The Mesenchymal Stem Cell Secretome: Implications for Treatment of Traumatic Brain Injury

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EDITORIAL

Since their discovery in the 1960s [1,2] mesenchymal stem cells (MSC), also known as mesenchymal stromal stem cells, are the subject of investigation of many research groups. MSC are an attractive cell source for the regenerative therapy because they can be easily procured from several adult tissues, have low or absent tumorigenicity, have ability to migrate to the site of injury, and can be used for the patient-specific therapy to circumvent immune response.

Over the years numerous studies including ours demonstrated beneficial effects of naive and genetically modified MSC for neurodegenerative disorders and brain injury [3-5]. Under particular circumstances and genetic modifications, MSC are able to differentiate into cells of neuronal lineage, which might contribute to the repair of diseased or the injured brain. Nevertheless, there is a growing body of evidence that MSC mainly achieve their therapeutic effects through secretion of different autocrine/paracrine factors including growth factors, cytokines, chemokines, metabolites, and bioactive lipids. Moreover, factors from MSC secretome exert neurotrophic, anti-apoptotic, neurogenic, angiogenic, anti-inflammatory, and immunomodulatory properties. Thus, MSC secretome promotes healing of the injured brain through stimulation of endogenous restorative mechanisms and modulation of immune system. This editorial discusses a potential of MSC secretome for the treatment of traumatic brain injury (TBI).

Chop and his colleagues were among first who demonstrated a therapeutic potential of MSC after different routes of administration in a rat model of TBI [6-8]. Studies from other groups also confirmed beneficial effects of bone marrow-, umbilical cord-, and amniotic-derived MSC following transplantation in rodent models of TBI [9-22]. Importantly, recent clinical trials in children and adults with TBI demonstrated safety and therapeutic efficacy of MSC transplantation [23-25]. Similar to the studies with MSC transplantation in different models of neurodegenerative disorders, preclinical TBI studies suggest that functional recovery following MSC transplantation is mainly achieved through secretion of various factors that stimulate recovery of the injured brain and lead to improvement of neurologic outcome [15,18]. Thus far, several mechanisms have been implicated in the MSC secretome evoked functional recovery following TBI. MSC secreted factors can decrease brain damage following TBI by promoting neuronal survival and reducing apoptosis and autophagy [11,15,18, 20]. Further, MSC secretome can evoke neuroregeneration through a stimulation of neurogenesis, increased axonal fiber length, axonal reorganization, and inhibition of the glial scar [14,18,26-28]. MSC secretome can also evoke angiogenesis and regulate blood-brain barrier integrity that can promote brain recovery [16,27]. In addition, MSC-secreted factors may modulate inflammation–associated immune cells and cytokines at the injury site that leads to the enhanced neuroprotection and repair. Although all the above mechanisms seem to be implicated in the MSC-evoked therapeutic effects in TBI, the primary mechanism responsible for the brain recovery is still elusive. However, it is plausible that several interconnected mechanisms may functionally underline the MSC evoked neuroprotection and neuroregeneration. Furthermore, depending upon the environmental cues, different factors secreted by MSC may cause therapeutic effects through various mechanisms.

Taken together, MSC are promising candidates for a novel treatment of TBI. However, specific therapeutic factors within the MSC secretome need to be specified, validated and further refined. A better understanding of factors derived from MSC secretome and underlying mechanisms of their actions are prerequisite to develop an effective therapy for TBI and other neurodegenerative disorders.

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REFERENCES

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