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Letter to Editor

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Cell-Free Therapy may Experience More Rapid Advancement "Pretended Bystander Effects" in Cell-Based Therapy for Treating Diseases

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To the Editor;

We read with great interest that the article by Chen et al. entitled "Protective Effect of adenovirus (Ad)-VEGF-Bone Mesenchymal Stem Cells on Cerebral Infarction" in Turkish Neurosurgery (1). In this article, Chen et al. reported that "intracerebroventricular transplantation of vascular endothelial growth factor (VEGF) gene-modified bone mesenchymal stem cells (BMSCs) in rats after cerebral infarction could reduce reactive gliosis, ameliorate neurological deficit, diminish the percentage of cerebral infarction volume in rats, and facilitate angiogenesis" (1).

We agree with the conclusions drawn from Chen et al. (1). MSCs-based therapies were anticipated to repair the structure and function of diseased or damaged tissues via direct cell replacement and/or pretended by-stander effect. More recently, MSC-derived extracellular vesicles (EVs), which include exosomes and microvesicles (MV), are being examined for their role in MSC-based cellular therapy. The exosomes and MVs can influence tissue responses to injury, infection, and disease (4). MSCs-free therapy maybe a promising therapy to treat some diseases, especially some intractable disease.

MSC-derived exosomes have a content that includes cytokines, exosomes, growth factors, signaling lipids, mRNAs, and regulatory miRNAs, etc. To the extent that MSC derived exosomes can be used for cell-free regenerative medicine, much will depend on the quality, reproducibility, and potency of their production, in the same manner that these parameters dictate the development of cell-based MSC therapies. Therefore, careful attention to detail in producing MSC exosomes may provide a new therapeutic paradigm for cell-free MSC-based therapies with decreased risk (5). We hold the opinion that both "Pretended Bystander Effects" (2) and Cell Replacement play a therapeutic role together (2,3). In the process of cell therapy, the former is the main one at the early stage (about a month after cell therapy) and the latter at the later stage (usually a month after cell therapy) (7).

We believed that stem cell free therapy would experience more rapid advancement in the future. The advantages of MSC-free therapy could avoid the transfer of cells which may block the microvessels; and the MSC-derived exosomes, growth factors, signaling lipids, mRNAs, and regulatory miRNAs are small which could circulate readily (5,6), and most of all MSC-free therapy can regulate the therapeutic doses scientifically. Therefore, careful attention to "MSC-free" treatment may provide a new therapeutic paradigm for MSC-based therapies.

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