *(UNITEFA-CONICET-UNC)*, Alejandro Javier Paredes *(UNITEFA-CONICET-UNC)*, María Celeste Morán *(CIVETAN-CONICET-CICPBA)*, Belkys Maletto *(CIBICI-CONICET-UNC)*, Santiago Daniel Palma *(UNITEFA-CONICET-UNC)*, Silvia Marcela Estein *(CIVETAN-CONICET-CICPBA)*, Elina Beatriz Reinoso *(INBIAS-CONICET-UNRC)*, Laura Noelia Cariddi *(INBIAS-CONICET-UNRC)*

In a previous study, we demonstrated the adjuvant capacity of the Minthostachys verticillata essential oil (EO) (2.5 mg/ml) or microencapsulated essential oil (EOMC) (5 mg/ml) on the humoral and cellular immune response against Enterococcus faecium in Balb/c mice. The aim of this study was to evaluate the functionality of the specific antibodies produced and to quantify the IFN-γ and IL-4 cytokines. Balb/c mice (n=4 per group) were inoculated by subcutaneous injection (days 0, 14 and 28) as follows: Group 1: 100 µl saline solution; Group 2: 100 µl bacterin+EO (2.5 mg/ml); Group 3: 100 µl bacterin+ microcapsule wall material (2.5 mg/ml); Group 4: 100 µl bacterin+EOMC (5 mg/ml). In all groups, bacterin was of E. faecium. Seven days after the last booster, blood was obtained and serum was separated. Mice were sacrificed by cervical dislocation and spleens were removed to obtain splenic lymphocytes for cell proliferation assay. To evaluate the functionality of the antibodies, the Opsonophagocytic Killing Assay was carried out using different

dilutions of the sera (1/100, 1/200, 1/500, 1/1000, 1/2000), E. faecium (1x107 CFU/ml), bovine PMNs (1x107cells/ml) suspensions and a source of bovine complement. Sera antibodies of mice from Group 4 mediated the opsonization of E. faecium and enhance the phagocytosis by PMNs up to the 1/500 dilution compared to Group 2, which was up to the 1/200 dilution (p<0.001). IFN-γ and IL-4 were quantified in the culture supernatants by sandwich ELISA. Higher levels of IFN-γ and IL-4 were detected in lymphocyte culture supernatants of Group 2 compared to other groups (p<0.001). In Group 2, IFN-γ levels were higher than IL-4 (p<0.001), indicating that the activation of CD4+ T cells by the vaccine formulation containing alone EO may result in a Th1 profile. The results obtained confirm that EO and EOMC activate humoral and cellular immunity and could be candidates for vaccine adjuvants.

385. (336) **CHARACTERIZATION OF SPECIFIC CAMELID SINGLE DOMAIN ANTIBODIES AGAINST MURINE IgG1 TO BE USED AS LIGAND IN CONVENTIONAL MONOCLONAL ANTIBODY PURIFICATION**

Marchese FA[1], Bozzo JI[1], López NM[1], Grippo V[1].
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In addition to classical antibodies (Abs), the adaptive immune system of camelids comprises heavy-chain only antibodies (HCAb), where antigen-binding is mediated exclusively by one variable domain. These single domains are the smallest functional Abs, known as VHH or nanobodies (Nbs). Due to their inherent favorable attributes, such as high affinity and specificity for their antigen, easy cloning and small size, VHH have great potential for diagnostic, therapeutic and biotechnological applications. Thus, Nbs are used as protein purification ligands because of their high stability, monomeric nature, and easy directional immobilization to solid supports. For this reason, our aim was to characterize VHH against murine IgG1 (mIgG1) to be used as ligands in a new affinity chromatography method to purify conventional monoclonal Abs (mAbs). To achieve our goal, two immune VHH libraries were previously constructed starting from llama blood, and specific Nbs against mIgG1 were selected by Phage Display methodology. Moreover, 9 out of the 24 most reactive selected VHH were confirmed as unique by sequencing. In this work, these Nbs were expressed as soluble protein in *E. coli* WK6 strain. Later, 4 of these VHH were purified from periplasmic extract by IMAC. Reactivity of these soluble-expressed Nbs against mIgG1 was confirmed by ELISA and Western Blot (WB). Also, the reactivity against IgGs from other species was evaluated by Dot Blot and WB. Moreover, all these VHH were able to successfully bind and immunoprecipitate IgG from mouse sera and ascites. In conclusion, we have characterized four specific VHH expressed as soluble protein, which showed high reactivity against mIgG1 in ELISA and WB as expected. All of them were able to recognize their target in a biological protein mixture. Even more, two of them were highly specific for only murine IgG. Further characterization of these Nbs will allow us to develop a new VHH-based method of mAb purification with potential advantages.

386. (338) **CHRONIC POLIOVIRUS INFECTION IN A FEMALE PATIENT WITH UNCHARACTERIZED IMMUNODEFICIENCY: CASE REPORT**

Lampugnani A, Bazán N, Carelli D, Ramis E
Hospital Dr. Guillermo Rawson, Departamento de Inmunología

Introduction: Patients with B-cell immune deficiency have increased risk of complications associated with enterovirus infections. Long-term excretors could reintroduce mutated polioviruses with increased neurovirulence into the general circulation. Treatments such as pocapavir can reduce environmental spread.
Objective: To present clinical behavior of a patient with uncharacterized immunodeficiency and chronic poliovirus infection.
Clinical case: A two-year-old female patient, term newborn, daughter of healthy non-consanguineous parents, without relevant family history is hospitalized at 9 months old due to a left brachiocrural hemiparesis. She is evaluated by Neurology who assumes acute disseminated encephalomyelitis and prescribes methylprednisolone and EV gammaglobulin. The patient responds favorably so she is discharged.
After 3 months, she is referred to Immunology for evaluation. Inmunological screening shows undosable IgA and IgM, IgG 228mg/dl. Lymphocyte subpopulations CD3 77% CD4 48% CD8 27% CD19 15% NK 8%. Subpopulations B Naive 98.9%, memory without change of isotype 1.04%. Absent plasma cells. Blood group 0+. Isohaemaglutinins anti A and anti B absent. Ac HBs non-reactive. Uncharacterized humoral immunodeficiency is assumed so EV gamma globulin is initiated. The patient had received sabin at 6 months old so samples are sent to Malbran Institute to rule out vaccine´s secondary infection, obtaining positive result for sabin 3 postvaccinal serotype. Actually the patient continues fecal viral shedding wich presents 30 mutations. Compassionate use of pocapavir is attempted but cannot be imported. Samples are sent to NIH in the United States for mutation testing.
Conclusions: Our case explain chronic poliovirus infection in a patient with humoral immunodeficiency. We consider important to provide an antiviral treatment wich stops the environmental spread of the virus, because it has suffered numerous mutations that can constitute a serious epidemiological risk.

387. (340) **QUANTITATIVE AND INTEGRATIVE ANALYSIS WITH HISTORICAL PERSPECTIVE OF INFLAMMATORY BOWEL DISEASE RESEARCH: UNDERSTANDING ETIOLOGY AND PATHOGENESIS AS A RESULT OF AN INTERACTOME OR "NETWORK EFFECT"**

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Inflammatory bowel diseases (IBD) present a complex etiology associated with multiple factors interacting at different functional levels (i.e., risk genes, molecules, immune cells, biological processes and environment). The wide diversity of factors and associated variables studied over the last 3 decades in the context of IBD has challenged our ability to integrate the empirical information available in humans. Thus, our goal was to quantitatively analyze how representativeness of components of different functional levels and their interactions have changed over the last 30 years of IBD research in humans. A bibliographic search in Pubmed was performed aimed at extracting experimental studies on IBD in humans published between July 1990 and June 2020. This resulted in 25971 valid abstracts. A search for 1380 specific variables in these abstracts was conducted automatically using customized code in Matlab. The selection of these variables was based on recent reviews and, genetic and molecular catalogues. Publications showed a 5-fold annual rate increase from 1990 to the present. Representativeness of molecular and cellular components remained relatively constant over time, while genes showed a peak increase in publications between 1990 and 2005, with an increasing diversity of genes studied. Microbiota-sensing related variables showed a constant increase in publications. Specifically, components such as IL-1, IL-6, IL-10, NOD2, IFNγ, NF-κB, ATG16L1, TNF, T helper, Treg, macrophages and monocytes emerged as the most frequently studied elements. These components appear as integrative nodes in the network of variables involved in the manifestation of IBD. Our quantitative analysis with historical perspective supports the need to comprehend IBD as the resultant of an inter-