



RESEARCH TOPIC MECM_21

Addressing metabolic and functional defects in neurons and oligodendrocytes in Nasu-Hakola Disease

Curriculum

MECM Standard

Research Area

Neuro

Laboratory name

Laboratory of Pharmacology and Brain Pathology

Research Supervisor

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Abstract

Nasu-Hakola disease (NHD) is a rare autosomal recessive disorder that manifests in early adulthood with rapidly progressive dementia induced by neuronal degeneration, synaptic loss and myelin disruption. NHD is caused by mutations in TREM2 gene that, in the Central Nervous System (CNS), is only expressed by microglia, the brain's resident immune cells. We demonstrated that TREM2 acts as a regulator in brain development, orchestrating immune responses, developmentally regulated synaptic elimination and neuronal metabolic activity. In this project we will pursue an integrated strategy to investigate NHD, analyzing the impact of TREM2 deficiency both on neurons and oligodendrocytes. First, we will evaluate the role of TREM2 in regulating oligodendrocytes maturation, metabolic activity and myelination at different developmental stages. Secondly, with the aim of identifying candidate therapeutic targets, we will validate different TREM2 interactors possibly implicated in orchestrating neuronal and oligodendrocyte functions. Finally, we will test a therapeutic strategy using hematopoietic stem cells engineered with lentiviral vectors to express TREM2 in microglia. This project will deepen our understanding of TREM2 in NHD and provide proof-of-concept data for future translational studies.

Main technical approaches

Previous experience with basic molecular biology (PCR, RT-PCR, RT-qPCR, WB) - Previous experience with cultures, immunocytochemistry / immunohistochemistry techniques and confocal microscopy - Willingness to work with animals

Scientific references

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3. Morini R, Tagliatti E, Bizzotto M, Matteoli M. Microglial and TREM2 dialogues in the developing brain. *Immunity*. 2025 May 13;58(5):1068-1084. doi: 10.1016/j.immuni.2025.04.022. Epub 2025 May 4. PMID: 40324380.
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Type of contract

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Borsa di dottorato pari a € 21.000 annui lordi erogata da Humanitas University. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.