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Human umbilical cord blood-derived mesenchymal stem cells improve neuropathology and cognitive impairment in an Alzheimer's disease mouse model through modulation of neuroinflammation

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- Abstract

Human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSC) have a potential therapeutic role in the treatment of neurological disorders, but their current clinical usage and mechanism of action has yet to be ascertained in Alzheimer's disease (AD). Here we report that hUCB-MSC transplantation into amyloid precursor protein (APP) and presenilin1 (PS1) double-transgenic mice significantly improved spatial learning and memory decline. Furthermore, amyloid-β peptide (Aβ) deposition, β-secretase 1 (BACE-1) levels, and tau hyperphosphorylation were dramatically reduced in hUCB-MSC transplanted APP/PS1 mice. Interestingly, these effects were associated with reversal of disease-associated microglial neuroinflammation, as evidenced by decreased microglia-induced proinflammatory cytokines, elevated alternatively activated microglia, and increased anti-inflammatory cytokines. These findings lead us to suggest that hUCB-MSC produced their sustained neuroprotective effect by inducing a feed-forward loop involving alternative activation of microglial neuroinflammation, thereby ameliorating disease pathophysiology and reversing the cognitive decline associated with Aβ deposition in AD mice.