Induced neural stem cell

Reprogramming adult human fibroblasts to iNSC by plasmid vectors and basic neural medium without small molecules is possible and feasible. However, a full set of pluripotency-associated transcription factors may indeed result in the acquisition of a transient (at least partial) pluripotent intermediate during reprogramming. In contrast to previous reports, the EBV-based plasmid system remained present and active inside the cells at all time points [1].

Transdifferentiation can be used to create induced neural stem cells (iNSCs). Previous in vivo research using induced pluripotent stem cells has been stymied by the formation of cancerous teratomas. However, iNSCs have not shown such in vivo teratoma formation, suggesting that iNSCs can provide safe, patient-specific cell transplantation therapy to treat disorders of the central nervous system [2] [3].

NSCs exhibit tumoritropic migration, allowing unprecedented access to glioblastoma GBM cancer cells. NSCs also have the ability to release anticancer molecules that could provide long-term drug delivery directly to the cancer cells [4].

However, NSCs are located deep within the adult brain and are not readily available without invasive surgery. A recent study by Bagó et al [5] shows a potential means of inducing NSCs from skin fibroblasts and specifically delivering tumoricidal treatments to GBM in vivo.

The use of iNSCs could potentially lead to highly selective delivery of therapeutics to brain tumors, reducing systemic toxicities and improving efficacy. Many clinical trials are currently underway that are using TRAIL-based treatments in a variety of cancers, including leukemia, lymphoma, colorectal cancer, and GBM [6].

Induced neural stem cells (iNSCs), similar to neural stem cells (NSCs), can accelerate neurological recovery in vivo and produce neurotrophic factors in vitro.

Whether iNSCs have immunomodulatory properties is unknown.

Mouse models of closed head injury (CHI) were established using a standardized weight-drop device and assessed by neurological severity score (NSS). Although these models fail to mimic the complete spectrum of human CHI, they reproduce impairment in neurological function observed in clinical patients. Syngeneic iNSCs or NSCs were separately transplanted into the brains of CHI mice at 12h after CHI. Neurological impairment post-CHI was evaluated by several tests. Animals were sacrificed for morphological and molecular biological analyses.

Gao et al. discovered that iNSC administration promoted neurological functional recovery in CHI mice and reduced cerebral edema, BBB disruption, cell death and astroglial scarring following trauma. Implanted iNSCs could up-regulate brain derived neurotrophic factor (BDNF) and glial derived neurotrophic factor (GDNF) levels to support the survival of existing neurons after CHI. In addition, engrafted iNSCs decreased immune cell recruitment and pro-inflammatory cytokine expression in the brain post-injury. Moreover, we found significant nuclear factor kappaB (NF-κB) inhibition in the presence of iNSC grafts. In short, iNSCs exert neurotrophic and immunomodulatory effects that mitigate CHI-induced neurological impairment [7].

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