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At the chronic stage of T. gondii infection, tissue cysts are located mainly in SNC. There are no treatments able to eliminate these resistant structures or to reduce the adverse effects associated with the infection. Currently, accumulated evidence links chronic infection with different pathologies, including neurocognitive and behavioral conditions. Herein, we study the effect of environmental enrichment (EE) as a non-invasive therapy against chronic toxoplasmosis and the impaired social behavior associated. Methods: The EE therapy involves increasing the available space and the addition of novel elements in the habitat. A three-chamber sociability device where a naive mouse (stranger) was placed was used to evaluate social abilities of C57BL/6 chronically infected treated (TE) or untreated (T) mice. The data was analyzed with t-student test. Brain cyst burden was evaluated at the end of the assay. Results: The results indicate that the EE treatment on infected mice improved its social ability measured as time of active contacts between the test mouse and novel mouse (TE vs T; p=0,0276). Indeed, TE mice showed higher exploration of the novel subject than T mice (up to 1,7-fold higher; p=0,0033). Moreover, 75% of TE mice showed a first impulse to approach that area while only 25% of T mice showed this behavior. Chronically infected treated mice showed a significantly better discrimination index compared to T group (p = 0,0443). All these data evidence that EE treatment improves social abilities in mice. Nevertheless, TE brain parasite load was similar to the T group. Conclusions: This environmental enrichment therapy showed a positive impact in social behavior, showing its potential to deal with the harmful effects of chronic toxoplasmosis, improving well-being of the affected individuals and the social environment that surrounds them and in which they develop. This type of non-invasive therapy could be easily incorporated into translational medicine approaches.

271. (805) **SKIN WOUND HEALING EFFECTS AND ACTION MECHANISM OF LACTIPLANTIBACILLUS PLANTARUN**

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The aim of this study was to investigate the wound healing effect of *Lactiplantibacillus plantarum* (Lp) and a posible underlying mechanism involved in its action using *in vitro* and *in vivo* models. Balc/c mice were used in the study and fulll-thickness excisional punch wound were created through the skin. Mice were divided into: group 1 (uninfected control), group 2 (infected on the wound with Methicillin resistant *Staphylococcus aureus* strains $1x10^7$ UFC/ml) and group 3 (infected and treated with topical applications of whole culture of Lp. Mice were sacrificed on day 4, 6 and 10 post-treatment. We investigated: a) Wound area, b) Histopathological study (H&E), c) Re-epithelialization and d) Microbial evaluation (CFU/g of tissue). *In vitro* studies: The fibroblast cell line L 929 was used. On day 2 after seeding (80% confluence), cells were incubated with 50, 100,150 and 200 ul of viable Lp, not viable Lp and supernatant for 24, 30 and 48hr and studied: 1) MTT assay for cell viability determination, 2) Scrath assay, 3) Collagen-I contraction assay and 4) Assessment of collagen deposition and quantitative analisys by Sirius red staining. H&E staining of skin biopsies showed trat Lp acelerated closure wound and complete re-epithelialization by day 6. In addition, the presence of granulation tissue favors the healing process. Mice in the group 2 displayed slower wound closure over time. Bacteria load was significantly reduced in the group 3 compared to the group 2 (10^3UFC/ml vs 10^7 UFC/ml p< 0.01). Viable Lp, not viable Lp and supernatant (50ul at 24hr) significantly promoted cell proliferation. This increase was significant (p< 0.05) compared to those without treatment. Lp and supernatant increased the content of soluble collagen in the supernatant in a concentration-dependent manner without reduction of the cell viability (300ug/ml vs 129ug/ml p <0.01). Lp promotes the healing process, reduced infection and promotes the development of granulation tissue.

272. (849) **GENOTYPIC CHARACTERIZATION OF CARBAPENEM-RESISTANT ISOLATES FOR EPIDEMIOLOGICAL SURVEILLANCE IN A PUBLIC HOSPITAL IN ROSARIO**

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Multi-resistant Gram-negative bacilli constitute a problem of great importance, as they can generate outbreaks making difficult the infection control. The characterization of a resistance mechanism in rectal swabs is a powerful tool to provide resources for the future implementation of prophylaxis treatments in case the patient develops symptoms. Objectives: To implement molecular biology techniques to evaluate the epidemiology of rectal colonization of multiresistant microorganisms in patients during their hospitalization in Intensive Care (IC). Material and Methods: 420 samples of rectal swabs from patients from IC, were cultured in selective and differential media. Isolated colonies were identified by MALDI-TOF, genotypically characterized by multiplex PCR by Malbrán Institute protocols, detecting the presence of genes coding for serino-carbapenemases (KPC, OXA-48) and metallo-β-lactamases (NDM, IMP, VIM). Results: Of the 420 samples, 157 were positive for Gram-negative (G(-)) bacilli resistant to carbapenems. Of these 157 samples, 108 were *Klebsiella pneumoniae*, (104 were KPC positive, 2 were NDM positive, and 2 were KPC/NDM double mechanism positive), 3 were *Pseudomonas putida* VIM positives, 4 were *Pseudomonas aeruginosa* and 42 were *Acinetobacter baumanii* MDR, both last two without presenting any of the resistance genes analyzed. The genotypic determinations of the samples were verified phenotypically, obtaining 100% correlation. Conclusions: During the last year, the percentage of colonization by G(-) bacilli resistant to carbapenems in swabbed patients was 37%, being KPC the most frequent mechanism detected. The prompt determination of resistance mechanisms by PCR is relevant for an early and effective diagnosis. The few therapeutic options to treat infections by multiresistant microorganisms make it necessary to implement an active surveillance by constantly searching for colonized patients to reinforce isolation measurements.

273. (860) **ADVANCED EXPERIMENTAL CYSTIC ECHINOCOCCOSIS: REPROGRAMMING THE INTERMEDIARY CARBON METABOLISM IN THE PARASITE UNDER METFORMIN TREATMENT *IN VIVO***

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Cystic echinococcosis is a progressive and chronic disease caused by the larval stage of the species complex *Echinococcus granulosus sensu latu.* New treatment options are needed especially for advanced disease. Since in these cestodes glycogen is the main energy storage molecule and glucose the major fermentative substrate, our approach was to target the metabolic pathways of the parasite involved in energy production, focusing on the AMPK/TOR pathway. Here, the aim was to assess the *in vivo* efficacy of met-

formin as an indirect AMPK agonist, in an advanced disease model (1year post-infection in mice), employing the highest dose of assayed drug (250 mg kg^{-1} day^{-1}). Metformin-treated mice exhibited a reduction of cellular integrity of the germinal layer of cysts, registering a drug concentration of 1.7 mM (which inhibits mitochondrial respiratory chain complex I), a reduction in intracystic glucose with an increase in lactate concentration, consistent with the rise in the glycogen breakdown and in the LDH activity. Interestingly, the fraction of reducing soluble sugars decreased by 3 times in the cystic fluid and germinal cells after of drug-treatment. However, non-reducing soluble sugars, such as sucrose and trehalose, were consumed in the cystic fluid but showed a significant increase at the intracellular level in presence of the drug. It is surprising that trehalose and sucrose biosynthesis was upregulated during starvation induced by metformin. That is, a futile cycle of non-reducing sugars synthesis and glycogen catabolism during starvation. Function of these disaccharides as stress protectants during starvation provides some resolution to this paradox, as it also occurs in others invertebrates and plants. In the same line evidence, fasting and starvation induce hepatic gluconeogenesis in mammalians. Thus, in this parasite metformin affects glucose-starvation-induced AMPK activation and restructures carbohydrate metabolism prior induction of cell death.

274. (890) **THE POTENTIAL USE OF CANNABIDIOL IN *MYCOBACTERIUM TUBERCULOSIS* INFECTION**

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Cannabidiol (CBD), the main non-psychoactive ingredient of the cannabis plant, is one of more than 100 cannabinoids that can be extracted from the *Cannabis sativa* L., many of which have been shown to be biologically active. Besides the scientific research, the societal acceptance of CBD oil for medical application has increased in recent years. However, in spite of the increasing research, all of CBD biological effects are not completely understood. The purpose of this work was to investigate the antimicrobial and immunomodulatory effects of CBD in *Mycobacterium tuberculosis* (*Mtb*) infection. Results: First, we evaluated the anti-mycobacterial effect of different concentrations of CBD (150µg/mL, 15µg/mL, 1.5µg/mL 0,15µg/mL and 0,015µg/mL) by colony forming units (CFU) counts after2hours and 24hours of treatment. We found that CBD treatment produced a decrease in *Mtb*H37Rv viability in a dose dependent manner at 2hours and 24hours (ANOVA test, $p<0,05$). Then, we investigated the anti-mycobacterial effect of CBD in macrophage infected cells with *Mtb*H37Rv (MOI 10). We observed a reduced intracellular *Mtb*H37Rv viability after CBD treatment (CFU counts, 24hours) at concentrations that displayed no cytotoxic effect on THP-1 cell lines determined by Trypan Blue assay (CBD: 150µg/mL $p<0,05$). Finally, we investigated de modulatory effect of CBD on healthy donors (HD) and tuberculosis patients (TB) PBMC´s IFN-γ and IL-17A secreted levels. After 5 days of PBMC´s *Mtb*-Ag stimulation, CBD treatment (15µg/mL) decreased the IFN-γ and IL-17A levels detected by ELISA in HD and TB patients. Conclusion: Overall, the data support the notion that CBD is immune modulator and antimicrobial for tuberculosis human infection.

275. (909) **ANTIVIRAL AND IMMUNOMODULATORY ACTIVITY OF A SYNTHETIC STEROID ANALOG AGAINST ZIKA VIRUS INFECTION IN OCULAR CELLS**

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Zika virus (ZIKV) is a mosquito-transmitted arbovirus in humans, with other modes of transmission including sexual, perinatal, and via blood transfusion. Most of infected patients are asymptomatic, but infection can be associated with viral neurotropism and Guillain-Barre syndrome. Conjunctivitis, uveitis, and unilateral acute maculopathy have been reported in adults after acute infection. Congenital Zika syndrome (CZS) is the distinctive phenotype of babies infected with ZIKV in utero, with neurological, ocular, hearing, and skeletal abnormalities. There are no vaccines or specific antiviral agents to treat ZKV infections. Virest, (22S, 23S)-22,23-dihydroxystigmast-4-en-3-one, is a steroidal analogue with stigmastane structure, with antiviral activity against diverse clinically relevant human virus with different structures and replicative strategies. In the present study we evaluated a potential direct antiviral activity of Vires against ZIKV, through virus yield reduction assays, and an indirect inhibitory activity by an immunomodulation of the infected cells, through the quantification of the secreted cytokines with enzyme linked immunoassays, in human cell lines derived from ocular tissue and in macrophages. Virest significantly reduced viral yields in retinal, conjunctival, and corneal cells, and it induced an increase in proinflammatory cytokines secretion. However, the compound induced a significative reduction of cytokine secretion in infected macrophages. ANOVA followed by Tuckey test, $p<0,001$ were performed ($n>2$). Virest exhibited antiviral activity against ZIKV in ocular epithelial cells and modulated the inflammatory response in infected epithelial cells and macrophages.

276. (927) **CELLULAR PHYSIOLOGICAL IMPROVEMENT BY SPINOCHROMES FROM SEA URCHIN EGGS. A POTENTIAL ALLY IN IMPROVING THE SECUELAES OF COVID-19**

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Spinochromes are marine polyphenols known for their antioxidant properties, enhance glutathione metabolism and reduce cellular inflammation. They are naturally concentrated in the eggs of sea urchins and there are two therapeutic pharmacological formulations marketed in Russia and Germany. In Argentina, a nutraceutic with Echinochrome A (EchA) has been formulated as a product equivalent to that used in Russia and is being used in a multicenter clinical trial focused on patients with sequalae of COVID-19 (Long COVID-19), under the hypothesis of decreasing cellular inflammation and increasing cell viability. Patient recruitment is closed, 54 patients have been recruited, with an average age of 51 years (60% women). The patients consume 6 ml of 0.025 mg/ml of EchA per day for 90 days and clinical, biochemical (biomarkers of inflammation and thrombosis) and psychological parameters are analyzed; all interconnected through a SKYMED telemedicine platform. In parallel, EchA was evaluated to demonstrate cell viability activity in Madin Darby Canine Kidney (MDBK) and Vero cells with neutral red in a concentration range of 0.0375 ug/ml to 1000 ug/ml with exposure for 2 hours and 72 hours. Differences in cell viability were found in cell