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Letter to Editor

The Hope for Pandora's Box: Mesenchymal Stem Cells for Promoting Angiogenesis in Stroke and Trauma Brain Injury

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To the Editor;

We read the articles with great interest by Li et al. entitled "2-Methoxyestradiol Inhibits Intracerebral Hemorrhage-Induced Angiogenesis in Rats" (6). In this paper, Li et al. reported that the Hypoxia-inducible factor-1α (HIF-1α) inhibitor, 2-Methoxyestradiol (2ME2) impaired post-intracerebral hemorrhage (ICH) angiogenesis and functional recovery and again in this paper the authors consider that HIF-1α may have a protective effect against ICH-induced damage. We agree with the conclusions drawn from Li et al., but there are some issues which are still in debate and further studies are needed to clarify to advance the rational design of the following clinical research. At the same time, we provide a promising paragon that can both promote vascular reconstruction (angiogenesis and arteriogenesis), and the lesion tissue repair which may provide a new perspective for the restoration and regeneration in neurological diseases.

Mesenchymal stem cells (MSCs) are a class of cells with significant self-renewal and multi-lineage differentiation properties, which are a class of seed cells in regenerative medicine (3,4). Over the years, our understanding of the nature and the function of MSCs has undergone a number of paradigm shifts. Initially, MSC-based therapies were anticipated to augment the structure and function of damaged or diseased tissues via direct cell replacement (5). However, it soon became apparent that relatively few MSCs engrafted at these sites of injury, and studies in rodents and dogs confirmed that intravenously administered MSCs are caught in the capillaries of the lung, and most MSCs are largely cleared (1,8). It had been long-known that MSCs produced abundant growth factors, and bio-active cytokines, many of which modulate the immune system, limiting inflammation, aiding healing, the field adopted the revisionist viewpoint that MSCs affect tissue repair largely via their paracrine factors and stimulation of host cells (7-9),which suggest that MSCs repair damaged tissue due to the 'faking by stander effect' or cell-to-cell communication or exosomes and/or some metabolites and cytokines.

Whether the cell replacement or 'faking bystander effect'of MSCs, the role of MSCs in promoting vascular regeneration and tissue repair has been widely recognized. The studies have demonstrated the central role of HIF-1α in angiogenesis (Figure 1) (2). In some central nervous system disease, such as traumatic brain injury (TBI), stoke, cerebral ischemia-reperfusion (CI/R) injury HIF-1α is up-regulated, which provides a local microenvironment that could promote angiogenesis and reconstruction. The implanted MSCs (seed cells) can further promote the regeneration and reconstruction of blood vessels by 'faking bystander effect' or/and cell replacement (4,5).

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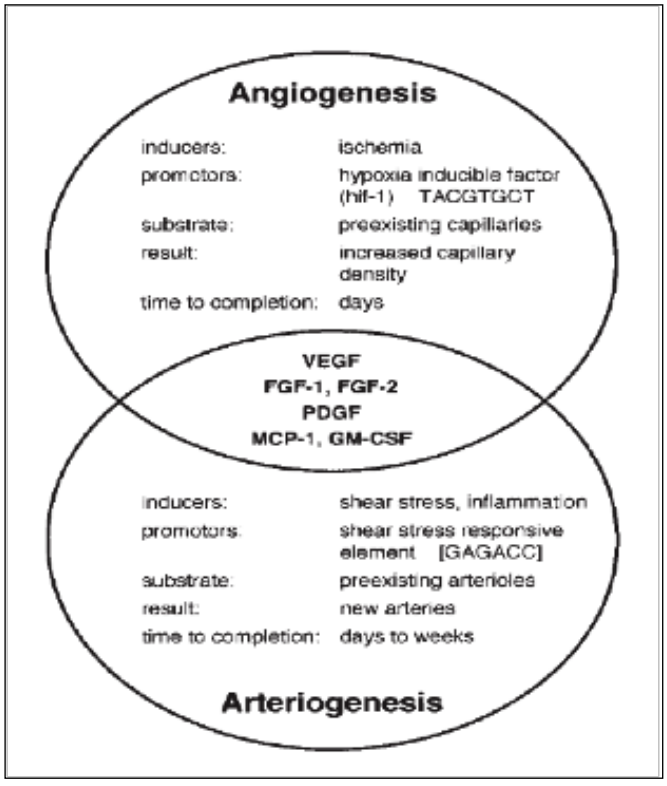

Figure 1: Arteriogenesis versus angiogenesis: Two mechanisms of vessel growth (2).

Based on the above, MSCs or temperature sensitive MSCs (10) transplantation may be a potential method for regeneration and reconstruction of blood vessels.

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■ REFERENCES

1. Aggarwal S, Moggio A, Bussolati B: Concise review: Stem/progenitor cells for renal tissue repair: Current knowledge and perspectives. Stem Cells Translational Medicine 2:1011-1019, 2013
2. Buschmann I, Schaper W: Arteriogenesis versus angiogenesis_ two mechanisms of vessel growth. News Physiol Sci 14:121-125, 1999
3. Ding DC, Chang YH, Shyu WC, Lin SZ: Human umbilical cord mesenchymal stem cells: A new era for stem cell therapy. Cell Transplant 24:339-347, 2015
4. Dong H, Li G, Shang C, Yin H, Luo Y, Meng H, Li X, Wang Y, Lin L, Zhao M: Umbilical cord mesenchymal stem cell (UC-MSC) transplantations for cerebral palsy. Am J Transl Res 10:901-906, 2018
5. Li G, Yang Y, Dong HJ, Lin L: The research progress of mesenchymal stem cells in the treatment of Traumatic brain injury. Turk Neurosurg 28:696-702,2018
6. Li HT, Zhou HJ, Zhong JH, Tang T, Cui HJ, Zhang QM, Zhou JH, Zhang Q: 2-Methoxyestradiol inhibits intracerebral hemorrhage - induced angiogenesis in rats. Turk Neurosurg 28:241-247, 2018
7. Oh SH, Choi C, Chang DJ, Shin DA, Lee N, Jeon I, Sung JH, Lee H, Hong KS, Ko JJ, Song J: Early neuroprotective effect with lack of long-term cell replacement effect on experimental stroke after intra-arterial transplantation of adipose-derived mesenchymal stromal cells. Cytotherapy 17:1090-1103, 2015
8. Phinney DG, Pittenger MF: Concise review: MSC-derived exosomes for cell-free therapy. Stem Cells 35:851-858, 2017
9. Savukinas UB, Enes SR, Sjoland AA, Westergren-Thorsson G: Concise review: The bystander effect: Mesenchymal stem cell-mediated lung repair. Stem Cells 34:1437-1444, 2016
10. Zhao WY, Chen SB, Wang JJ, Xu C, Zhao ML, Dong HJ, Liang HQ, Li XH, Tu Y, Zhang S, Chen C, Sun HT: Establishment of an ideal time window model in hypothermic-targeted temperature management after traumatic brain injury in rats. Brain Research 1669:141-149, 2017