ImmunoTools *special* Award 2013

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MODULATION OF NEUROINFLAMMATION IN A MOUSE MODEL OF PARKINSONISM

Parkinson's disease (PD) is a neurological disorder characterized by a significant loss of dopaminergic neurons in the substantia nigra (SN) resulting in reduced striatal dopamine (DA). Parkinson's disease is progressive, age-related, whose main clinical signs are bradykinesia, resting tremor and rigidity. The initial cause of the neurodegeneration in Parkinson's disease has not been clearly identified, but recent evidence demonstrates that chronic neuroinflammation plays a key role in disease. The analysis of brains from Parkinson's disease patients has revealed increased levels of proinflammatory mediators such as tumor necrosis factor (TNF)-alpha, interleukin (IL)-1beta, IL-6, and nitric oxide (NO). In these patients, the loss of dopaminergic neurons in the SN is associated with a massive astrogliosis and excessive microglial activation. CD11-beta is a marker of microglia, and microglia activation is associated with neuroinflammation processes. Glial fibrillary acidic protein (GFAP) is a marker of astroglia activation, and astrogliosis is associated with the elevation of pro-inflammatory cytokines levels in the brain. Thus, it is very interesting to find innovative methods to modulate the glial activation and the conseguent inflammatory damage in Parkinson's disease, such as the modulation of ILs cross talk among these cells and / or neurons.

The neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) causes the degeneration of mesencephalic dopaminergic neurons. The neurotoxic effects of MPTP are exherted by its metabolite 1-methyl-4-phenylpyridinium ion (MPP+), which is selectively taken up by the dopamine transporter and subsequently accumulated within the mitochondria, where it blocks the respiratory chian, leading to oxidative stress and consequent neuronal cell death. MPTP was discovered as a side-product of an illicit drug synthesis; humans that took MPTP developed Parkinson-like symptoms of idiopathic Parkinson's disease and responded to antiparkinsonian. MPTP-treated animals, including non-human primates and mice, are widely used as models of Parkinson's disease. In addition, the robust glia activation found in MPTP-induced animal models of Parkinson's disease, together with proinflammatory mediators and their respective receptors expression, make this model particularly suitable for the study of neuroinflammation in Parkinson's disease.

Therefore, in this study we propose to modulate inflammation by both systemic and intraventricular administration of ILs and /or their agonists followed by glia activation evaluation by means of immunohistochemistry and western blot.

Specific cytokines and their agonists will be very useful, such as rm IFN-gamma, rm IL1F1, rm IL1F2, rm IL1F3, rm IL1F11, rm IL1RA, rm IL-1alpha, rm IL-1beta, rm IL-6, rm TNF-alpha, rm TNF-alpha (strep.liv.), rm NGF-beta, rm MIP3α / CCL20, rh Neuregulin. Moreover mouse anti CD11b antibody purified for IHC (if available) and / or FITC conjugated and will provide a valuable tool for microglia activation evaluation.