

# *medicina*

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$p < 0.05$ ). In addition, the pesticide exposure decreases the protein levels of ER- $\beta$  while increasing the GPR30 expression (Western blot;  $p < 0.05$ ). These results indicate that HCB exposure induces a dysregulation in the expression of the different types of estrogen receptors, collaborating with the promotion and tumor growth in the HER2-positive breast cancer model.

**577. (462) BIOSYNTHESIS OF IRON NANOPARTICLES BY MICROORGANISMS: CHARACTERIZATION AND EFFECTS ON HUMAN KERATINOCYTES**

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Metallic nanoparticles (NPs) can be obtained by biosynthesis using microorganisms, as bacteria. Iron is abundant in nature, an essential metal for humans, and a suitable candidate for NPs synthesis with possible microbicidal activity. In this work we biosynthesized iron NPs (FeNPs) and studied possible toxic effects in the human keratinocyte cell line HaCaT.

FeNPs were synthesized using *Escherichia coli* (ATCC 25922), characterized by UV-Vis spectroscopy and by transmission electron microscopy. HaCaT cells were incubated for 4 and 24 h at different FeNPs concentrations (535; 214, 107, 53.5 and 26.75  $\mu\text{g/ml}$ ). Controls: culture medium, metal precursor salt solution  $\text{FeSO}_4$  (0.1 and 0.25 mM), and bacterial growth control of biosynthesis (CCB, dilutions 1/2, 1/5, 1/10, 1/20, 1/40). We investigated cell viability by MTT and neutral red test (NRT), reactive oxygen species (ROS) by DCF-DA and by NBT, superoxide dismutase (SOD) activity by the riboflavin-NBT method, and glutathione (GSH) content by the Ellman method.

FeNPs had a spherical shape with an average size of  $\approx 20$  nm. Cell viability decreased after 4 and 24 h incubation with FeNPs 535  $\mu\text{g/ml}$ , and CCB 1/2. However, no changes in NRT uptake were observed at 4 and 24 h. The ROS levels were significantly increased after 4 h and 24 h incubation with all the treatments assayed. In addition,  $\text{O}_2^-$  production significantly increased at 24 h of incubation with FeNPs 535  $\mu\text{g/ml}$ , and CCB 1/2. SOD activity was increased at all treatments tested. Finally, the GSH content was not modified by any treatment at 24 h.

Altogether these results suggest that the highest FeNPs concentration significantly modifies the cell viability with increase in  $\text{O}_2^-$ , ROS, and SOD. In contrast, other stimuli were able to modify HaCaT oxidant/antioxidant cell balance, but not cell viability. Prolonged incubation studies are needed in order to determine if cell viability is altered at lower concentrations and to unravel the mechanisms underlying these alterations.

**578. (471) EFFECTS OF INTRAUTERINE EXPOSURE TO BENZOPHENONE-3 IN LACTATING MURINE MAMMARY GLAND**

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Benzophenone-3 (BP3), an ultraviolet radiation filter commonly used in sunscreens, has been shown to alter mammary gland (MG) development. Previously, we have demonstrated that exposure to BP3 alters beta-casein (CSN2) and alpha-lactalbumin (LALBA) milk protein expression during functional differentiation of the MG *in vitro*. Here, our aim was to evaluate whether intrauterine exposure to BP3 alters the lactating mammary gland in the F1 female offspring. Pregnant F0 C57BL/6 mice were dermally exposed to vehicle (sesame oil; Control), 0.15 (0.15BP3) or 50mg BP3/kg/day (50BP3) from gestation day 8.5 to 18. At 8 weeks-old, female offspring (F1) were bred and MG samples were obtained on lactation day 10. The protein expression of the myoepithelial cell biomarker alpha-smooth muscle actin, CSN2 and LALBA was assessed by immunohistochemistry. The perimeter and area of the alveoli and the myoepithelial linear density were measured to establish either the proportion of large/small alveoli per group or the maturation and differentiation of the myoepithelial cells. CSN2, LALBA and whey acidic protein (WAP) mRNA expression was evaluated by qRT-PCR. The alveolar perimeter in 0.15BP3 animals was the lowest among groups ( $p < 0.05$ ). Conversely, 50BP3 animals showed the highest alveolar area compared to 0.15BP3 ones ( $p < 0.05$ ). In addition, BP3 treatments had opposite effects on the proportion of large/small alveoli: whereas it was similar in control animals (47.3/52.7), it was diminished in the 0.15BP3 group (31.7/68.2) and augmented in the 50BP3 group (60.7/39.2). Also, the myoepithelial linear density was lower in 0.15BP3 than in control animals ( $p < 0.05$ ). In contrast, the protein expression of CSN2 and LALBA, and the mRNA expression of CSN2, LALBA and WAP were similar between groups ( $p > 0.05$ ). In conclusion, the intrauterine exposure to BP3 altered the lactating MG, and these effects could be related to the alveolar secretory content and/or its contractile function.

**579. (515) CHRONIC ORAL EXPOSURE TO A GLYPHOSATE-BASED HERBICIDE IMPAIRS FEMALE REPRODUCTIVE OUTCOMES IN WISTAR RATS**

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Glyphosate-based herbicides (GBHs) are the most globally used herbicide increasing the environmental exposure risk. The chronic effects on reproductive outcomes associated with long-term exposure to GBHs remain unexplored. In the present work, we investigated, in Wistar rats, the effects of chronic oral administration of a safe dose of a commercial GBH on: 1) body weight and food intake; 2) reproductive performance and fetoplacental parameters. Female rats were exposed to GBH through food, in a dose of 2 mg of glyphosate/kg bw/day, from postnatal day 21 (PND21) and during 11 weeks. Control group (CON) was provided with a laboratory pellet chow-based paste. Body weight and food intake were registered along the exposure. Females at the proestrus stage were caged with males with proven fertility. We evaluated the pregnancy rate by assessing the number of pregnant females/number of females housed with a male  $\times 100$ . In addition, we determined the reproductive performance by quantifying the number of corpora lutea, the implantation sites (IS) and the resorption sites on gestational day 19 (GD19). The fetuses and the placentas pairs were removed and weighted. The placental index was calculated as follows: placental weight/fetal body weight. Last, fetal length and litter size were determined.

We detected an increase in body weight of the rats exposed to GBH 8 days after the beginning of treatment (PND30). However, no differences were found on food intake between CON and GBH-treated rats. Regarding reproductive performance, we detected a lower number of IS in GBH group compared to CON group. Fetal development was impaired, we detect a decrease in weight and length of the