IJAE
Vol. 117, n. 2 (Supplement): 24, 2012
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

NPP1 inhibits intimal hyperplasia in ApoE knockout mice

Francesca Bonomini[1], Frank Rutsch[2], Yvonne Nitschke[2], Stefania Castrezzati[1] and Rita Rezzani[1]

[1] Human Anatomy Division, Department of Biomedical Science and Biotechnology, University of Brescia, Brescia, Italy
[2] Department of General Pediatrics, Muenster University Children's Hospital, Muenster, Germany

Atherosclerosis is an important cause of morbidity and mortality, which is increasingly recognized and reported on a global scale. This pathology is due to multiple metabolic toxicity including increased levels of reactive oxygen species (ROS). Excessive ROS are damaging to proteins, lipids, carbohydrates and nucleic acids, which prompt a classic "response to injury" mechanism including inflammation supporting a cytokine surge, granulation and fibrosis. ROS are excessive, robustly produced in atherosclerosis associated with endothelial dysfunction. Excessive ROS due to osteopontin (OPN) increase may be the driving force promoting atherosclerotic process.

Recently has been shown that ecto-nucleotide pyrophosphatase/phosphodiesterase 1 (NPP1) promotes atherosclerosis, potentially mediated by OPN expression in ApoE knockout mice (Nitschke et al., 2011).

Hence, this study tested the hypothesis that NPP1 deficiency modulates intimal hyperplasia and oxidative stress in the atherosclerotic process.

For this study were used ApoE null mice and Npp1/ApoE double deficient mice. Atherosclerotic lesion area, calcification and vascular alterations were examined at 13, 18, 23 and 28 weeks of age.

Morphological changes in vessels were evaluated by histological procedures and immunohistochemical analysis using thrombospondin-1 (TSP-1), transforming growth factor-β1 (TGF-β1), plasminogen activator inhibitor-1 (PAI-1) and oxidative stress markers such as superoxidodismutase (SOD) and inducible nitric oxide synthase (iNOS). In ApoE null mice vessels we demonstrated vascular alterations with extensive accumulation of collagen and elastic fibers and also an increase of TSP-1, TGF-β1, PAI-1 expression and oxidative stress related protein levels compared to Npp1/ApoE double deficient mice. Moreover, histological analysis showed neointima formation only in ApoE deficient mice.

Our findings suggest that NPP1 could be involved in intimal hyperplasia and oxidative stress in the atherosclerosis pathway.

References

Nitschke Y, Weissen-Plenz G, Terkeltaub R, Rutsch F. Npp1 promotes atherosclerosis in ApoE knockout mice. J Cell Mol Med. 2011;15(11):2273-83.

Keywords: ApoE, NPP1, intimal hyperplasia, oxidative stress.