**Title**
Extracellular Vesicles mediators of anti-inflammatory and neuroprotective action and potential novel biomarkers for Alzheimer's Disease

**Name and affiliation:** Maria Luisa Malosio CNR, Institute of Neuroscience - URT c/o IRCCS Humanitas Clinical and Research Center, Rozzano (Milano).

**Abstract**
Considerable evidence has recently suggested that neuroinflammation and the soluble form of amyloid-\(\beta\)_{1-42} proteolytic fragment of the APP protein are etiological mechanisms at the basis of Alzheimer’s Disease (AD). Mesenchymal Stem Cells (MSCs) are multipotent non-hematopoietic adult stem cells, which are able to mediate repair of injured tissues and to mediate immunoregulatory actions on innate and adaptive immune responses (1). Exploiting the immunomodulatory and neuroprotective effects of the MSC derived Extracellular Vesicles (EVs) is a promising approach overcoming the risks associated with cell therapy (2). EVs, such as exosomes and microvesicles, are phospholipid bilayer-delimited structures, which are involved in intercellular communication (3).

We have recently shown that intracerebral injection of MSC-EVs can reduce the A\(\beta\) burden in the brain of the double Tg APPswe/PS1dE9 (APP/PS1) preclinical model of AD, at early stages of the disease (4) and that intranasally injected huMSC-EVs exert anti-inflammatory and neuroprotective actions in 3xTg mice (5). In addition MSC-EVs ameliorate synaptic plasticity in APP/PS1 mice and protect hippocampal neurons from oxidative stress and synapse damage induced by A\(\beta\) oligomers (A\(\beta\)O) (6).

Based on these data the objective of this project is to investigate the cellular and molecular mechanisms underlying the neuroprotective and anti-inflammatory properties of MSC-EVs and to explore to possibility to enhance the production of anti-inflammatory EVs by means of novel mechanical stimulations with translational potential. In particular shock wave therapy (SWT), a mechanical treatment, has been shown to stimulate beneficial EVs production (7, 8).

Moreover an ongoing effort is being made in collaboration with Research Hospitals within the Italian IRCCS Network of Neuroscience and Neurorehabilitation to standardize methods and procedures for isolation and characterization of EVs of brain origin from the blood and cerebrospinal fluid of patients with neurodegenerative diseases for using them as biomarkers of disease diagnosis and prognosis.

**References:**


**Keywords:** Extracellular Vesicles; therapeutical strategy; biomarkers; Alzheimer’s Disease; Mesenchymal Stem Cells.

**Contacts:** marialuisa.malosio@in.cnr.it

**Website(s):** http://www.in.cnr.it/index.php/it/9-people/52-maria-luisa-malosio

**Other:**
Collaborators:
Silvia Coco, Università degli Studi di Milano Bicocca, Monza (MI)
Maria Cristina D’Agostino, IRCCS Humanitas Clinical and Research Center, Rozzano (MI)
Achille Anselmo, IRCCS Humanitas Clinical and Research Center, Rozzano (MI)
Michela Matteoli CNR, Institute of Neuroscience & Humanitas Clinical and Research Center, Rozzano (MI)
Luisa Benussi, IRCCS Fatebenefratelli San Giovanni di Dio, Brescia
Daniela Galimberti, Università degli Studi di Milano & IRCCS Ca’ Granda Ospedale Policlinico di Milano (MI)