

## T14-059B

**Decoding damage-associated microglia in post mortem hippocampus of Alzheimer's disease patients**

**E. Sanchez-Mejias**<sup>1,2,3</sup>, M. Mejias-Ortega<sup>1,2,3</sup>, V. Navarro<sup>5,2,4</sup>, A. Gomez-Arboledas<sup>1,2,3</sup>, C. Nuñez-Díaz<sup>1,2,3</sup>, R. Sanchez-Varo<sup>1,2,3</sup>, M. Vizuete<sup>5,2,4</sup>, J.C. Davila<sup>1,2,3</sup>, J. Vitorica<sup>5,2,4</sup>, A. Gutierrez<sup>1,2,3</sup>

<sup>1</sup>Department of Cell Biology, Genetics and Physiology, University of Malaga, Malaga, ES

<sup>2</sup>CIBERNED, Malaga, ES

<sup>3</sup>IBIMA, Malaga, ES

<sup>4</sup>IBIS, Sevilla, ES

<sup>5</sup>Department of Biochemistry and Molecular Biology, University of Seville, Sevilla, ES

The relationship between Alzheimer's disease (AD) and neuroinflammation has become stronger since the identification of several genetic risk factors related to microglial function. Though the role of microglial cells in the development/progression of AD is still unknown, a dysfunctional response has recently gained support. In this sense, we have reported an attenuated microglial activation associated to amyloid plaques in the hippocampus of AD patients, including a prominent degenerative process of the microglial population in the dentate gyrus, which was in contrast to the exacerbated microglial response in amyloidogenic models. This microglial degeneration could compromise their normal role of surveying the brain environment and respond to the damage. Here, we have further analyzed the phenotypic profile displayed by the damage-associated microglial cells by immunostaining and qPCR in the hippocampus of *postmortem* samples of AD patients (Braak V-VI) and control cases (Braak 0-II). Damage-associated microglial cells of Braak V-VI individuals were clustered around amyloid plaques and expressed Iba1, CD68, Trem2, TMEM119 and CD45<sup>high</sup>. A subset of these cells also expressed ferritin. On the contrary, these microglia down-regulated homeostatic markers, such as Cx3cr1 and P2ry12. The homeostatic and ramified microglial cells of non-demented Braak II cases were characterized by Iba1, CX3CR1, P2ry12, TMEM119 and CD45<sup>low</sup> expression. The dynamic of the microglial molecular phenotypes associated to AD pathology needs to be considered for better understand the disease complexity and, therefore, guarantee clinical success. Correcting dysregulated brain inflammatory responses might be a promising avenue to prevent/slow cognitive decline.

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**Dysfunctional astroglial phagocytosis in Alzheimer's disease**

**A. Gomez-Arboledas**<sup>1,2,3</sup>, J.C. Davila<sup>1,2,3</sup>, **E. Sanchez-Mejias**<sup>1,2,3</sup>, C. Nuñez-Díaz<sup>1,2,3</sup>, R. Sanchez-Varo<sup>1,2,3</sup>, V. Navarro<sup>4,2,5</sup>, M.V. Sanchez-Mico<sup>4,2,5</sup>, M. Vizuete<sup>4,2,5</sup>, J. Vitorica<sup>4,2,5</sup>, A. Gutierrez<sup>1,2,3</sup>

<sup>1</sup>Cell Biology, Genetics and Physiology, University of Malaga, Malaga, ES

<sup>2</sup>CIBERNED, Malaga, ES

<sup>3</sup>IBIMA, Malaga, ES

<sup>4</sup>Biochemistry and Molecular Biology, University of Seville, Sevilla, ES

<sup>5</sup>IBIS, Sevilla, ES