Resultado do Prêmio José Ribeiro do Valle 2004

O prêmio José Ribeiro do Valle, oferecido a cada ano pela SBFTE em parceria com a Eli-Lilly do Brasil, visa identificar a cada ano os melhores trabalhos científicos desenvolvidos por jovens investigadores na área da Farmacologia. Entre os trabalhos inscritos para esta sétima edição do prêmio, foram selecionados cinco finalistas, que fizeram apresentações de seus respectivos trabalhos perante comissão julgadora, em sessão pública durante o XXXVI Congresso Brasileiro de Farmacologia e Terapêutica Experimental, em Águas de Lindóia, SP. Os cinco finalistas escolhidos para a edição de 2004 foram:

Primeiro lugar

João A. de Moraes

VLO5, A HETERODIMERIC VGD/MLD-PEPTIDE LIGAND OF a_9/ a_4b1 INTEGRIN INHIBITS NEUTROPHIL APOPTOSIS Moraes, J. A. de[1]; Ferreira Gomes Saldanha da Gama, R.[2]; Mariano de Oliveira, A.[2]; Souza, P. B.[3]; Coelho, A. L.[3]; Sampaio de Freitas, M.[2]; Marcinkievicz, M.[4]; Barja Fidalgo, T. C.[3] - [1]UERJ - Farmacologia e Bioquímica Celular; [2]UERJ Farmacologia e Psicobiologia; [3]UERJ - Farmacologia; [4]Temple University - Biology

During inflammation, different cytokines and adhesion molecule interactions can accelerate or delay PMN surv ival, interfering in the resolution of this process. Integrin-mediated downstream signals modulate survival in different cells, activating intracellular pathways, as PI3K and MAPK, which interfere with the balance between BclxL and Bad. We have shown that disintegrins, peptides ligands of a_2 or a_9 integrins, activate integrin-coupled signaling in PMN, interfering in the apoptotic processes. VLO5 is a MLD/VGD disintegrin that was shown to activate integrin signaling pathways in PMN, inducing FAK activation, cytoskeleton mobilization and chemotaxis. In this study, we evaluated the effect of VLO5 on human PMN apoptosis and the involvement of PI3K and MAPK pathways and superoxide (O^{-2}) production. PMN were incubated with VLO5 (1mM) and apoptosis was evaluated morphologically (18h-microscopy), DNA fragmentation (8h-agarose gel) and Bad degradation (30 min-blotting). VLO5 potently inhibited spontaneous apoptosis and induced PI3K activation and ERK2 nuclear translocation. In agreement, PI3K and ERK2 inhibitors reverted VLO5 effect, accelerating PMN apoptosis. Although, discrete O^{-2} production induced by VLO5 might contribute to its anti-apoptotic effect since DPI, an inhibitor of oxidative burst, partially reverted it. The data suggest that interaction of VLO5 with PMN integrin might be related with its anti-apoptotic effect, which is dependent on PI3K and ERK2 activation and O^{-2}production. **Supported by:** FAPERJ, CNPq, IFS-Sweden

Segundo lugar

Maria do Carmo Franco

PROGRAMMING THE ENDOTHELIUM DYSFUNCTION *IN UTERO*: ROLE OF SUPEROXIDE ANION, NITRIC OXIDE AND ANGIOTENSIN II. Franco, M. C.; Akamine, E. H.; Fortes, Z. B.; Tostes, R. C. A; Carvalho, M. H. C.; Nigro, D. ICB-USP Farmacologia

Aim: It is well known that intrauterine undernutrition (IU) contributes to the development of cardiovascular disease in adulthood. In addition, the vascular diseases that have been linked to IU are characterized by endothelial dysfunction. The aim of this study was to explore the mechanisms involved in programming of endothelium dysfunction *in utero*. **Methods:** Female pregnant Wistar rats were fed either normal or 50% of the normal intake diets, during the whole gestational period. In male offspring, arteriolar diameter was measured *in vivo* by intravital microscopy before and after application of bradykinin (BK) or acetylcholine (ACh) in the absence or presence of SOD mimetic, tetrahydrobiopterin (BH_4) (NOS cofactor) or apocynin (NADPH-oxidase inhibitor). Superoxide anion generation

(hydroethidine method) was studied in the absence or presence of apocynin, BH_4 or losartan. Arterial blood pressure, NOS and SOD activities, NO production (DAF-2), angiotensin II (ANGII) concentration (HPLC) and AT_1, $p22^{phox}$, $gp91^{phox}$ and eNOS gene expression (RT-PCR) were determined. **Results:** IU induced hypertension, decreased vasodilation to ACh (4.53± 0.4*vs.*10.3± 0.4%) and BK (5.87± 0.6*vs.* 10.9± 0.9%). Topical application of SOD mimetic, apocynin and BH_4 significantly improved the altered arteriolar responses to ACh and BK. Decreased SOD and NOS activities, reduction in NO production (2.1 ± 0.2*vs.*2.9 ± 0.2), increased superoxide concentration (25.84 ± 2.60 *vs.*10.83 ± 1.72%), enhanced local ANGII concentration, attenuation of oxidative stress by BH_4, apocynin and losartan and improvement of NO production after treatment with BH_4 were observed. IU did not alter the gene expression for eNOS, AT_1, $p22^{phox}$ and $gp91^{phox}$. **Conclusion:** This study shows that IU programmed endothelium dysfunction by: 1) enhancing oxidative stress, which is associated with decreased SOD activity and increased activation of NADPH oxidase via ANGII-mediated mechanism; 2) decreasing NO production by impairment of BH_4 pathways. **Supported by:** FAPESP

Outros trabalhos apresentados

Tatiana R. Rosenstock

ALTERAÇÕES MITOCONDRIAIS E DA HOMEOSTASE DE Ca^{2+} EM UM MODELO ANIMAL DA DOENÇA NEURODEGENERATIVA DE HUNTINGTON Rosenstock, T. R.[1]; Bertoncini, C. R. A.[2]; Frussa-Filho, R.[1]; Smaili, S. S.[1] - [1]UNIFESP - Farmacologia; [2]UNIFESP - CEDEME

Fabricio A. Pamplona

AGONISTA CANABINÓIDE WIN55,212-2 PREJUDICA A AQUISIÇÃO DE MEMÓRIAS AVERSIVAS Pamplona, F. A.; Takahashi, R. UFSC Farmacologia

Nelson Carvalho Farias Jr.

Lys-[Leu^{8}des-Arg^9]-Bradykinin blocks lipopolysaccharide-induced SHR aorta hyperpolarization by inhibition of Ca^{++}- and ATP-dependent K^+ channels Farias Junior, N. C.; Feres, T.; Paiva, A. C. M.; Paiva, T. B. UNIFESP-EPM Biofísica

Comissão Julgadora

Ivan Antonio Izquierdo, Universidade Federal do Rio Grande do Sul (UFRGS) (como Presidente)
Jamil Assreuy, Universidade Federal de Santa Catarina (UFSC)
Roberto Soares de Moura, Universidade do Estado do Rio de Janeiro (UERJ)

Patrocinadora do Prêmio José Ribeiro do Valle