RESEARCH TOPIC MEM13

Role of microglial receptor trem2 in controlling bioenergetic profile of neurons during development and aging

Curriculum MEM standard

Research Area

Neuro

Laboratory name

Laboratory of Pharmacology and Brain Pathology

Research Supervisor

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Abstract

Microglia represent the main brain residential immune cells. The continuous crosstalk occurs between the nervous and the immune systems is particularly relevant during development and aging. In the brain, the communication and the interactions between glial and neuronal cells are fundamental in maintaining the brain metabolic homeostasis (Paolicelli et al., 2022). In particular, the Triggering Receptor Expressed on Myeloid cells 2 (TREM2), an immune receptor expressed in the brain microglia, has recently emerged as central in controlling the metabolic fitness of neurons in the developing hippocampus, in addition to directing synapse elimination and shaping the functional brain connectivity (Filipello, Morini et al., Immunity 2018; Tagliatti, Desiato et al., Immunity 2024). In the present project, We propose that the microglial receptor TREM2 could play a pivotal role in regulating neuronal metabolism in the hypothalamus, fundamental structure involved in different body functions including the control of feeding and systemic energy expenditure. We thus hypothesize that alterations in neuronal hypothalamic metabolism due to lack of trem2 represent a crucial step in the development of metabolic diseases. By using a combination of transcriptomics analysis and cell-based imaging methods, we will characterize in a gender- specific manner hypothalamic cells populations to uncover how defective Trem2 impacts the transcriptomic profile, morphology and function of selected neuronal cell populations and determine which subsets of microglia cooperate within hypothalamic centers. Data from this study will provide comprehensive knowledge of microglia functions in shaping hypothalamic complexity and endocrine output. Also, they will offer a targeting potential for new therapeutic strategies that could reverse immune-metabolic dysfunction by modulation of hypothalamic microglial function.

Main technical approaches

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

- molecular biology;
- confocal microscopy ;
-morphological and functional analysis of microglia and CNS synapses.

Bioinformatic analysis

-mouse behavior

The candidate will use a variety of experimental models:

-in vitro primary cultures from neurons and glia

-ex vivo brain slices

-Transgenic mouse models

Scientific references

Filipello F, Morini R, Starvaggi C, Canzi A, Corradini I, Erreni M, Otero K, Piccio L, Perrucci F, Tamborini M, Rajendran L, Menna E, Vetrano S, Michalski B, Fahnestock M, Paolicelli R, Matteoli M (2018) The microglial innate immune receptor TREM2 is required for neuronal synapse elimination. Immunity 48(5):979-991

-Tagliatti E, Desiato G, Mancinelli S, Bizzotto M, Gagliani MC, Faggiani E, Hernández-Soto R, Cugurra A, Poliseno P, Miotto M, Argüello RJ, Filipello F, Cortese K, Morini R, Lodato S, Matteoli M. Trem2 expression in microglia is required to maintain normal neuronal bioenergetics during development. Immunity. 2024 Jan 9;57(1):86-105.e9. doi: 10.1016/j.immuni.2023.12.002. Epub 2023 Dec 29. PMID: 38159572; PMCID: PMC10783804.O56+O57Dec 29. PMID: 38159572; PMCID: PMC10783804.

Type of contract

PhD scholarship of € 21.000 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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