Emerging targets on non neuronal cells and new phenotypes of microglia in chronic neuroinflammatory diseases

L. Luongo[1], V. de Novellis[1], L. Cristino[2], R. Nisticò[3,4], F. Gardoni[5], D. Salvemini[6], F. Rossi[1], A. Usiello[7,8], S. Maione[1]

[1]Dept. of Experimental Medicine, Second University of Naples, Italy
[2]Endocannabinoid Research Group, Institute of Biomolecular Chemistry, Consiglio Nazionale delle Ricerche, Pozzuoli, Italy
[3]European Center for Brain Research, Rome, Italy
[4]Dept. of Physiology and Pharmacology, Sapienza University of Rome, Rome, Italy
[5]Dept. of Pharmacological Sciences, University of Milan, Milan, Italy
[6]Saint Louis University School of Medicine, Saint Louis, MO USA
[7]Laboratory of Behavioural Neuroscience, CEINGE Biotecnologie Avanzate, Naples, Italy
[8]Dept. of Environmental, Biological and Pharmaceutical Sciences and Technologies, The Second University of Naples (SUN), Caserta, Italy

In the last two decades, the neuroscientists have dedicated an important part of their attention for investigating the complex roles of non neuronal cells into the brain homeostasis and pathophysiology. In particular, it is now confirmed a role for microglia and astrocytes in the induction and maintenance of several chronic neuroinflammatory and neurodegenerative diseases including Alzheimer, Parkinson and Huntington Disease, Multiple sclerosis and neuropathic pain. In particular, astrocytes and microglia show different phenotypes in vivo and in vitro, depending on the microenvironment. Two different phenotypes of microglia have been deeply described, the pro-inflammatory activated (M1) and the alternatively activated neuroprotective (M2) phenotypes. Another microglia phenotype, partly described only in *post-mortem* human brain, is represented by the dystrophic microglia. In the studies I will present, we indentified new possible pharmacological target in glia and microglia cells and we described, for the first time in mice, the dystrophic phenotype of microglia. In particular, in a model of neuropathic pain induced by partial nerve ligation (spared nerve injury, SNI), we have identified new targets on non neuronal cells that could be suitable as a new pharmacological tool for treating neuropathic pain conditions. In another set of experiments we found in a transgenic model of hyperexcitation, beside the sensorial and neuropsychiatric changes, the new dystrophic microglia phenotype.
These results pave the way for future studies for better understanding the real involvement of the non neuronal components of the brain in the chronic neurodegenerative diseases.