RESEARCH TOPIC MEM10
Role of Pentraxin 3 in prenatal inflammation on foetal neurodevelopment
Curriculum MEM

Laboratory name
Pharmacology and brain pathology

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Abstract
The association between inflammation in pregnancy and increase risk of neurodevelopmental disorders (NDD), such as autism, is now clear.
Work of our group contributed to demonstrate that immune molecules produced upon an inflammatory condition during pregnancy can directly influence the process of formation and development of synapses in the offspring thus affecting the foetal neurodevelopment.
We have demonstrated that the innate immune molecule Pentraxin 3 (PTX3) plays a key role in the process of synaptogenesis promoting the maturation of excitatory synapses.
PTX3 is stimulated by inflammatory stimuli and single nucleotide polymorphisms of the PTX3 gene are associated with changed susceptibility to infections, altered inflammatory response and PTX3 deficiency in humans.
This project aims at understanding at the cellular and molecular level if alterations of PTX3, occurring in the offspring brain upon prenatal inflammation, may affect neurodevelopment. Furthermore, we will also investigate whether genetic variants of PTX3 associate to an increased risk of NDD in a human cohort of prenatal infection.

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.
- mouse behaviour.

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 mouse model of maternal immune activation and prenatal inflammation.

Scientific references

'Fossati G, Pozzi D, Canzi A, Mirabella F, Valentino S, Morini R, et al. Pentraxin 3 regulates synaptic function by inducing AMPA receptor clustering via ECM remodeling and beta1-integrin. EMBO J. 2019;38(1).

Fossati G, Matteoli M, Menna E. Astrocytic Factors Controlling Synaptogenesis: A Team Play. Cells. 2020;9(10).

Mirabella F, Desiato G, Mancinelli S, Fossati G, Rasile M, Morini R, et al. Prenatal interleukin 6 elevation increases glutamatergic synapse density and disrupts hippocampal connectivity in offspring. Immunity. 2021;54(11):2611-31 e8.

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Type of contract

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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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