Neuroprotective properties of marrow-isolated adult multilineage-inducible cells in rat hippocampus following global cerebral ischemia are enhanced when complexed to biomimetic microcarriers

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Résumé en anglais	Cell-based therapies for global cerebral ischemia represent promising approaches for neuronal damage prevention and tissue repair promotion. We examined the potential of marrow-isolated adult multilineage-inducible (MIAMI) cells, a homogeneous subpopulation of immature human mesenchymal stromal cell, injected into the hippocampus to prevent neuronal damage induced by global ischemia using rat organotypic hippocampal slices exposed to oxygen-glucose deprivation and rats subjected to asphyxial cardiac arrest. We next examined the value of combining fibronectin-coated biomimetic microcarriers (FN-BMMs) with epidermal growth factor (EGF)/basic fibroblast growth factor (bFGF) pre-treated MIAMI compared to EGF/bFGF pre-treated MIAMI cells alone, for their in vitro and in vivo neuroprotective capacity. Naive and EGF/bFGF pre-treated MIAMI cells significantly protected the Cornu Ammonis layer 1 (CA1) against ischemic death in hippocampal slices and increased CA1 survival in rats. MIAMI cells therapeutic value was significantly increased when delivering the cells complexed with FN-BMMs, probably by increasing stem cell survival and paracrine secretion of pro-survival and/or anti-inflammatory molecules as concluded from survival, differentiation and gene expression analysis. Four days after oxygen and glucose deprivation and asphyxial cardiac arrest, few transplanted cells administered alone survived in the brain whereas stem cell survival improved when injected complexed with FN-BMMs. Interestingly, a large fraction of the transplanted cells administered alone or in complexes expressed betaIII-tubulin suggesting that partial neuronal transdifferentiation may be a contributing factor to the neuroprotective mechanism of MIAMI cells.
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