RESEARCH TOPIC MEM5

Investigating the physiological and molecular effects of inflammation episode on neurodevelopment and ASD risk
Curriculum MEM

Laboratory name
Laboratory of Pharmacology and Brain Pathology, IRCCS Humanitas Research Hospital

Pre-clinical Supervisor
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Abstract
Autism spectrum disorder (ASD) is a genetically heterogeneous neurodevelopmental disorder with an estimated prevalence of 1% in the childhood population. ASD is characterized by impairments of social interaction and communication accompanied by a pattern of repetitive and restrictive behavior, typically diagnosed in the first 3 years of life. Besides the genetic basis of ASD, it is known that fever or other inflammatory insults may precipitate the ASD-core symptoms unveiling an interplay between genetic and environmental factors at the root of the pathology. We aim to investigate the physiological and molecular effects of inflammation on neurodevelopment by using a genetic mouse model of ASD (Shank3 het) and maternal immune activation (MIA) mouse model.

In these models, we will define the effect of inflammatory responses on synapses and role of microglia and astrocytes. We will investigate the role of proinflammatory cytokines, such as IL1beta, and innate immune molecules, such as PTX3, on synapse formation and refinement.

Main technical approaches
Project execution requires a multidisciplinary approach based on a combination of techniques including:

- biochemistry;

- molecular biology;

- FACS sorting

- confocal imaging

- morphological and functional analysis of CNS synapses.

The candidate will use a variety of experimental models:

-in vitro primary cultures from neurons and glia (microglia and astrocytes);

-Transgenic mouse models and a prenatal inflammation mouse model.

Scientific references

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Fossati, G., et al. (2019). Pentraxin 3 regulates synaptic function by inducing AMPA receptor clustering via ECM remodeling and β1-integrin. EMBO J. 2019 Jan 3;38(1):e99529. doi: 10.15252/embj.201899529.

Pozzi et al (2018) The Communication Between the Immune and Nervous Systems: The Role of IL-1β in Synaptopathies. Front Mol Neurosci. 2018 Apr 5;11:111. doi: 10.3389/fnmol.2018.00111.

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Type of contract

Scholarship of € 21.000 gross per year awarded by Istituto Clinico Humanitas. This sum is subject to IRPEF income tax and exempt from social security contributions.

Borsa di studio pari a € 21.000 annui lordi erogata da Istituto Clinico Humanitas. Importo soggetto a tassazione IRPEF ed esente da contribuzione previdenziale.

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