



RESEARCH TOPIC MEM5

Investigating the role of the innate immune molecule,PTX3, in neurodevelopmental diseases.

Curriculum MEM Standard

Laboratory name

Pharmacology and Brain Pathology, Humanitas University

Pre-clinical Supervisor

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Abstract

In the developing central nervous system (CNS), the control of synapse number and function is critical to the formation of healthy brain circuits. Astrocyte-secreted molecules, such as thrombospondins, have been identified to play a key role in the build up of silent synapses. We have recently discovered that the innate immune molecule Pentraxin 3, (PTX3) is produced and released from glial cells and promotes the maturation of excitatory synapses enhancing the recruitment of AMPA receptors at the synapse. We have also demonstrated that, in this context, PTX3 activity is regulated by Thrombospondin 1 (TSP1). These data indicate that the interplay of PTX3 and TSP1 sets the proper balance between synaptic growth and synapse function during development. Prenatal inflammation is a recognized risk factor in neuropsychiatric disorders. PTX3 expression is strongly stimulated by inflammation indicating that the levels of PTX3, TSP1 and of their complex may change upon prenatal CNS infections, possibly affecting synaptogenesis and brain development. Objective of the study is to define the impact of prenatal inflammation on the PTX3/TSP1 complex, and the cellular and molecular mechanisms involved.

Main technical approaches

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

- biochemistry;
- molecular biology;
- 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
- -ex vivo brain slices
- -Transgenic mouse models and a prenatal inflammation mouse model.

Scientific references

Fossati, G., Matteoli, M., Menna, E. Astrocytic Factors Controlling Synaptogenesis: A Team Play. *Cells*. 2020 Sep 26;9(10):2173. doi: 10.3390/cells9102173.

Fossati, G., et al. (2019). Pentraxin 3 regulates synaptic function by inducing AMPA receptor clustering via ECM remodeling and β 1-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-1 β in Synaptopathies. *Front Mol Neurosci*. 2018 Apr 5;11:111. doi: 10.3389/fnmol.2018.00111.

Corradini et al (2018) Maternal Immune Activation Delays Excitatory-to-Inhibitory Gamma-Aminobutyric Acid Switch in Offspring. *Biol Psychiatry*. 2018 Apr 15;83(8):680-691. doi: 10.1016/j.biopsych.2017.09.030.

Type of contract

Place without scholarship.

Posizione senza borsa.