The roles of mesenchymal stem cells secretome in diabetic wound healing

There has been a fourfold rise in the number of diabetics from 108 million in 1980 to 422 million in 2014 and by 2040 the number will reach to 642 million. Diabetes mellitus drastically influences normal functioning of the affected individual including the natural process of wound healing which is impaired. Therefore, diabetic foot ulcer have become a significant cause of diabetes related amputations, which lead to high medical cost and poor life quality of patients.

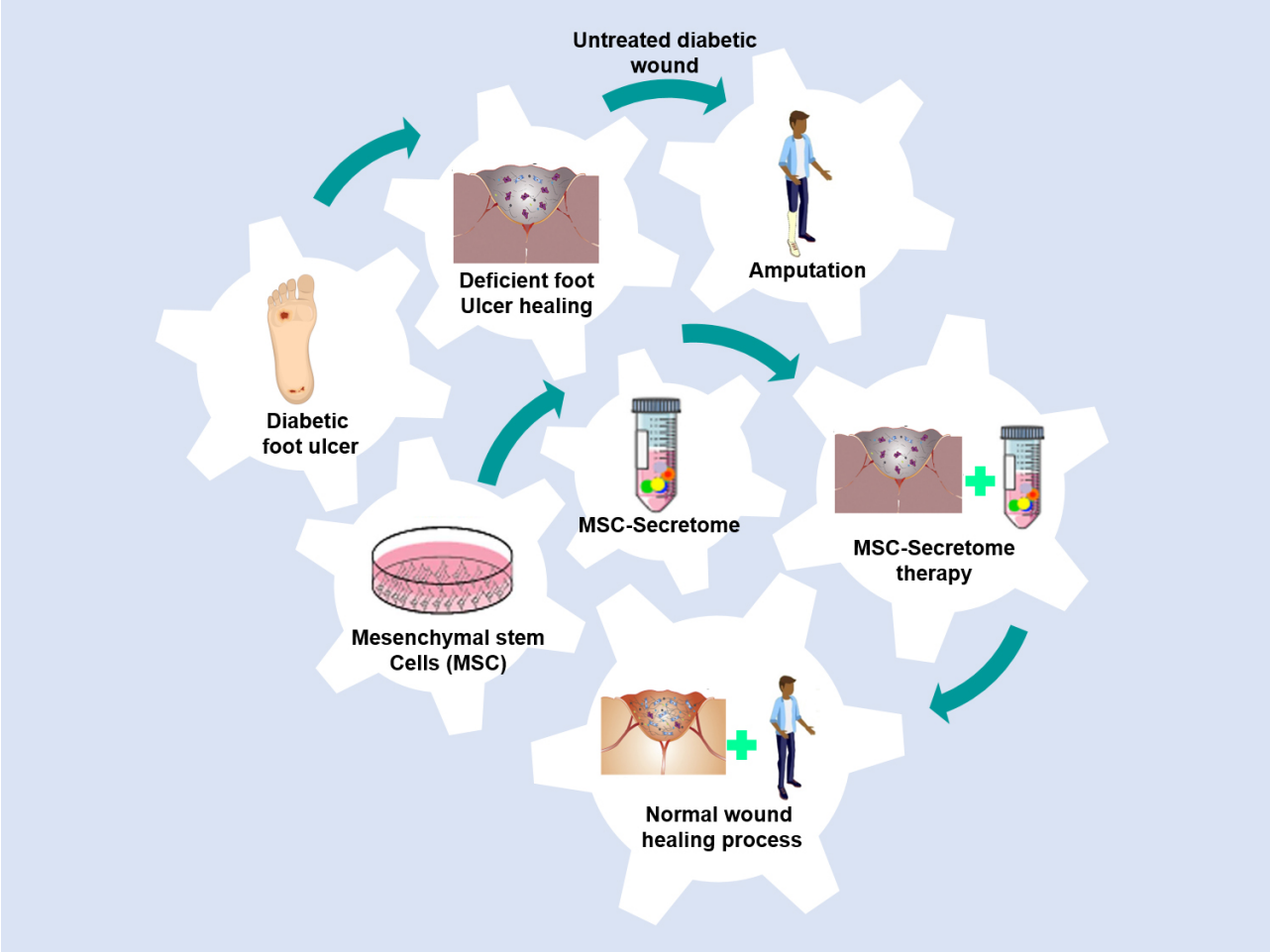

Fig. 1. Potential applications of MSC-CM in diabetic wound healing.
In patients with diabetes mellitus, the wound healing processes are affected, starting with a decrease in fibrinolysis and an imbalance of cytokines, which causes an alteration in wound healing which causes diabetic foot ulcer and amputation. Mesenchymal stem cells secretome contains trophic factors that facilitate wound healing via advance proliferation and migration of keratinocyte, endothelial cell, and fibroblastes into the injury site. Actually the potent paracrine chemoattractant and angiogenic factors affect the microenvironment by acting on different cell

types, leading to normal wound healing and tissue repair and may rescue the pations from foot ulcer and amputation.

Skin wound healing involves distinct but overlapping phases of hemostasis, inflammation, proliferation, and remodeling. A diverse set of cells such as neutrophils, macrophages, and fibroblasts contribute to the process of different phases of skin wound healing. Mechanisms underlying poor healing of diabetic wounds are still unclear, yet the reasons for this dread complication of diabetes mainly involves hypoxia, impaired angiogenesis, damage from reactive oxygen species (ROS), and neuropathy, leads to long-time medical burden and compromised life quality of those patients. Conventional clinical treatment of diabetic wounds often seem ineffective for many patients due to impaired cell function around the wound sites.

To solve these problems, therapies based on mesenchymal stem cells (MSCs) showed great potential for wound healing due to their secretome. It is shown that MSC secretome contains a variety of cytokines, chemokines, and growth factors that enhance wound healing through improvement of epithelial and endothelial cell migration, granular tissue formation, and angiogenesis.

Since fibroblast plays a key role in wound healing, and the advantages of mesenchymal stem cellssecretome in wound healing have been reported we scrutinized the impact of MSC-secretome on diabetics wound healing and skin regeneration. Our findings revealed significant improvements in some healing kinetics of diabetic wound which received MSC-secretome Particularly, MSC-secretome-treated diabetic wounds reached considerably higher percentages of wound closure. Also, the granulation tissue of these wound had less pronounced inflammatory response, better tissue remodeling, and more vascularization compared with non-treated diabetic ones. Based on these findings, it is suggested that MSC-secretome could promote wound repair and skin regeneration, in some major processes, via improvement of cellular behaviors of fbroblasts in the diabetic microenvironment. The beneficial advantages of mesenchymal stem cells-secretome on fibroblast cellular behaviors and wound healing may lead to establish a novel approach as an alternative therapeutic procedure to cure chronic wounds in diabetic conditions.

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