Preparation of peripheral blood-derived microglia-like cells and its intra-hippocampal injection to ameliorate amyloid-β burden and cognitive impairment in a mouse model of Alzheimer's disease

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Amyloid-β (Aβ) accumulation in the brain is the first trigger for the onset of Alzheimer's disease (AD), and its prevention and elimination are promising strategies for AD therapy. Previously, we demonstrated that injection of mouse bone marrow (BM)–derived microglia-like (BMDML) cells into the brain decreases Aβ and ameliorates cognitive impairment in a mouse model of AD. In this study, considering majority of AD patients are elderly and less invasive ways for preparing autologous microglia-like cells are needed, we focused on hematopoietic stem cells (HSCs) in peripheral blood (PB). Mouse HSCs were mobilized from BM to PB by administration of granulocyte colony-stimulating factor (G-CSF) and CXCR4 antagonist and were collected from PB. Collected HSCs were subsequently differentiated into microglia-like cells upon stimulation with colony- stimulating factor 1 (CSF-1) and interleukin-34. The PB-derived microglia-like (PBDML) cells expressed macrophage/microglia markers and effectively phagocytosed Aβ. We further found that PBDML cells injected into the hippocampi of AD model mice diffused in the brain with phagocytosing Aβ, and contributed to the reduction of brain Aβ and improvement of cognitive impairment. These results suggest that PBDML cells could be promising candidate source for the development of cell therapy against AD.