Toxicología / Toxicology II

Chairs: Pablo Evelson | Paola Ingaramo

0086 - EFFECTS OF GLYPHOSATE (G) AND ROUNDUP (R) ON IMMATURE RAT SERTOLI CELL (SC) PROLIFERATION

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CENTRO DE INVESTIGACIONES ENDOCRINOLÓGICAS "DR. CÉSAR BERGADÁ" (CEDIE)-CONICET

Abstract/Resumen: A declining trend in human fertility has been described and exposure to xenobiotics, such as herbicides, emerges as a potential cause. We have shown that G and its commercial formulation R alter blood-testis barrier between neighboring SC, which would partly explain the decrease in reproductive function observed after herbicide exposure. This observation points the SC as a plausible target for G or R effects. In rats, SC proliferation occurs during fetal and postnatal periods up to 15 days of age. As each SC supports a limited number of germ cells, the number reached during proliferative periods will be decisive for spermatogenic capacity. Thus, disruption of any SC proliferative stage would compromise fertility. The aim of this work is to analyze whether exposure to G or R can alter postnatal SC proliferation. SC cultures from 8-day-old rats were treated with 100 ppm of G or R in the absence or presence of FSH, the main SC mitogen. Proliferation was evaluated by BrdU incorporation. It was observed that R, but not G, decreased FSH-stimulated SC proliferation (FSH: 19.8 ± 2.3; FSH + R: 9.7 ± 1.4*, X ± DS, *p<0.05). Additionally, it was observed that R decreased cyclin D1 and D2 and increased p21Cip expression (p<0.05), evaluated by RT-qPCR. For in vivo studies, male pups were assigned to control and R groups receiving daily sterile saline solution or 50 mg/kg R ip, from postnatal day (pnd) 3 to 7, respectively. At pnd8, pups were injected with BrdU (50 mg/kg) before sacrifice to evaluate cell proliferation. No changes in BrdU incorporation in SC and in testis weight was observed (n= 4/group). In addition, histological analysis showed normal organization of the seminiferous epithelium. The results obtained show that although R could decrease in vitro SC proliferation, these effects could not be observed in vivo. Altogether the results suggest that the harmful effects of R on adult reproductive function would not be mediated by alterations in SC proliferation.

0264 - LENS REDOX IMBALANCE AFTER URBAN AIR POLLUTION EXPOSURE

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Abstract/Resumen: Particulate matter (PM) present in air pollution produces adverse effects on the eye. Oxidative stress has been suggested to play a key role in the toxic mechanism. Lens antioxidant system maintains the redox status of nearby ocular structures. The aim of the study was to evaluate the redox balance in mice lens after the exposure to urban air pollution. 8-week-old Balb/c male mice were exposed to urban air or filtered air (UA-group and FA-group, respectively) in exposure chambers located in highly populated area of Buenos Aires city (average level of PM: 25.6 ± 0.8 μg/m³). The animals were exposed for 8 h/day, 5 days/week, up to 12 weeks (CICUAL-FFYB, CUDAP 50946/16). Superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR) activity, levels of reduced and oxidized glutathione (GSH and GSSG) and protein oxidation (PO) were evaluated in lens lysates. After 1 and 2 weeks of exposure, UA-group presented no significant differences in all measurements compared to the FA-group, except for SOD activity that was increased after 1 week (107 %, p<0.05). After 4 weeks, an increase in GR activity was shown in UA-group (47 %, p<0.05). After 12 weeks, GPx activity was increased in UA-group (63 %, p<0.05), meanwhile GR activity decreased (40%, p<0.05) as well as the GSH/GSSG index (62 %, p<0.05), compared to FA-group. PO increased in UA-group (113 %, p<0.05), and an inverse correlation was found between PO and GSH/GSSG index (r= -0.9114, p<0.001). GPx activity and GSH/GSSG index also presented an inverse correlation (r= -0.7421, p<0.001) in UA-group. These results suggest that urban air pollution exposure alters the redox balance of the lens, which could affect the antioxidant defenses of nearby ocular structures. The correlation between the PO and GSH/GSSG index indicates that lens GSH pool could prevent the protein oxidation, which has been suggested as one of the triggers of cataracts.

0290 - EXPOSURE TO HEXACHLOROBENZENE INDUCES ENDOCRINE ALTERATIONS ASSOCIATED WITH ENDOMETRIOSIS PROGRESSION

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Abstract/Resumen: Endometriosis is a chronic illness hormone-dependent which is defined by the presence of endometrial tissue outside the uterus. The endocrine disrupting chemicals may be involved in the development and progression of disease. Hexachlorobenzene (HCB) is a pesticide that acts as an endocrine disruptor modulating the hormonal signaling. Aberrant expression of estrogen and progesterone receptors (ER, PR) has been associated with progression of endometriosis, which is referred to as estrogen-dependent and progesterone-resistant. Aromatase is the key enzyme in the estrogen biosynthesis and it is essential for establishment and growth of endometriosis lesions. Previous results showed that HCB induces cell migration and invasion of endometrial cells, increases ERalfa; and reduces PR levels in lesion and eutopic endometrium in rat model. Our aim was to evaluate the dependence of ER on migration (scratch motility assay) and invasion (transwell assay) in endometrial stromal cells (T-HESCs), and to investigate the hormone receptor profile (WB) in T-HESCs and primary cultures of endometrial stromal cells from eutopic endometrium of control (CESC) women. Cells were exposed to HCB (0.005, 0.05, 0.5 and 5 μM) for 24h. Results showed that the pesticide enhanced cell migration (HCB 5 μM, p<0.001) and invasion (HCB 0.5 μM, p<0.001) in an ER dependent manner in T-HESCs. Moreover, HCB increased expression of Aromatase (0.005, 0.05 and 0.5 μM, p<0.01) and ERalfa; (0.5, p<0.05), while it reduced PR protein levels (5 μM, p<0.05). Instead, the ERß levels were not modified. In CESC, HCB enhanced ERalfa (0.5 μM, p<0.05), ERß (0.05, μM p<0.05) and Aromatase (0.5 μM, p<0.05) protein levels. Also we compared the HCB exposure effects with 17-ß-estradiol, observing that both showed a similar action on REalfa protein expression. In conclusion, our results demonstrated that HCB would act as a xenoestrogen inducing an invasive profile contributing to the development and progression of the disease.

0303 - NEUTRALIZING CAPACITY OF ANTISERA OBTAINED BY IMMUNIZATION WITH BOTHROPS