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## Extracellular vesicles from CS fluid are possible biomarkers of multiple sclerosis disease status

F. Geraci<sup>1,2</sup>, M. M. Barreca<sup>1,3</sup>, E. Aliotta<sup>1</sup>, P. Ragonese <sup>4</sup>, G. Sconzo<sup>1</sup> and G. Salemi<sup>4</sup>

## Giuseppe, salemi@unipa.it

Multiple sclerosis (MS) is an autoimmune disease and several researches have been focused on identifying molecular biomarkers that could reflect its heterogeneous clinical course and determine the best treatment option for patients. Some studies identified extracellular vesicles (EVs) in both the cerebrospinal fluid (CSF) and also in blood samples of patients affected by inflammatory neurodegenerative diseases and multiple sclerosis. To monitor the disease onset and its progression we compared the amount of CSF-EVs and their surface markers in subjects affected by either MS or other neurological disorders correlating the EVs with clinical indicators of MS disease severity. EVs isolated by ultracentrifugation from CSF were characterized by flow cytometry. We identified their cellular origin by using a panel of fluorescent antibodies, such as CD4, CD193, CD195, CD19 and CD200, and the lectin IB4. We found a higher EV concentration in progressive MS and in clinically isolated syndrome when compared to EV amount of all the other groups examined. In relapsing MS patients, in course of clinical relapse, we observed an increase in CSF-EV level, and also a reduction of CD19+/CD200+ EVs, markers that are expressed by immature and naïve B lymphocytes. In contrast, in the presence of gadolinium enhancing lesions, we observed an increase of CSF-EV CD193+/CD195+, CD4+/CD193+, and CD4+/CD195+. In conclusion, our results indicate that CSF-EVs could be a promising tool to investigate the immunopathology of MS and to identify biomarkers specific to the different phases of the disease.

<sup>&</sup>lt;sup>1</sup> Department of Biological, Chemical, and Pharmaceutical Sciences and Technologies, University of Palermo. Italy. <sup>2</sup> Euro-Mediterranean Institute of Science & Technology, Palermo, Italy

<sup>&</sup>lt;sup>3</sup> UOC Neurology with Stroke Unit & Neurophysiopathology, Palermo, Italy.

<sup>&</sup>lt;sup>4</sup>Department of Experimental Biomedicine & Clinical Neuroscience, University of Palermo. Italy.