BOOK OF ABSTRACTS
6th MEETING OF YOUNG RESEARCHERS OF UNIVERSITY OF PORTO

IJUP'12

PORTO
CREDITS

Livro de Resumos IJUP’12

5º Encontro
de Investigação
Jovem da U.Porto

© Universidade do Porto
AA ID+i
T. 22 040 81 46
secidi@reit.up.pt

Design
Tiago Campeã
Rui Mendonça

Impressão e acabamentos
Invulgar – artes gráficas

Tiragem
1300 exemplares

Depósito Legal
340336/12

ISBN
978-989-8265-82-1
Neuregulin attenuates pulmonary endothelial dysfunction in an experimental model of pulmonary hypertension

Adão R¹, Maia-Rocha C¹, Mendes-Ferreira P¹, Mendes MJ¹, Cerqueira RJ¹, Castro-Chaves P¹, De Keulenaer GW², Lette-Moreira AF¹, and Brás-Silva C¹,³

¹ Department of Physiology, Faculty of Medicine, University of Porto, Portugal.  
² Laboratory of Physiology, University of Antwerp, Belgium.  
³ Faculty of Nutrition and Food Sciences, University of Porto, Portugal.

Neuregulin-1 (NRG-1) is implicated in the maintenance and structural integrity of the cardiovascular system [1]. No studies have determined the effects of NRG-1 in pulmonary vasculature, in health or disease. Pulmonary arterial hypertension (PAH) is characterized by a complex proliferation and dysfunction of the endothelium and pulmonary vascular remodeling [2]. Therefore, the role of this work was to evaluate the effects of a NRG-1 chronic treatment on pulmonary endothelial dysfunction in an animal model of pulmonary arterial hypertension (PAH).

Male Wistar rats (180-200g) randomly received monocrotaline (MCT, 60mg/Kg,sc) or vehicle. After 14 days, animals from these groups were randomly assigned to receive treatment with either NRG-1 (4ug/Kg/day,ip) or vehicle. The study resulted in 3 groups: control (CTRL, n=8); MCT (n=8); MCT+NRG (n=5). 21 to 24 days after MCT administration, animals were anesthetized, heart and lungs were excised en bloc and pulmonary arterial rings were isolated and mounted in a myograph. Endothelial function was determined by a dose-response curve to acetylcholine in phenylephrine pre-contracted rings. After the experimental protocol arterial rings were stored in formalin (10%) for histological analysis. Only significant results are presented (mean±SEM, p<0.05).

MCT animals presented PAH associated with endothelial dysfunction, has shown by a decreased relaxation, mediated by acetylcholine in phenylephrine pre-contracted rings, when compared with the CTRL group (MCT vs CTRL: 35.41±4.02% vs 86.27±1.85%). Treated animals (MCT+NRG) presented a significant improvement in endothelial function (48.31±5.69%). Histological analysis revealed vascular remodeling in arterial rings of MCT animals when compared with the CTRL group, as shown by an increase in tunica media thickness (MCT vs CTRL: 53.24±1.84mm vs 31.33±0.83mm), tunica media area (MCT vs CTRL: 104.50±7.48mm² vs 67.85±3.93mm²) and the tunica media area/lumen area ratio (MCT vs CTRL: 41.23±1.48% vs 31.97±2.99%). Treated animals presented a significant decrease in vascular remodeling as shown by improvements in all parameters studied (34.26±0.91mm, 75.64±5.10mm² and 29.56±2.46% respectively).

NRG-1 chronic treatment significantly reduced the severity of PAH associated physiopathological processes, namely endothelial dysfunction and vascular remodeling. These results suggest that the NRG-1 system has a crucial role in vascular function, specifically in PAH, proving to be a potential therapeutical target.
