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Evaluation of the effect of exosomes isolated from stem cells in in vivo model of ALS

Raffaella Mariotti, Roberta Bonafede, Chiara Buoso, Ilaria Scambi, Lorenzo Schiaffino

Università di Verona, Dipartimento Neuroscienze Biomedicina e Movimento, Verona, Italia

Amyotrophic lateral sclerosis (ALS) is a late-onset fatal neurodegenerative disease: its peculiarity is represented by the progressive loss of the upper and lower motor neurons (LMNs) at the spinal or bulbar level. The ALS sporadic form affects 90-95% of the cases, while the remaining 5-10% are familiar. The superoxide dismutase 1 (SOD1) gene was the first identified gene to be correlated with familiar form.

An effective treatment is currently not available; some drugs seem to modestly slow down the disease progression, influencing minimally the survival of the patients. A promising therapeutic approach for ALS is represented by mesenchymal stem cells, in particular, adipose stem cells (ASC). The beneficial effect of these cells seems to be due to a paracrine action via the release of exosomes (ASC-exosomes).

Exosomes are small vesicles (30-100 nm) containing lipids, proteins, and nucleic acids related to the type of cell that secretes them. Exosomes, through the release of their content, enhance the repair of the damaged area and could be used as a novel cell-free therapeutic approach, avoiding all the risks associated with the use of cells, there are also evidence in in vitro model of ALS.

On this basis we wanted to assess the efficacy of ASC-exosomes in in vivo model of ALS, the SOD1(G93A) mice. We injected ASC-exosomes intravenously, every four days, from the onset of the animals until the end stage. The progression of disease was monitored through the behavioural motor test and the evaluation of neurological score. Despite we did not observe a postponement of the treated animal's survival, we show that the treatment delays the symptoms progression of the disease of the treated animals compared to the control group. Moreover, the evaluation of the motoneurons number and the inflammatory state, through the assessment of astrocytes and microglia activation, is ongoing. In addition, in order to identify some of the molecular pathways by which exosomes could exert the neuroprotective effect on motoneurons, we performed the protein content characterization of ASC-exosomes. These data suggest that ASC-exosomes exert a neuroprotective role in in vivo model of ALS, underlining a possible therapeutic use of exosomes in this neurodegenerative disease and also suggest molecules that could be responsible for these neuroprotective effect in order to potentiate their effect in the future.