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Editorial

Multimodal Repair of Spinal Cord Injury With Mesenchymal Stem Cells: An Editorial Perspective

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The science of regenerative medicine has undergone significant advances in the past 2 decades with the development of stem cells as a potential therapeutic option. Mesenchymal stromal cells (MSCs) represent a conceptually relatively safe therapeutic option owing to their low tumorigenicity and potential to differentiate into various cell types including osteogenic, adipogenic, chondronic, and myogenic lines. MSCs are highly viable, nonimmunogenic, and are known to provide structural support in spinal cord injuries when continually transfused.[1]

As Ma and colleagues report,[2] the regenerative contribution MSCs afford lies in their anti-inflammatory, structural, and trophic support in injury environments. As trophic supporters, MSCs are amongst the highest secreting cell types, allowing them to exert large effects by secreting numerous cytokines and growth factors. In fact, when injected intravenously into rats, MSCs have been shown to home to the spleen, where they exert immunomodulatory effects by increasing circulating levels of interleukin-10, thereby reducing lesion volume and tissue loss, ultimately improving functional recovery.[3] In the present paper, the authors reference a previous study uncovering a novel role for MSCs in establishing neuroprotective sheaths that deposit extracellular matrix components and prevent oxidative damage to nerve fibres. These MSC-derived sheaths, investigated by Ma and colleagues,[4] were found to enwrap neurites stretching across the lesion site, despite lacking expression of myelin basic protein and Schwann cell markers. These findings demonstrate the potential for MSCs to act as reparative supporting cells that may be used to complement endogenous glial scarring and lesion compaction mechanisms in order to encourage axonal regeneration.

The authors describe previous unsuccessful attempts to differentiate MSCs into neurons using chemical treatment, and go on to explain more recent approaches using growth factors and morphogens to achieve a 'neuron-like' cell phenotype potentially capable of firing action potentials and synapse formation. While these findings provide an avenue for further investigation, MSCs appear most relevant in structural repair, acting as a sponge when administered systemically in order to limit immune cell infiltration into lesion sites, and inflammatory modulators when administered focally. Optimizing the survival and reparative phenotypes of these cells is an attractive field for further investigation. The authors describe

multiple strategies including ischemic preconditioning, 3-dimensional culturing, and tissue engineering that have been used to effectively yield cells with greater viability and anti-inflammatory potential. Use of these approaches with complementary therapies is likely to achieve the greatest neuroprotection and regeneration. Recent findings have successfully stimulated axonal regrowth in mature spinal neurons using osteopontin, insulin-, fibroblast-, and epidermal- growth factors, and ciliary- and glial-derived neurotrophic factors.[5] MSCs may be used in combination with these approaches to facilitate a structural and trophic niche for functional regeneration, which may be further encouraged by rehabilitative therapy.

MSCs and stem cells in general show great potential for the future that has yet to be fully harnessed and understood. The mechanisms by which MSCs impose angiogenic, neurotrophic, and structural benefits continue to elude definition, though these represent attractive targets for optimizing their therapeutic capacity. In their review, the Zeng group describes current states of knowledge, existing gaps, and future directions of MSC research and highlights the necessity of continued research in this field. This represents a promising area of translational research.

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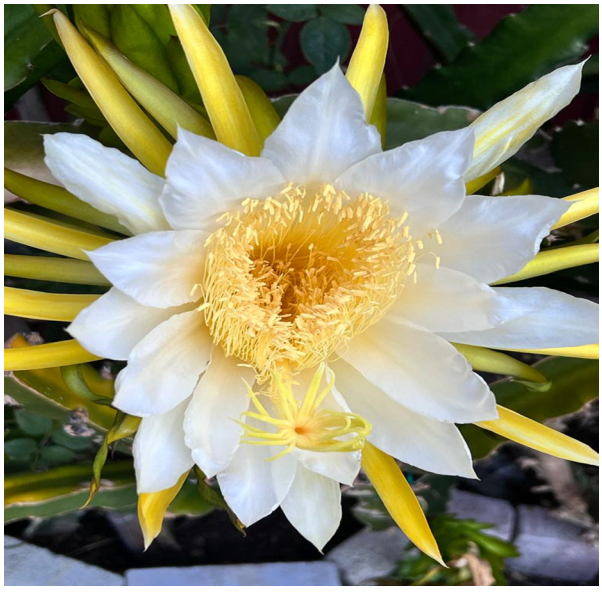

Artist: Michael G. Fehlings
Title: Sunflower in a Toronto Garden
Year: 2022