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LXIII REUNIÓN ANUAL DE LA

SOCIEDAD ARGENTINA DE INVESTIGACIÓN CLÍNICA (SAIC)

LXVI REUNIÓN ANUAL DE LA

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CON LA PARTICIPACIÓN DE

SOCIEDAD ARGENTINA DE VIROLOGÍA (SAV)

ASOCIACIÓN ARGENTINA DE NANOMEDICINAS (NANOMED-ar)

14-17 de noviembre de 2018
Hotel 13 de Julio – Mar del Plata

EDITORES RESPONSABLES

Claudia Pérez Leirós
Pablo Baldi
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JOINT MEETING SAIC SAI SAFIS 2018

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RESPONSIBLE EDITORS

Claudia Pérez Leirós
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locomotor activity. Then, we selected the lower dose of nicotine that induced sensitization which interestingly cannot induce CPP. Locomotor sensitization was increased by 103% with nicotine and 166% with cocaine. Following this, sensitized zebrafish were trained using a two-chamber nicotine-driven CPP protocol. Cocaine-sensitized animals showed the highest score for the establishment of nicotine-CPP compared to previously nicotine-sensitized fish. Furthermore, detailed behavioral and molecular analyses confirmed these findings. The levels of nicotinic receptor subunits α7 and α6, but not β2, mRNA were increased in both nicotine- and cocaine-sensitized zebrafish. Only cocaine-sensitized zebrafish showed significant increases of the dopamine transporter (DAT). Nicotine-CPP but not control CPP showed similar values compared to sensitized animals for practically all the markers measured, suggesting that some specific markers are sensible to both processes. These findings suggest that doses of nicotine that can induce sensitization might be not enough to induce nicotine-place conditioning. On the other hand, suggest that previous exposure to low doses of drugs of abuse can increase subjects' sensitivity to the rewarding properties of drugs of abuse.

267. (143) **EPIGENETIC TRANSGENERATIONAL BEHAVIOURAL EFFECTS INDUCED BY TELLURIUM (TE) ADMINISTRATION IN MATURING RATS.**

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Previous evidence from our laboratory, showed that after systemic administration of K2TeO3 in non-toxic doses to pregnant mother and its litter rats, several behavioural parameters related to motivated and lateralized exploration in the offspring (F1) were affected. The objective of the present work was to determine if F2 generation still might be influenced by the previous Te administration to its parents. For this purpose, parent rats and its litters were exposed to K2TeO3 1.55 nM in drinking water (n=10;F1). Te treatment ended at 35 day-old of litters. After that, animals remained at rest until 90 day-old, when female rats were mated with normal males. Behavioural tests were performed when offspring reached 30 days of age (F2, n=10). Tap water administration was considered control (n=9). Behavioural tests performed at 30 day-old (F1 andF2) were: Double Lateral Hole-Board Labyrinth (LDHB) to register motivated lateralized exploration; Resident-Intruder Challenge (RIC), to register social behavioural parameters, and Forced Swimming (FS), to register survival motivation. Experiments were videotaped and behavioural activity recorded by a digital automatic counter in Counts/3min (C/3m). Results showed in F2 generation: loss of lateralized exploration in a similar way that in F1 parents (34±5.1, left Vs. 36±3.4, right C/3m, F2, n.s.; 50,5±4.7, left Vs 46,5±7.1 right C/3m, F1, n.s.; LDHB), increased latency to confront the intruder animal (45±13 Vs 15.5±1.5 C/3m, F2 Vs Control, p<0.01, RIC), and decreased active swimming (158±7.1 Vs 188±16 C/3m, F2 Vs Control, p<0.01, FS). In conclusion, Te treatment on F1 animals extended to its progeny, supporting the epigenetic action of Te.

ONCOLOGÍA / ONCOLOGY 5

268. (272) **HEMATOLOGIC TOXICITY ANALYSIS OF METRONOMIC CHEMOTHERAPY IN PEDIATRIC PATIENTS WITH ADVANCED SOLID TUMORS**

Juan Manuel Cáceres[1], Marcelo Coirini[2], Andrea Schifino[2], Julia Jotomliansky[2], Viviana R. Rozados[1, 3], O. Graciela Scharovsky[1, 4]
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Metronomic chemotherapy (MCT) is a novel approach for treating cancer; it consists in the chronic administration of low doses of conventional chemotherapy drugs, without prolonged drug-free periods. It was originally conceived to overcome drug resistance, targeting the tumor blood vessels rather than the tumor cells. Recent clinical studies have demonstrated the ability of MCT to control disease and improve life quality in children with different types of advanced cancer that do not have other therapeutic options available. Our objective was to study hematologic variables in children with relapsed/resistant/high risk solid tumors treated with MCT in order to test our hypothesis of lack of severe hematologic toxicity caused by the treatment. Complete Blood Count (CBC) results from ten patients (6 boys and 4 girls, mean age 10,9 years, SD: 5,7) were analyzed. Samples were obtained before, and every 8 weeks during 6 months of treatment with 1) cyclophosphamide (25mg/m^2/day, PO) / vinblastine(3mg/m^2/week, IV) or 2) cyclophosphamide (25mg/m^2/day, PO) / vinorelbine (25mg/m^2 day 1-8-15, IV) or 3) etoposide (50mg/day, 28 days cycles; 21 days YES, 7 days NO, PO). Data was compared with the CTCAE v. 5. CBC values showed no statistical differences during treatment in RBC (P=0.99), hemoglobin (P=0.87), hematocrit (P=0.87), Mean Corpuscular Volume (P=0.89), platelets (P=0.97), WBC (P=0.99) and neutrophils (P=0.99), after six months of treatment. Interestingly, a high percentage of patients had normal hematologic values; moreover, there were no grade 3 toxicities. We conclude that MCT with cyclophosphamide/vinblastine, cyclophosphamide/vinorelbine or etoposid administered to pediatric patients with advanced oncological diseases is safe, from the hematologic point of view. The lack of toxicity, which leads to a good quality of life and avoids additional treatments, together with the expected therapeutic effect, supports its use in pediatric cancer.

269. (212) **ANTITUMOR ROLE OF HEME OXYGENASE-1 IN BREAST CANCER**

Norberto Ariel Gandini, Eliana Alonso, María Eugenia Fermento, Georgina Pamela Coló, Marilina Mascaró, María Julia Ferronato, Josefina Guevara, Martín C Abba, Julián Arévalo, Silvina Grioli, Agustina Ibarra, Nazarena Barrera Lamas, María Marta Facchinetti, Alejandro Carlos Curino
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It has been reported that HO-1 can translocate to multiple subcellular compartments and can have non-enzymatic signaling roles. Thus, in the nucleus the protein may act as a transcriptional co-regulator protein and may bind and modulate other important proteins. HO-1 is an enzyme involved in cellular responses to oxidative stress and has also been shown to regulate processes related to cancer progression. In this regard, HO-1 has been shown to display a dual effect with either antitumor or protumor activity, being this also true for breast cancer (BC). In this work we intended to address this discrepancy regarding the role of HO-1 in BC. HO-1 was detected in human BC tissues, and its protein levels correlated with reduced tumor size (p=0.046) and longer overall survival time of patients (p=0.004). Contrariwise, nuclear localization of HO-1 correlated with higher tumor grade (p=0.05). However, nuclear HO-1 was not significantly associated to patient overall survival time (p = 0.13). In vivo experiments showed that both pharmacological activation and genetic overexpression of HO-1 reduced the tumor burden in two different animal models of BC. Furthermore, the activation of HO-1 in several BC cell lines reduced cellular viability by inducing apoptosis (p<0.05) and cell cycle arrest (p<0.003) and decreased the cellular migration, invasion and adhesion rates by modulating pathways involved in the epithelial-mesenchymal transition. Furthermore, HO-1 activation impaired in vivo the metastatic dissemination (p=0.020). In concordance, HO-1 expression associated with reduced number of lymph node metastases (p=0.0243) and higher levels of E-cadherin (p=0.0026) in human BC. In addition, the enzymatic activity of HO-1 in nuclear and cytoplasmic fraction was studied by ICP-AES. In conclusion, we demonstrate that HO-1 displays antitumor activities in BC. Furthermore, our studies suggest that HO-1 subcellular localization may explain the differential effects observed for the protein in different tumor types.

270. (355) **ROLE OF HEME-OXYGENASE 1 IN THE CELLULAR METABOLISM OF PROSTATE CANCER**

Florencia Cascardo[1, 2], Alejandra Páez[1, 2], Florencia Velaz-