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Aerobic training and N-acetylcysteine delay the progression of diabetic nephropathy through the control of purinergic receptors

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Previous studies in our laboratory showed that N-acetylcysteine supplementation or aerobic training reduced oxidative stress and the progression of diabetic nephropathy in rats. The P2X₇ receptor is up-regulated in pathological conditions, such as diabetes mellitus. This up-regulation is related to oxidative stress and induces tissue apoptosis or necrosis. The aim of the present study is to assess the role of P2X₇ receptor in the kidneys of diabetic rats submitted to aerobic training and/or N-acetylcysteine (NAC) supplementation. Diabetes was induced in male Wistar rats by streptozotocin (60mg/kg, i.v.) and the training was done on a treadmill; NAC was given in the drinking water (600mg/L). By confocal microscopy, as compared to control, the kidneys of diabetic rats showed increased P2X₇ receptor expression and a higher activation in response to 2'(3')-O-(4-benzoylbenzoyl) adenosine 5'-triphosphate (specific agonist) and adenosine triphosphate (nonspecific agonist) (all p<0.05). All these alterations were reduced in diabetic rats treated with NAC, exercise or both. Proteinuria, albuminuria (early marker of diabetic nephropathy) and creatinine clearance in DM groups were attenuated with these treatments. Lipoperoxidation was strongly correlated with P2X₇ receptor expression, which was also correlated to NO•, thus associating this receptor to oxidative stress and kidney lesion. We suggest that P2X₇ receptor inhibition associated with the maintenance of redox homeostasis could be useful as coadjuvant treatment to delay the progression of diabetic nephropathy.

Biography

Elisa Mieko Suemitsu Higa graduated from Medical School in São Paulo, Brazil. After obtaining the Master and PhD degree at the Nephrology Division of Universidade Federal de São Paulo (UNIFESP), she has been at University of Colorado Health Sciences Center in Denver, Colorado, USA, for a Post Doctoral Program. Currently, she works at UNIFESP as an Associate Professor of Medicine Department, where she is the Supervisor for the 6th year students from Medical School, at the Emergency Division (Internship). She is the Chief of Nitric Oxide and Oxidative Stress Laboratory and is involved in the Translational Medicine and Nephrology Post graduation Programs. She is an elected member of Physiology/ Physiopathology Department of Brazilian Society of Nephrology. She served as a peer reviewer for Scientific Journals like PLOS ONE, Nitric oxide, ETAP and Medical Principles and Practice.

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