PRÊMIO JOSÉ RIBEIRO DO VALLE 2018

O prêmio José Ribeiro do Valle, oferecido a cada ano pela SBFTE, visa identificar a cada ano os melhores trabalhos científicos desenvolvidos por jovens investigadores na área da Farmacologia. Entre os trabalhos inscritos para esta vigésima edição do prêmio, foram selecionados cinco finalistas, que fizeram apresentações de seus respectivos trabalhos perante comissão julgadora, em sessão pública durante o 50º Congresso Brasileiro de Farmacologia e Terapêutica Experimental, em Ribeirão Preto, SP. O resultado foi o seguinte:

Primeiro prêmio

Bruna da Silva Soley

04.012 Participation of kinin receptors in the imiquimod-induced psoriasis-like skin inflammation. Soley BS[1], Pesqueiro JB[2], Bader M[3], Otuki MF[1], Cabrini DA[1] [1]UFPR – Farmacologia, [2]Unifesp – Biofísica, [3]Max-Delbrück-Center for Molecular Medicine – Molecular Medicine

Introduction: It is known that all kinin system components are constitutively expressed on skin; furthermore, both receptors are upregulated during cutaneous disorders, such as psoriasis. We have previously shown that kinin receptors are involved in the control of the keratinocyte hyperproliferative process (Pietrovski et al. 2011). However, it is unclear how the kinin receptors modulate inflammatory parameters observed in psoriasis. **Methods**: C57bl/6 wild type (WT) and knockout (KOB1, KOB2 and KOB1B2) animals were subjected to the chronic inflammation induced by *imiquimod* (IMQ). Animals were trichomized and received IMQ topical administrations (80 mg) on the back for 6 consecutive days. On the seventh day, skin samples were collected for analysis. In addition, C57bl/6 animals were submitted to the same experimental protocol, but 1h before the IMQ administration received daily the pre-treatment with captopril (10; 30 or 100 mg/kg, p.o.). **Results:** The PASI (Psoriasis area and severity index) showed improvement in knockout animals (KOB1, KOB2 and KOB1B2) submitted to IMQ model, when compared to the WT group. In addition, knockout animals showed reduction on myeloperoxidase activity, 31.11 ± 1.80% (KOB1), 30.82 ± 1.75% (KOB2) and 51.60 ± 2.28% (KOB1B2). Similarly, the N-acetyl-BD-glucosaminidase (NAG) enzyme activity was lower in the knockout groups, equal to 31.54 ± 7.41% (KOB1), 41.11 ± 1.66% (KOB2) and 29.56 ± 6.73% (KOB1B2). Histological analyzes showed reductions of 80.16 ± 6.26% (KOB1), 98.27 ± 5.92% (KOB2) and 94.01 ± 5.22% (KOB1B2) in the number of colored nuclei. Still, KOB1, KOB2 and KOB1B2 groups showed epidermis thickness declines of 9.12 ± 2.92%, 13.63 ± 6.60% and 68.59 ± 1.60%, respectively. The PCNA analysis showed reduction in the number of immunoreactive cells in 30.95 ± 5.8% (KOB2) and 62.05 ± 2.13% (KOB1B2), while no changes were observed in KOB1 group. In addition, IMQ promotes increase in the number of immunolabelled cells for cytokeratin 14, reducing this parameter in the groups KOB1 (34.15 ± 2.95%), KOB2 (75.35 ± 1.19%) and KOB1B2 (81.69 ± 1.57%). On the other hand, captopril treatment (100 mg/Kg) worsened PASI evaluation, increased in 73.09 ± 7.82% NAG activity, epidermis thickness (31.99 ± 8.16%) and the influx of inflammatory cells (51.74 ± 3.08%),

when compared to the vehicle group (saline). **Conclusions**: The kinin receptors absence improves the morphological features of IMQ-induced psoriasis, where both receptors seem to modulate inflammatory cells influx. The B1 receptors seem to be also involved in the modulation of keratinocyte proliferation, while B2 receptors seems to be more related to the differentiation process of these cells. Furthermore, the increase in bradykinin levels associated with captopril administration led to worsening of inflammatory parameters associated with psoriasis. Thus, once again there are data supporting the involvement of the kinin system in psoriasis. Further studies are carried on evaluating the behavior of kinin receptors on other signs related to the chronic inflammation of psoriasis. **Acknowledgment:** CNPq, INCT and CAPES. **Reference:** Pietrovski, et al. "B1 and B2 kinin Receptor Participation in Hyperproliferative and Inflammatory Skin Processes in Mice." J Dermatol Sci (2011). **Número da licença do comitê de ética:** Número 1185 (CEUA/BIO - UFPR). **Auxílio financeiro:** CNPq, INCT and CAPES.

Segundo prêmio

Alexandre Gomes de Macedo Maganin

05.018 ***Spinal kynurenine monooxygenase-expressing astrocytes mediate the maintenance of neuropathic pain.*** Maganin AGM, Souza GR, Silva RL, Lopes AH, Alves-Filho JC, Cunha FQ, Cunha TM FMRP-USP – Farmacologia

Introduction: Neuropathic pain is a chronic pain caused by injury or disease in the nervous system. Previous study forms our group has identified that after peripheral nerve injury there is a up regulation of kynurenine metabolic pathway, leading to an increase in kynurenine in the plasma, which seems to be involved in the maintenance of neuropathic pain. However, the mechanisms by which peripheral kynurenine (Kyn) mediates neuropathic pain is unknown. Kynurenine-3-monooxygenase (KMO) is the rate-limiting downstream enzyme in the kynurenine pathway that oxidatively metabolizes Kyn into 3-Hk and could be involved in maintenance of neuropathic pain. **Objectives:** The aim of the present study was to test the hypothesis that peripheral Kyn reaches the spinal cord and maintain neuropathic pain through its metabolism by KMO that forms downstream nociceptive metabolites. **Methods**: Spared Nerve Injury (SNI) model of neuropathic pain was induced in C57BL/6 mice and the following test and methods were used: von frey filaments nociceptive test, spinal cord were harvested for Real-time PCR and western blotting. KMO activity was pharmacologically (Ro-18048) and genetically (ShRNA) inhibited. Astrocytes primary cultures were also used. This study was approved by Local Ethical Commission in Animal Research: Protocol n°045/2013. **Results**: SNI induced mechanical allodynia in a time dependent manner, which peaked from 7 up to 21 days. SNI-induced mechanical allodynia was associated with an increase in the expression (protein and mRNA) of KMO in the spinal cord, mainly at day 10 and 14 after peripheral nerve injury. KMO expression was restrict to spinal cord astrocytes but was not detected in microglia and neurons. Functionally, pharmacological inhibitor and ShRNA against KMO injected intrathecally after SNI reduced mechanical allodynia. As a control, ShRNA against KMO reduced KMO expression. Kyn injected systemically (i.v) also promoted mechanical allodynia, which was also reduced when KMO was pharmacological inhibited in the spinal cord. In vitro, primary cultured astrocytes stimulated with TNF increased the expression of activation cell makers including GFAP and also of KMO. **Conclusions:** In summary, **t**hese results indicated that after peripheral nerve injury spinal astrocytes-expressing KMO plays a critical role in the development of neuropathic pain. In conclusion, these data reveal a previously unappreciated role for the kynurenine metabolic pathway as a critical link between peripheral nerve injury, spinal cord glia cells (astrocytes) and the maintenance of neuropathic pain. **Número da licença do comitê de ética** 045/2013. **Auxílio financeiro:** CAPES, CNPq, FAPESP

Menção Honrosa

Domingos Magno Santos Pereira

04.038 ***TRPV1 contributes to the development of cerebral malaria by modulating the integrity of the blood-brain barrier and oxidative stress in mice.*** Pereira DMS[1], Teixeira SA[2], Murillo O[3], Peixoto EPM[3], Araújo MC[1], Sousa NCF[1], Monteiro-Neto V[4], Calixto JB[5], Cunha TM[6], Marinho CRF[3], Muscará MN[2], Fernandes ES[1] [1]Ceuma – Imunofarmacologia, [2]USP – Farmacologia, [3]USP –Parasitologia, [4]Ceuma – Microbiologia, [5]CIEnP – Farmacologia, [6]FMRP-USP – Bioquímica e Imunologia

Fernanda Verdini Guimarães

04.047 ***Quercetin accelerates resolution of lung pathological changes caused by silica particles in mice.*** Guimarães FV[1], Ferreira TPT[1], Arantes ACS[1], Jannini-Sá YAP[1], Oliveira TAL[1], Silva CD[1], Moraes JA[2], Martins MA[1], Silva PMR[1] [1]Fiocruz - Laboratório de Inflamação, [2]UFRJ - Labio Redox

Aleksandro Martins Balbino

04.024 Novel Histamine H_3/H_4 Receptor Antagonist LINS01005 and LINS01007 modulate lung inflammatory response in murine asthma model. Balbino AM[1], Lima LJS[1], Corrêa FM[1], Fernandes GAB[1], Landgraf MA[1,2], Fernandes JPS[1], Landgraf RG[1] [1]Unifesp-Diadema – Ciências Farmacêuticas, [2]Uninove – Farmacologia e Inflamação

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