



## SEMINARIO PRESENCIAL

Viernes, 5 de Abril de 2024

12:30 h. Instituto Cajal - CSIC

**Dra. AMANDA SIERRA**

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# BORN TO BE A PHAGOCYTE: DEVELOPMENTAL MATURATION OF MICROGLIAL PHAGOCYTOSIS EFFICIENCY

## Abstract

Microglia, the resident macrophages of the brain, originate from yolk sac progenitors and invade the brain at embryonic stages to progressively become integrated in the parenchyma. However, the mechanisms driving the acquisition of the mature microglia phenotype during development are yet unclear. To understand this process, we focused on the hippocampus and the cerebellum, two structures with protracted development and developed a series of mathematical simulations using differential equations and Monte Carlo simulations. The optimal model fitness was obtained using a two-cell type model, in which a small population of proliferative (P) microglia faded off by P5 and gave rise to a large population of quiescent (Q), post mitotic microglia, with minimal contributions of microglial apoptosis and migration to the colonization process. Morphofunctional maturation occurred after the switch, and was characterized by increased morphological complexity, phagocytosis efficiency, and response to apoptotic challenges. These results suggest an inverse correlation between proliferation and phagocytosis efficiency that challenges our current understanding of the role of microglia in neurodegenerative diseases.

## Affiliation and short bio

Amanda Sierra graduated in Biology at the University Complutense of Madrid in 2000 and obtained her PhD degree from the same university in 2003, under the supervision of Luis Miguel García Segura, at the Cajal Institute. She did her postdoctoral training in the Rockefeller University, Stony Brook University and Baylor College of Medicine in the USA. In 2011, she returned to Spain as an Ikerbasque Research Professor and head of the Glial Cell Biology Lab at Achucarro Basque Center for Neuroscience. She has served as board member of the Spanish Glial Network (2008-2015), as Secretary and Vice-president of the Spanish Society for Neuroscience (2015-2019), and since 2021 serves as adjunct member of Life Science office at the Spanish Confederation of Scientific Societies.

## Related publications with the topic

Beccari S, Sierra-Torre V, Valero J, Garcia-Zaballa M, Carretero-Guillen A, Capetillo-Zarate E, Domercq M, Huguet-Rodriguez PR, Ramonet D, Umekawa T, Osman A, Han W, Dominguez C, Faust T, Touzani O, Boya P, Schaffer D, Mariño G, Canet-Soulas E, Blomgren K,\* Plaza-Zabala A, \*Sierra A. Microglial phagocytosis dysfunction in stroke is driven by energy depletion and induction of autophagy *Autophagy* 2023 19(7):1952-1981

Paolicelli R, Sierra A, Stevens B, Tremblay ME et al. Microglia states and nomenclature: a field at its crossroads. *Neuron* 2022, 21:3458-3486.

Diaz-Aparicio I, Paris I, Sierra-Torre V, Plaza-Zabala A, Rodriguez-Iglesias N, Marquez-Ropero M, Beccari S, Huguet P, Abiega O, Alberdi E, Matute C, Bernales I, Schulz A, Sperlagh B, Lemke G, Maletic-Savatic M, Valero J, Sierra A. Microglia actively remodel adult hippocampal neurogenesis through the phagocytosis secretome, *J Neurosci* 2020, 40 (7) 1453-1482

Sierra-Torre V, Plaza-Zabala A, Bonifaci P, Abiega O, Diaz-Aparicio I, Tejelberg S, Lehesjoki AE, Valero J, Sierra A. Microglial phagocytosis dysfunction is related to local neuronal activity in a genetic model of epilepsy. *Epilepsia* 2020, 61(11):2593-2608.