Neuroprotective and inflammatory factors in neurodegenerative diseases: potential biomarkers

A member of the chemokines family, the Bv8/Prokineticin (PROK2), interacting with two G-protein coupled receptors (PKR1 and PKR2) has recently emerged as a critical player in immune system and inflammatory diseases (Negri and Ferrara, 2018).

In the contest of neurodegenerative diseases, an involvement of PROK2 and its receptors has been demonstrated in Aβ toxicity, indicating a deleterious role of this chemokine, up-regulated by Aβ mainly in astrocytes (Severini et al., 2015; Maftei et al., 2019). More recently, we demonstrated a significant up-regulation of PROK2 levels in brain tissues of both Aβ1-42 i.c.v. injected rats and of transgenic Alzheimer’s disease (AD) mice (Tg2576) and in the hippocampus of AD patients. Additionally, by a pilot study, a significant increase of PROK2 levels has been proved in the serum of AD patients, as compared to control subjects, identifying a potential plasma marker of the disease (Lattanzi et al., 2019).

Conversely, PROK2 seems to exert a neuroprotective activity in Parkinson’s disease (PD), as demonstrated by Gordon et al. (2014). PROK2 expression was highly induced in nigral dopaminergic neurons during early stages of degeneration in multiple models of PD, including PK2 reporter mice and MitoPark mice and brain of PD patients.

In the proposed research, we are planning to test the serum, CSF and olfactory neuroepithelium levels of PROK2, comparatively in a cohort of PD patients and sex/age-matched controls, correlating biochemical findings to clinical parameters, in order to dissect the role of PROK2 in PD.

Additionally, to confirm and extend data from patients, we aim to study a PD rat model overexpressing α-synuclein, analyzing the amount of the mRNA of this chemokine and of its cognate receptors by qPCR, respect to the corresponding controls, and examining their localization by immunofluorescence studies.

References:
- Maftei, D. et al., 2019. The prokineticin receptor antagonist PC1 rescues memory impairment induced by β amyloid administration through the modulation of prokineticin system. Neuropharmacol. 158, 107739

Keywords: Alzheimer’s and Parkinson’s diseases, chemokines, biomarkers, blood, cerebrospinal fluid

Contacts: Severini Cinzia, IBBC Department of Sense Organs, Sapienza University of Rome

Website(s):

Other: This project research is carried out in collaboration with the Department of Physiology and Pharmacology, Sapienza University of Roma (Prof. Lattanzi Roberta, Dr. Maftei Daniela), and with the Department of Systems Medicine, University of Rome Tor Vergata (Prof. Mercuri Nicola, Prof. Possenti Roberta, Dr. Schirinzi Tommaso).