INSTITUTO CAJAL

SEMINARIO PRESENCIAL

Viernes, 4 de Octubre de 2024
12:30 h. Instituto Cajal - CSIC

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TARGETING MICROGLIAL MITOCHONDRIAL METABOLISM TO HALT CHRONIC CENTRAL NERVOUS SYSTEM INFLAMMATION.

Abstract

Microglia, the resident immune cells of the central nervous system (CNS), exhibit dynamic metabolic reprogramming in response to chronic inflammation. We have previously uncovered that mitochondria play a key role in this process and that their dysfunction is linked with enhanced pro-inflammatory activity of microglia. However, the underlined molecular mechanism remained to be resolved. Here we show that the heightened expression of mitochondrial complex I (CI) genes and proteins characterise a specific cluster of persistently activated microglia in vivo. This unique cluster first appears during the acute phase of multiple sclerosis (MS)-like disease in mice, persists throughout the chronic phase, and can be found at the edge of chronic-active MS lesions in the brain. Importantly, interfering with CI function in microglia reduces their pro-inflammatory activation and secretion of neurotoxic reactive oxygen species. Focusing on this novel pathway and its relationship with mitochondrial function and metabolites, we identify new metabolic targets for therapeutic approaches aimed at reducing chronic CNS inflammation.

Affiliation and short bio

Luca obtained his MD from University Vita-Salute San Raffaele of Milan, Italy (2007). He completed a residency program in Neurology at the same University (2013) and a following PhD in Clinical Neurosciences at the University of Cambridge, UK (2018). During his graduate studies, he was a visiting scientist in major European universities, such as the University Hospital in Zürich (Switzerland), University of Aarhus (Denmark), Laboratory of Stem Cells and Restorative Neurology of Lund (Sweden) and University of Innsbruck (Austria). He later progressed towards a post-doctoral position in Cambridge (2018) and became Group Leader within the Department of Clinical Neurosciences and Cambridge Centre for Myelin Repair (2020). Over the last 10+ years, Luca has made key contributions to the understanding of inflammation in central nervous system (CNS) diseases. His research in regenerative neuroimmunology led to novel experimental advanced therapeutics with neural stem cells, extracellular vesicles, and small molecules for the treatment of ischemic stroke, spinal cord injury, and multiple sclerosis. Luca’s most recent work is focusing on cellular metabolism and mitochondria to find novel ways to modulate chronic inflammation and favour CNS regeneration. Luca’s research is documented in >60 PubMed indexed publications, □9,000 citations, with a Hirsch Factor of 29.

Related publications with the topic

1. Peruzzotti-Jametti L, Willis CM, Krzak G, Hamel R, Pirvan L, Ionescu RB, Reisz JA, Prag HA, Garcia-Segura ME, Wu V, Xiang Y, Barlas B, Casey AM, van den Bosch AMR, Nicaise AM, Roth L, Bates GR, Huang H, Prasad P, Vincent AE, Frezza C, Viscomi C, Balmus G, Takats Z, Marioni JC, D'Alessandro A, Murphy MP, Mohorianu I, Pluchino S.
Mitochondrial complex I activity in microglia sustains neuroinflammation.
Nature, 2024, doi: 10.1038/s41586-024-07167-9.

2. Krzak G, Willis CM, Smith JA, Pluchino S, and Peruzzotti-Jametti L.
Succinate Receptor 1: An Emerging Regulator of Myeloid Cell Function in Inflammation.
Trends in Immunology, 2021, doi: 10.1016/j.it.2020.11.004.

3. Peruzzotti-Jametti L, Bernstock JD, Manferrari G, Rogall R, Fernandez-Vizarra E, Williamson J, Braga A, Van den Bosch A, Leonardi T, Kittel A, Beninca C, Vicario N, Tan S, Bastos C, Bicci I, Iraci N, Smith JA, Lehner P, Buzás E, Faria N, Zeviani M, Frezza C, Brisson A, Matheson N, Viscomi C, Pluchino S.
Neural stem cells traffic functional mitochondria via extracellular vesicles.
Plos Biology, 2021, doi: 10.1371/journal.pbio.3001166.

4. Peruzzotti-Jametti L, Bernstock JD, Vicario N, Costa ASH, Kwok C, Leonardi T, Booty L, Bicci I, Balzarotti B, Volpe G, Mallucci G, Manferrari G, Iraci N, Braga A, Hallenbeck JM, Murphy MP, Edenhofer F, Frezza C and Pluchino S.
Macrophage-derived extracellular succinate licenses neural stem cells to ameliorate chronic neuroinflammation.
Cell Stem Cell, 2018, doi: 10.1016/j.stem.

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