POSTER N.º 52

Introduced by: Marina Mejías Ortega

Principal Investigator: Antonia Gutiérrez Pérez, Universidad de Málaga

Title:
MONOCYTE-DERIVED CELLS INVADE AMYLOID PLAQUES IN HUMAN ALZHEIMER'S DISEASE HIPPOCAMPUS

Main Author: Marina Mejías Ortega

Authors: Marina Mejias-Ortega (1,2) | Clara Muñoz-Castro (2,3,4) | Elisabeth Sanchez-Mejias (1,2) | Sebastian Jimenez (2,3) | Laura Trujillo-Estrada (1,2) | Marisa Vizuete (2,3,4) | Javier Vitorica (2,3,4) | Antonia Gutierrez (1,2)

Filiation: 1- Dpto. Biología Celular, Genética y Fisiología, Instituto de Investigación Biomédica de Málaga-IBIMA, Facultad de Ciencias, Universidad de Málaga, Spain. | 2- Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Spain. | 3- Dpto. Bioquímica & Biología Molecular, Facultad de Farmacia, Universidad de Sevilla, Spain. | 4- Instituto de Biomedicina de Sevilla (IBiS)-Hospital Universitario Virgen del Rocío CSIC/Universidad de Sevilla, Sevilla, Spain.

Abstract:
Microglia, the brain-resident myeloid cells, play a major role in the immune responses of the nervous system and in the pathogenesis of Alzheimer's disease (AD). However, the presence of peripheral myeloid cells in the AD brains, and their contribution to disease progression, remain to be demonstrated. In this work, cellular (immunostainings and image analysis) and molecular (qPCR and western blots) approaches have been carried out in post-mortem hippocampal samples from patients with dementia (Braak V-VI) and age-matched asymptomatic cases (Braak II). Our study provides evidence that circulating monocytes infiltrate the AD brains. Our findings showed that a high proportion of demented individuals was associated with up-regulation of genes rarely expressed by microglial cells and abundant in monocytes-derived cells (MDC), among which stands the scavenger receptor Cd163. These Cd163-positive MDC invaded the brain parenchyma, acquired a microglial-like morphology, and were located in close proximity to blood vessels. These cells infiltrated the nearby amyloid plaques contributing to plaque-associated myeloid cell heterogeneity. Besides, asymptomatic individuals with high amyloid pathology, showed no signs of MDC brain infiltration or plaque invasion. The MDC infiltration was associated with the progression and severity of AD pathology. These results reveal the co-existence of distinct myeloid populations associated with amyloid plaques during disease progression, as well their region-specific contribution to neuroimmune protection. The recruitment of monocytes could be a consequence rather than the cause of the severity of the disease. Whether monocyte infiltration is beneficial or detrimental to AD pathology remains to be fully elucidated. These findings open the opportunity to design targeted therapies, not only to microglia, but also to peripheral immune cell population to modulate amyloid pathology and provide a better understanding of the immunological mechanisms underlying AD progression. Supported by ISCiii grants (PI21-0915 (to AG),PI21-00914 (to JV) co-financed by FEDER funds from European Union, by Junta de Andalucia grants P18-RT-2233 (to AG) and US-1262734 (to JV) co-financed by Programa Operativo FEDER 2014-2020, and by grant PPIT.UMA.B1-2019-07 (to ESM).