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Pluripotent Properties of Multipotent Adult Progenitor Cells

Transplantation of stem cells into the brain has been proposed as a method to both replace cells lost following ischemic stroke and to minimize ischemic damage via neuroprotection. In rodent stroke models, trophic effects of transplanted bone marrow derived stem cells have been shown to decrease infarct size and enhance behavioral recovery. Multipotent adult progenitor cells (MAPCs) are a type of bone marrow derived stem cell that is unique due to its capacity to generate tissues from all three embryonic germ layers *in vitro* and *in vivo*. Recent improvements in cell isolation and culture technique have yielded MAPCs expressing high levels of Oct4, a marker of pluripotency characteristic of embryonic stem cells (ESCs). We here describe the capacity of these high Oct4 MAPCs to form teratoma-like structures after transplantation into the ischemic brain. Although fewer cell types were observed than in control ESC-derived teratomas, spontaneous differentiation into multiple tissues has not previously been described from adult stem cells. Tumor formation was replicated in multiple lines of high Oct4 MAPCs including cells from rat and mouse. By contrast, cells with low Oct4 expression failed to form tumors. Cytogenetically abnormal cells were observed in some lines, but did not correlate positively with tumor formation. Of note, tumor formation has not been observed after systemic delivery of MAPCs, suggesting that like embryonic stem cells, high local cell density in the confined brain space likely facilitates differentiation into teratoma-like structures.



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