



Research Project Proposal
Academic year 2015-2016

Project Nº 52* ASIGNADO

Title: Study of inflammation and dopaminergic degeneration in a model of progressive parkinsonism

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Summary

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the presence of motor abnormalities, due to the degeneration of dopaminergic neurons in the substantia nigra (SN), and the presence of intraneuronal inclusions containing aggregated α -synuclein. Given that motor signs of PD appear when the dopaminergic loss is higher than 50%, a progressive neuronal death thus takes place years before PD is diagnosed. The underlying mechanisms of this process are not well known, but neuroinflammation might play an important role as several markers of inflammation in brain areas depleted of dopaminergic neurons have been described in both post-mortem and in vivo studies on PD patients, and in animal models. Concerning the latter, as toxins are used to induce an acute and severe state of dopaminergic lesion, it is not clear yet whether inflammation plays a role in the pathological process as a causative factor in the origin or progression of the disease, or if it is a mere consequence of the neurodegenerative process. Recently, the overexpression of α -synuclein in the SN of rats was shown to cause a progressive degeneration of the dopaminergic cells which, after 2.5 months, reached a threshold for the presence of parkinsonian signs, thus mimicking the process of dopaminergic loss in PD. The aim of this project is to study the temporal and spatial relationship between inflammation and dopaminergic denervation in this model of progressive parkinsonism, in both the pre-symptomatic period and once the first signs of parkinsonism appear, using histochemical techniques.

References

Hirsch and Hunot. Neuroinflammation in Parkinson's disease: a target for neuroprotection? *Lancet Neurol.* 2009;8(4):382-97.



Eschbach and Danzer. α -Synuclein in Parkinson's Disease: Pathogenic Function and Translation into Animal Models. *Neurodegener Dis.* 2014;14(1):1-17.

More et al. Cellular and molecular mediators of neuroinflammation in the pathogenesis of Parkinson's disease. *Mediators Inflamm.* 2013;2013:952375.

POSSIBILITY OF PhD

YES Basque Country Government Predoctoral grant required