INDUCTION OF METALLOTHIONEIN I AND II ISOFORMS IN DAMAGED NERVOUS SYSTEM

González B., Acarin L., Vela J. M., Hidalgo J.M., Castellano B., Autonomous University of Barcelona, Barcelona, Spain.

Metallothioneins (MTs) are a family of metal-binding proteins which are expressed in most tissues and organs including the central nervous system (CNS). MT-I and MT-II isoforms are present throughout the brain and spinal cord in a population of astrocytes, ependymal cells, epithelial cells of the choroid plexus, meningeal cells of the pia mater and endothelial cells of the blood vessels, whereas microglia and oligodendrocytes are essentially devoid. In the brain, MT-I and MT-II can be upregulated in vivo by several factors such as metals, corticoids and also factors involved in the regulation of the inflammatory response. However the role of MT-I and MT-II induction in pathological conditions or after CNS injury is still unclear.

In this sense, in the present study we analyzed the MT-I and MT-II induction in astrocytes and microglia, as they are the most important cells associated with CNS response to tissue damage.

In the jimpy mouse, a myelin-deficient mutant whose genetic disorder results in severe alterations of the CNS, a very significant astroglial and microglial MT-I+II synthesis induction was observed. Moreover, MT induction was more pronounced in areas showing strong affectation of the tissue with hypomyelination, oligodendrocyte death and important astroglial and microglial reaction. Also in the immature brain, the intracerebral injection of N-methyl-D-aspartate (NMDA), a model for hypoxic-ischemic insult, caused a strong induction of MT-I+II synthesis in reactive astroglial and microglial cells in the damaged area within days after the insult. The results indicate that reactive but not resting microglial cells are able to synthesize MT-I+II in vivo and, in addition, they suggest a close correspondence between the degree of MT induction and the degree of glial reactivity. MT-I and MT-II induction in damaged tissue implies not only an increase in protein production by astrocytes but also the *de novo* synthesis by microglia. MT induction in glial cells under pathological conditions could be related to the protective role of MT against oxidative damage.