The Role of Mesenchymal Stem Cells in Organ Transplantation: Immunomodulatory and Anti-inflammatory Properties of Mesenchymal Stem Cells for Application in Organ Transplantation

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As a clinical practice, transplantation is a strategy for overcoming disease that could not be readily curable by any existing therapies. The scarcity of the organ number for transplantation in the continuously growing population makes the overall picture critical for meeting the requirement. The prevention of organ rejection, which is caused by the destruction of transplanted tissue by the tissue recipient’s (host) immune system, is mainly focused in routine application. The immunosuppressive drugs provide some benefits against organ rejection, but the immune system with its factors is still a major obstacle in successful transplantation.

The crucial role of mesenchymal stem cells in tissue function is widely known of their effect on the tissue components by paracrine and autocrine factors. Until the last decades, the self-renewal capacity and multi-lineage differentiation potency of these cells were mainly focused for the tissue regeneration applications. On the other hand, the chemical factors secreted by mesenchymal stem cells can promote differentiation of stem cells and tissue remodelling, but they can also affect the immune system by suppressing maturation of Dendritic Cells (DCs) and the functions of T cells, B cells and Natural Killer (NK) cells, as well as by inducing regulatory T (Treg) cells. The immunomodulatory effects of MSCs have been shown in otoimmune diseases such as Graft Versus Host Disease (GVHD), osteogenesis imperfecta, arthritis, encephalomyelitis [1,2]. The allo-reactivity caused by the immune system is prevented by use of immunosuppressive drug, which might lead severe side effect. The use of mesenchymal stem cells could be considered as an alternative approach to control the immune response in clinical transplantation settings.

Combined with the immunosuppressive therapy, MSCs administrations following transplantation were shown to prolong cardiac allograft survival, and attenuate graft rejection earlier [3]. MSCs together with low dose of drug treatment improved the donor-specific graft tolerance and reduce the immune response in this case. Similar studies also provide supportive results that MSCs enhance both transplant acceptance and physiologic functions [4]. The development of ischemia then reperfusion occur following kidney transplantation. This leads the formation of reactive oxygen species and lipid peroxidation. Thus, necrosis and apoptosis rates escalate in tissue in parallel with the intensifying inflammation. Consequently, tissue destruction is followed by the organ rejection [5]. In the MSC treatment with conventional immune suppressing drug therapy after the kidney transplantation, the IL-2 mediated role has been shown in recent study [6]. The point of use the immunosuppressive drugs is the control of inflammation and the inhibition of transplant rejection triggered by the immune system. Treg cells are the important regulatory components of the immune system, the function of which was inhibited by inflammatory cytokines, like IL-1β, IL-2, IL-6 and TNFa. In response to down-regulation of Treg activity, the attack of cytotoxic T-cells against the transplanted tissue surge significantly [7]. The regulation of the cytokine expression by MSCs mainly provides the control over immune response.

The role of MSCs in transplantations is not limited only with the regeneration and anti-inflammatory effect, but the prevention of fibrosis is well-recognized in the studies involving solid organ transplantation. The anti-inflammatory factors, including IL1ra, TGFb, Hepatocyte Growth Factor (HGF), nitric oxide (NO) and HLA-G, secreted by MSCs were also shown to function in reduce fibrosis in the heart [8], and other organs such as the lung, liver, and kidney [9-12] in the experimental animal models. The attenuated fibrosis level in tissue engrat will also reduce the rejection by MSC treatment [13].

MSCs might be accepted as an attractive cell immunotherapy tool in cell and organ transplantation. In addition to their regenerative potential, immunosuppressive effects of MSCs could participate in the successful organ grafting and regeneration of the transplanted organ. Some recent reports provided the evidences for their support in the engrafted tissue by multiple paths, but additional knowledge and well-designed studies are required to understand their effect on the immune system before clinical applications.

References

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