



RESEARCH TOPIC MEM18

Unveiling the Neurobehavioral Implications of Inborn Error of Immunity Disorders: A Focus on WHIM Syndrome MECM standard

Research Area

Neuroscience

Laboratory name

Developmental neurobiology Lab

Research Supervisor

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Abstract

Inborn errors of immunity (IEI) are genetic disorders marked by congenital immune defects and often co-occur with neurobehavioral issues. Using a WHIM syndrome mouse model (caused by *Cxcr4* hyperactivation), we found cerebellar foliation defects, motor dysfunctions, and anxiety-like behaviors, mirroring patient symptoms. Single-cell profiling revealed transcriptional changes in granule progenitors and Purkinje cells. Embryonic AMD3100 (a CXCR4 antagonist) treatment rescued both structural and behavioral phenotypes, confirming a cerebellar *Cxcr4*-driven mechanism. We aim to (1) study how *Cxcr4* mutations disrupt cerebellar development, using spatial transcriptomics to track granule progenitor migration and niche alterations; and (2) determine how inflammation worsens WHIM phenotypes by exposing mice to infections. Clinical correlations will help link genetics to neurobehavior in WHIM, guiding patient stratification and therapy.

Main technical approaches

- Mouse handling and maintenance
- In utero surgical procedures
- Spatial transcriptomics
- Behavioral testing in neonatal and juvenile mice
- Stem cell culture and maintenance
- Neuronal differentiation

Scientific references

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2. Galli, Jessica, Lorenzo Pinelli, Serena Micheletti, Giovanni Palumbo, Lucia Dora Notarangelo, Vassilios Lougaris, Laura Dotta, Elisa Fazzi, and Raffaele Badolato. 2019. "Cerebellar Involvement in Warts Hypogammaglobulinemia Immunodeficiency Myelokathexis Patients: Neuroimaging and Clinical Findings." *Orphanet Journal of Rare Diseases* 14 (1): 61.
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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.

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.