Amyotrophic Lateral Sclerosis: Analysis of Oxidative Damages in SOD1^{G93A} Transgenic Rat Tissues

Sanchez, A.B.[1], Garcia, C.C.M. [1], Freitas, F.P. [1], Angeli, J.P.F. [1], Gomes, O.F. [1], Di Mascio, P. [1], Medeiros, M.H.G. [1],
Departamento de Bioquímica, Instituto de Química, Universidade de São Paulo, Av. Prof. Lineu Prestes 748, CEP 05508-900, São Paulo, Brazil.

Amyotrophic lateral sclerosis is a disease characterized by progressive motor neuron degeneration causing atrophy, paralysis and death. Several studies have shown that neuron degeneration is a result of complex mechanisms involving oxidative damage, excitotoxicity by glutamate, protein dysfunction and genetic factors. Mutations in Cu,Zn-Superoxide Dismutase (SOD) have been linked to familiar amyotrophic lateral sclerosis (FALS) leading to a gain of a “toxic function”, not completely understood. Oxidative lesions in DNA, proteins and lipids have been detected in tissues of ALS patients and in animal models of the disease. Here we examined DNA damage and lipid peroxidation in liver and brain tissues of mutant G93A SOD1 transgenic rats. The levels of 8-oxo-7,8-dihydro-2´-deoxyguanosine (8-oxodGuo) was measured by HPLC with electrochemical detection and the levels of malondialdeyde (MDA), a lipid peroxidation product, by HPLC with fluorescence detection. Significantly higher levels of MDA and increased 8-oxodGuo tendency were observed in transgenic animals when compared to presymtomatic and non-transgenic control animals. These results suggest that oxidative stress is involved in the development of the disease and can contribute to elucidate the mechanisms of ALS. Furthermore, 8-oxodGuo can be used as a possible biomarker of the disease development.

Acknowledgements: FAPESP, CNPq, INCT de Processos Redox em Biomedicina-Redoxoma, Pró-reitoria de Pesquisa-USP

Keywords: DNA damage, SOD and ALS.