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(i) ESCI members can now submit abstracts for presentation at the joint Annual Meetings of the AFMR, AAP and ASCL.
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can cause various cutaneous diseases, such skin carcinoma, dermatitis, and sunburn. ROS play an important role in the initial step of these diseases; therefore, IDH2 deficient mice (KO) could be a useful model to investigate UV-mediated skin damage. When we exposed the dorsal skin of KO mice to UVB, pyrimidine dimers and (6-4) photoproducts (6-4PPs), marker of photoproducts generated by UVB, were found in the dermis of the knockout mice. Increased collagen degradation, apoptosis, inflammation, and ROS levels in the dermis were also observed. These results indicated that UVB could reach the dermis by penetrating the epidermis. We then attempted to determine how the epidermis was breached, and observed a decrease in the expression level of delnNp63, a major protein required for epidermis generation, in the KO mice. The mito-TEMPO supplement significantly ameliorates UVB-induced damage in the skin of KO mice. In the present study, we provided a role for IDH2 in protection against UVB-induced skin damage and a new connection between IDH2 and delnNp63.

**P051-T**  Effects of the caffeine on the snails training through the regulation of Ca^{2+} concentration through ryanodine receptors of the endoplasmic reticulum and mitochondria

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Calcium ions play a critical role in the regulation of a great variety of neuronal processes due to their specific physicochemical characteristics. They are the most versatile intracellular mediator linking the processes developing in the surface membrane of the cell and reactions occurring within the cell. It is generally accepted that intracellular calcium, which is ionized, has the function of universal secondary mediator involved in the regulation of many intracellular reactions, down to gene expression. One of the agents that cause the increasing of intracellular concentration of Ca^{2+} in cell, which acts on the ryanodine receptors in the endoplasmic reticulum and mitochondria. That is, the regulation of intracellular concentration of Ca^{2+} ions occurs through these receptors. In this regard, the aim of our study was to investigate the effects of chronic administration of caffeine on the formation of conditioned defensive reflex in snails. It was used 5 groups of animals: intact (n = 18), snails, received a saline injection 30 minutes before training (active control, n = 11), snails, injected with caffeine 30 minutes before training (n = 18), snails injected with caffeine immediately after the training (n = 18), snails, which were injected daily with caffeine during the study period (n = 8). Our experiments showed that the chronic injection of caffeine increases elaboration of defensive conditioned reflex in snail. The injection of caffeine immediately after the training procedure was produced learning faster than when caffeine applied before training. Thus, changes in intracellular Ca^{2+} concentration by caffeine, which occurs by activation of the ryanodine receptors of the endoplasmic reticulum and mitochondria serves as regulator of plastic processes during learning.

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**P052-T**  Dynamics of nitric oxide production in the rat hippocampus as one of the mechanisms of inflammation during ischemic and hemorrhagic insult

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It is known that nitric oxide (NO) and peroxynitrite are involvement in the pathophysiology of well-characterized acute and chronic inflammatory diseases and play an important role in the development of organ damage and inflammation triggered by various drugs and chemical agents (Patchett et al., 2007). Those processes characterized the hypoxia that occurs includes the development of tissue ischemia. According to this the study of the pathogenesis, the methods of correction and the mechanisms of stroke is important both from the theoretical and practical points of view. The main purpose of our investigation was to study the dynamics of NO production in the hippocampus of rats after modeling both ischemic and hemorrhagic stroke.

Electron paramagnetic resonance (EPR) was used as a method to record NO production in the tissues of the brain of healthy rats and rats after modeling of ischemic and hemorrhagic stroke. Direct measurement of the dynamics of NO production by EPR spectroscopy in our experiments showed that after the emergence of signs of ischemic stroke, 5 hours after the start of ischemia, the content of
NO in the hippocampus decreased 2–3 times and this decrease is maintained at 24 and 72 hours.

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**P053-T**  |  Effects of inhibition of tryptophan hydroxylase synthesis on context memory

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It is established that serotonin (5-HT) is a basic neurotransmitter for defensive behavior in mollusks and learning on the basis of defensive reflexes. In behavioral experiments it was shown that the disruption of serotoninergic system by the neurotoxin 5,7-DHT did not change the original memory, however, led to a memory impairment after repeated reactivation. An unavailability of reactivation under the action of the antagonist of serotonin receptors methysergide was also shown. These results demonstrated the relevance of analysis of long-term memory after inhibition of 5-HT synthesis. Tryptophan hydroxylase (TPH) is the first and presumably rate-limiting enzyme in 5-HT biosynthesis. P-chlorophenylalanine (p-CPA) is one of the various drugs that depletes TPH, it causes long and deep depletion of brain 5-HT-depot.

Here, we investigated the possible changes of the reconsolidation under the conditions of 5-HT deficit, caused by injection of inhibitor of TPH synthesis (intermediate stage of the synthesis of 5-HT) p-CPA. It was shown that the forgetting process for conditioned situational reflex after reminder and inhibition of protein synthesis did not occur if the 5-HT transmission in nervous system was impaired. This effect was significantly different from the direct action of inhibitor of protein syntheses ansiomycin, which completely blocked the reconsolidation of context memory. We concluded that the 5-HT system was included to the process of memory reconsolidation (in our system of situational memory).

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**P056-T**  |  Cytotoxicity of doxorubicin-loaded PLGA and PLGA-PEI nanoparticles: relevance for anti-tumor effects and cardiotoxicity

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Background: Doxorubicin (Dox) is an anti-neoplastic antibiotic widely used in therapeutics, although its high cardiotoxicity limits its use. Our objective was to use pharmaceutical technology to improve Dox biodistribution and consequently reduce toxicity, without sacrificing the anti-tumor efficacy. We developed two Dox delivery nanoparticle systems of poly (D,l-lactide-co-glycolide)-based nanoparticles (PLGA-NPs) and PLGA-NFs bearing surface polyethyleneimine (PEI)/PLGA-NPs and tested cytotoxicity on human breast tumor cells (MDA-MB-231) and MCF-7, normal human breast cells (MCF-12A) and rat cardiomyoblast (193C2).

Material and methods: Tumor and normal cell lines were incubated with free Dox, Dox-PLGA-NPs and Dox-PEI/PLGA-NPs for 24 hours (0.1–2.0 µM Dox). Cytotoxicity analysis was performed by resazurin, sulforhodamine B assay, and determination of ATP levels. p53 levels were detected by immunoblotting.

Results: Cytotoxicity assays demonstrated that all Dox formulations induced dose-dependent cell death in the tested cell lines (with exceptions for MDA-MB-231). No differences in cell death were observed between free Dox and the NP systems in the normal cell lines. However, for the MCF-7 cell line the Dox-PEI/PLGA-NPs showed higher reduction of cell mass vs observed in free Dox or Dox-PLGA-NPs treatments. Although no statistically differences were observed between the different treatments on 193C2 cells, with the NPs systems p52 levels were decreased by ap. 30% when compared with free Dox.

Conclusion: Dox chemotherapy efficiency is compromised by the cardiac side effects and drug delivery systems have been explored in an attempt to overcome off-target toxicity. We tested the cytotoxicity of two NPs systems for drug encapsulation and observed increased toxicity of Dox-PEI/PLGA-NPs in the breast tumor cell line MCF-7, while both NPs formulation seem to lower the activation of p53 in the cardiomyoblast cell line. The study was supported by CAPES (ref.88881.132300/2016-01); FCT (PTDC/CTP-FPG/1180/2012, SFRH/BD/52