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MEETING ABSTRACT

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Extracellular vesicles as a potential novel therapeutic tools against neurodegenerative diseases

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We and others have demonstrated that extracellular vesicles (EVs) display neuroprotective and anti-inflammatory properties. Increasing evidence suggests that neuroinflammation has a causal role in the pathogenesis of chronic neurodegenerative diseases, therefore, new therapies directed against neuroinflammatory processes may be beneficial. In the present study we investigated the effects of EVs derived from human dental pulp stem cells (DPSCs) on migration and phagocytic activity of human microglial cells. To determine phagocytic activity of immortalized human microglial cells (purchased from ABM) we used apoptotic bodies (AB) derived from ReNcell VM human neural stem cells (Millipore). ABs were prepared and labeled according to the described protocol, with some modifications [1]. The microglial polarization into M1 and M2 states was induced according to the protocol described by Gaikwad and Heneka [2]. EVs were purified by differential ultracentrifugation from DPSCs grown in serum- and xeno-free medium. Control and EV-treated M0, M1 and M2 cells were stained with CellTrace calcein green AM (Thermo Fisher Scientific) and incubated with ABs at a ratio 3:1 for 2 hours. Digital images of randomly selected fields were captured by confocal microscope (Leica SP8) and phagocytic activity calculated according to the following formula: number of microglial cells containing engulfed ABs / total number of counted cells × 100. Internalization of phagocytosed material was verified by using Z stacks acquired through confocal microscopy. For wound-healing assays we used 2-well silicone inserts (Ibidi) and Leica SP8 live-cell imaging system. Time-lapse microscopy revealed that EVs significantly promoted migration of unpolarized M0 cells. We also detected increased phagocytic activity of M1 and M2 microglial cells (by 40 % when compared with M0 cells). Importantly, EV treatment increased phagocytic activity of M0 and M2 cells by 46 % and 17 %, respectively. By contrast, EVs did not affect phagocytic activity in M1 cells.

Our findings demonstrate that EVs derived from human dental pulp stem cells can act as potent immunomodulators of human microglial cells.

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Keywords: extracellular vesicles – neuroinflammation – human microglial cells – human dental pulp stem cells

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