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Envenomation by the South American *Lonomia* saturniid caterpillars, named lonomism, constitutes an emerging and somewhat neglected public health issue in Argentina, mainly in the province of Misiones covered by the Atlantic Forest. Our aim was to assess the 24-hour kinetics of the local and systemic damage induced by the Argentinean *Lonomia* sp. venom (50 μL of 1 mg/Kg body weight, i.d., dissolved in PBS prior to injection) in male CF1 mice (n = 3 for each time point). After 2, 5, 10 and 24 h of injection, animals were anesthetized with ketamine 100 mg/Kg and xilazine 10 mg/Kg (i.p.), and tissue fragments were removed for histological analysis. By direct macroscopic examination, we evidenced an erythematous reaction that developed rapidly at the injection site. The microscopical data showed detachment of the epidermis, and disorganization of the dermal structure; the latter is apparently caused by inflammatory infiltrate and edema, both of which decreased considerably by 24 h after venom injection. Systemically, we revealed liver damage characterized by infiltration of polymorphonuclear inflammatory cells, centrilobular vascular congestion, dilation of sinusoids, and necrosis of hepatocytes; the last injury was preferentially observed in zones 2 and 3 of the hepatic acinus. In lung sections, we observed loss of the alveolar wall structure associated with detachment of type II pneumocytes, and large areas of hemorrhage and atelectasis. The systemic pathological changes were more pronounced at later time points. These findings have implications within the clinical setting for lonomism in Argentina, and support the need for looking further into an effective therapy available for this envenomation in this country.

584. (544) **SOY PROTECTS AGAINST CADMIUM-INDUCED FIBROSIS IN LUNG. ROLE OF HEAT SHOCK PROTEINS (HSP)**

Gabriel Boldrini[1,2], Verónica Pérez Chaca[1], Glenda Martin Molinero[1,2], María Evelyn Córdoba[3], Gisela Pennacchio[3], Mariel Fanelli[3], Nidia Gómez[1,2], Silvina Álvarez[1,2].
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Cadmium (Cd) is a toxic metal and an important environmental contaminant. We studied its effects on lung fibrosis and HSP expression under different diets. 4 lots of female Wistar rats were used: 2 lots received casein (Cas) and 2 lots received soy (So) as protein sources. Within each group: 1 lot received regular water (control-Co) and the other 15ppm of Cd in the drinking water for 60days. Lungs were hydrolyzed and hydroxyproline (Hyp) was quantified by the chloramine-T method. The color was read in a spectrophotometer at 550 nm. Lung tissues were fixed, dehydrated, cleared in xylene, and embedded in paraffin. Sections of 5–6μm thickness were stained with Masson's trichrome solution for histology assessment. Immunohistochemistry was performed by using Hsp27 and Hsp70 antibodies. Hyp showed an increase in CasCd group vs CasCo ($p<0.005$); in SoCd, Hyp levels were higher than SoCo ($p<0.01$) but lesser compared with CasCd ($p<0.05$). Masson's Trichromic exposed that CasCo and SoCo have normal alveolar septa, without deposits of connective tissue. In CasCd, advanced pulmonary fibrosis and blue collagen deposits were evident throughout the lung. In SoCd, collagen deposition was observed around the intrapulmonary tree and lung vessels. Hsp27 showed an increase of its expression in Cd intoxicated groups, being only significant in CasCd vs CasCo ($p<0.05$). Hsp70 exhibited higher levels in SoCd vs SoCo, without differences among casein-fed groups. We conclude that Cd induce lung fibrosis, and soy might have a protective effect. It has been proven that Hsp27 promotes fibrosis in animal models. The higher expression of Hsp70, a demonstrated anti-fibrotic protein, induced by soy could protect against Cd-induced fibrosis.

585. (560) **LUNG AND KERATINO CYTE CELLS DIFFERENTIAL RESPONSE TO RURAL AIR PARTICULATE MATTER IN VITRO**

Orona Nadia S.[1], Astort Francisco[1], Fenoy Ignacio[1]; Palavecino Imanol[1]; Ramirez Haberkon Nancy B.[2], Mendez Mariano[2], Randi Andrea[3], Panebianco Juan E. [2], Goldman Alejandra[1].
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Atopic disorders susceptibility depends on interactions between genetic and environmental factors. The prevalence of these disorders has increased in the last 5 decades indicating that environmental factors might be responsible for this increase. Airborne particulate matter (PM) is one of environmental health problems affecting the world's population. Although several studies related the exposure to urban PM with the onset or exacerbation of allergies such as asthma and atopic dermatitis, there are few studies that link rural PM with the development of these allergic disorders. Rural PM comes mainly from agricultural activity, where agrochemical compounds are frequently used. Although agrochemical exposure has been related to allergic diseases, an approach considering the synergistic effects of PM and agrochemicals is necessary. Therefore, the aim of this study was to evaluate the effect of soil generated-PM_{10} from an intensive cultivation area where the use of agrochemicals prevails (Rural PM) from the central Pampas region on pulmonary (A549) and skin (HaCaT) cells. A549 or HaCaT cells were exposed to Rural PM (1-100μg/ml) or to glyphosate (0.75–7500pg/ml). After 24h, cell metabolic activity, lactate dehydrogenase (LDH) and cytokine release (IL-8, TSLP, IL-1β) was assessed. We found that A549 cells exposed to PM showed a marked increase in IL-8 production ($P<0.001$), without alterations in cell metabolic activity or LDH release. Regarding HaCaT cells, we found that exposure to PM or glyphosate provoked an alteration in metabolic activity at the highest dose employed ($P<0.01$), without changes in the release of LDH. Moreover, the levels of TSLP, IL-1β and IL-8 increased significantly in PM exposed-HaCaT cells. These results indicate a differential response of the pulmonary and dermal epithelia against rural PM. Interestingly, the increased levels of TSLP observed in keratinocytes may point to the skin as the initial sensitization site for different atopic disorders.

586. (561) **LUNG AND KERATINO CYTE CELLS DIFFERENTIAL RESPONSE *TO* RURAL AIR PARTICULATE MATTER *IN VITRO***

Orona Nadia S.[1], Astort Francisco[1], Fenoy Ignacio[1]; Palavecino Imanol[1]; Ramirez Haberkon Nancy B.[2], Mendez Mariano[2], Randi Andrea[3], Panebianco Juan E. [2], Goldman Alejandra[1].
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587. (564) **SUBCHRONIC INTOXICATION WITH CADMIUM INDUCES MORPHOLOGICAL ALTERATIONS IN RAT CEREBELLUM: THE PROTECTIVE ROLE OF A SOYBEAN DIET**

Glenda Martin Molinero [1,2], Gabriel Boldrini [1,2], Pablo Héctor Horacio López [3], Silvina Mónica Álvarez [1,2].
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Cadmium (Cd) is an environmental contaminant. The aim of this study was to characterize its toxicity in cerebellum and the potential reversal by a soybean-based diet. The glial fibrillary acid protein (GFAP), indicator for neurotoxic effects in mature brain, was evaluated. Besides, we performed a morphometric and stereological analysis. Female Wistar rats (n=12) were fed with casein (Cas) and soybean diets (So) as protein source for 60 days. Simultaneously, half of the animals were administered either 15 ppm of Cd in water or regular tap water as control. The cerebellums were fixed and processed for immunofluorescence. The samples were visualized by fluorescence microscopy and the positive fluorescence area for GFAP was quantified by IMAGE J Software. Morphometric analysis included quantifying the number of granule cell neurons (CGn) and Purkinje cells neurons (Pkn) in serial 20µm-thick sections stained with cresyl violet along the different lobules. We performed a three-dimensional volumetric reconstruction of the tissue through the use of the software Stereo Investigator. The thicknesses of the molecular and granular layers of the cerebellar cortex of lobules I-X were determined on digital images. We found a decrease in the number of CGn in the CasCd group vs. CasCo group ($p<0.05$) and SoCd group ($p<0.01$). On the contrary, the number of Pkn remained unchanged. In addition, there was a significant reduction in the internal granular layer of CasCd group vs. SoCd group, while no effect was observed in the thickness of the molecular layer. The cortical thicknesses of the different regions of each folium base from cerebellar lobules I-X did not show significant differences between the groups. Overall, these results unmask an irreversible toxic effect of low dose-sub chronic Cd intoxication on cerebellum and identify a protective role of a soy-based diet with potential as a therapeutic strategy for those individuals exposed to this dangerous environmental contaminant.

588. (578) **ONTOGENIC VARIATION ON CYTOTOXIC POTENTIAL OF *Bothrops alternatus* (SERPENTES, VIPERIDAE)**

Karen Yamila González[1,2], Bustillo Soledad[1,,3], Sánchez Matías Nicolas[4], Maruñak Silvana[4], Valdovinos Zaputovich, Bertha[5], Gladys Pamela Teibler[4], María Emilia García Denegri[1,,3,4,6]
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Argentina presents a vast richness of snakes species, but only eighteen are venomous (Viperidae and Elapidae families). Snake venom plays a critical role in food acquisition, digestion, and defense. Venoms are known to change throughout the life of some snake species, but little is known about the venom composition during juvenile stage. In the northeast (NEA), venom from *B. alternatus* species, are known to display ontogenetic variation in both, biochemical and biological activities. We reported a comparative cytotoxic analysis of venoms from juvenile and adult specimens of *B. alternatus* and correlate it with the histological evaluation of crucial venom injuries from juvenile. Cytotoxic activity was assessed with undifferentiated myoblasts as cultured murine muscle cells (C2C12). After 3 h of venom incubation, cell viability was quantified by crystal violet staining. To support the *in vitro* damage, myotoxicity in gastrocnemius muscle from mice was assayed (6.9 μg/g) and submitted to routine histological processing and H&E staining. The venoms of *B. alternatus* juvenile and adult exhibited concentration-dependent cytotoxic activities toward the C2C12 cell line tested. Both venoms exhibited differential cytotoxic effects, with venom from juvenile species being significantly more potent in inhibiting the growth of the myoblast cells (~55%) with venom concentrations of 5 μg/mL. The histological effects from juvenile muscle envenomation exhibited marked and persistent hemorrhage, edema forming, polymorphonuclear infiltrations and necrosis. We demonstrated that the ontogenetic shift in diet, from ectothermic prey in early life to endothermic prey in adulthood, and in animal size are associated with changes in the venom proteome in *B. alternatus* species. Altogether, these results point out the different toxic features between juvenile and adult snakes in ontogenetic development.

TRANSDUCCIÓN DE SEÑALES

589. (010) **THIOREDOXIN-LIKE PROTEINS AS MEDIATORS OF FORMALDEHYDE TOXICITY AND THEIR ROLE IN CANCER**

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Formaldehyde (FA) is a mutagen and a carcinogen also produced inside cells as a byproduct of essential biological processes such as epigenetic demethylations and the one carbon cycle. We have previously shown that FA toxicity can not only be inflicted by damaging the DNA but also through the accumulation of reactive oxygen species.
To further identify the mechanism by which FA is triggering cell death through oxidative stress, we searched for factors that are affected upon FA treatment. We found that the protein thioredoxin like-1 (TXNL1), which has been found associated with the 19S proteasome, is downregulated upon acute exposure to FA in HCT116 colorectal cancer cells. The protein level of TXNL1 drops 31.7±7.9% upon 5-h exposure to 200 uM FA, and 48.1±14.4% upon 5-h ex-