RESEARCH TOPIC-MEM4
IMMUNE-SYNAPTOPATHIES: DISSECTING THE CONTRIBUTION OF INFLAMMATION TO SYNAPTIC DYSFUNCTIONS

Curriculum MEM Standard

Laboratory name: Laboratory of Pharmacology and Brain Pathology, Humanitas Clinical and Research Center - IRCCS

Pre-clinical Supervisor: Prof. Michele Matteoli, michela.matteoli@hunimed.eu

Abstract

In the last fifteen years, groundbreaking genetic progress has underlined the convergence of the pathogenetic mechanisms underlying a plethora of diverse psychiatric and neurodevelopmental disorders onto coherent synaptic pathways (synaptopathies) and the key contribution of environmental factors to these diseases has been unveiled. Among these, inflammation is known to influence the risk and/or severity of a variety of synaptopathies. Our recent data (Tomasoni et al., 2017) show that inflammation, and in particular the pro-inflammatory cytokine IL-1beta, negatively impacts synapse structure and function (Pozzi et al., 2018). Furthermore, we have evidence that IL-1beta modulates the expression of two transcription factors, MeCP2 (Tomasoni et al., 2017) and REST, which bind promoters of neuronal genes, thereby orchestrating epigenetic remodeling and silencing of neural genes under inflammatory situations (Corradini et al., 2018).
The overall goal of the project is to explore whether and how MeCP2 and REST dysregulation contribute to the pathogenesis of these diseases to ultimately identify novel molecular targets and therapeutic strategies. To this aim we will adopt a multidisciplinary approach exploiting cell biology, electrophysiology, calcium imaging and biochemistry techniques both in vitro and in vivo.

Main technical approaches

The position will suit an ambitious and talented individual who is interested in applying his/her skills in the study of the role of inflammation and immune response in the neurodevelopmental disorders aetiology . Familiarity with the following techniques will be an advantage but is not mandatory: flow cytometry, cell culture, and microscopy.

Scientific references

1.R Tomasoni, R Morini, J P. Lopez-Atalaya, I Corradini, A Canzi, M Rasile, C Mantovani, D Pozzi, C Garlanda, A Mantovani E Menna, A Barco and M Matteoli (2017) Lack of IL-1R8in neurons causes hyperactivation of IL-1 receptor pathway and induces MeCP2-dependent synaptic defects. eLife Mar 28;6. pii: e21735. doi: 10.7554/eLife.21735.

2.I Corradini, E Focchi, M Rasile, R Morini, G Desiato, R Tomasoni, M Lizier, E Ghirardini, D Morone, I Barajon, Fl Antonucci, D Pozzi and M Matteoli (2018) MATERNAL IMMUNE ACTIVATION DELAYS EXCITATORY-TO-INHIBITORY GABA SWITCH IN THE OFFSPRING. Biol. Psy. 83(8):680-691

3.Pozzi D, Menna E, Canzi A, Desiato G, Mantovani C and Matteoli M (2018) The communication between the immune and nervous systems: the role of IL-1beta in synaptopathies. Frontiers Mol Neurosci Apr 5;11:111. doi: 10.3389/fnmol.2018.00111

Type of contract

PhD scholarship awarded by Humanitas University of € 18.000 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

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