

# Transcendence of Medicine Regenerative Strategies in the Treatment for Diabetic Foot Ulcers

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## Abstract

The Diabetes Mellitus type 2 and one of its complications, the diabetic foot ulcer (DFU), are a great problem of public health that affects millions of people around the world. Due to its complexity, DFUs treatment and handling are expensive and complex. In addition, amputations of lower limbs and death are relatively frequent because conventional treatment cannot avoid them. In other hand, the use of growth factors, 3D scaffolds and mesenchymal stem cells, called regenerative medicine (RM), have created new perspectives about the treatment of this kind of injuries. The RM has demonstrated favorable clinical outcomes not only in the case of DFUs, so that, this new medicine area promises to become an important tool that supports or substitutes to conventional treatment in cases of tissue or organic damage caused by the different chronic and traumatic diseases.

**Keywords:** Diabetes foot ulcer; Mesenchymal stem cells; Regenerative medicine

## Introduction

Diabetes mellitus type 2 (DM2) is a great problem of world health that affects to millions of people around the world and it has been anticipated that the number of patients will be increase in the next decades [1]. Some of its complications as peripheral neuropathy and peripheral vascular disease are related to development cutaneous injures in lower limbs that are known like diabetic foot ulcers (DFUs) [2-4]. In addition, due to the generalized inflammatory state, characteristic of this disease, the healing process are affected, causing a slowly and costly recovery [2,5-11].

In spite of current treatments, a great number of people with DFUs will suffer lower limb amputation along its life [2,12], this fact becomes to DFUs as the first cause of non-traumatic amputation in world [13], and if this was not enough, the patient's lifespan will decrease drastically within first five years after the surgery [9,14-16]. The treatment of DFUs is focus in promote the scarring of wound through different methods, for example; hydrocolloid dressings, surgeries, drugs and skin grafts, among others [17-22], also, the therapy should be accompanied by educational health programs and changes in lifestyle. Even though, there are not enough when the problem is severe because it will progressive into amputation [23,24].

In other hand, in the last years it has been increasing the use of growth factors, 3D scaffolds and mesenchymal stem cells [25-31]-this has been called regenerative medicine (RM) [32,33]- for these wounds, where the treatment has had better healing and economical outcomes than conventional therapy [12,34]. A key factor of medicine regenerative's development was the discovery of mesenchymal stem cells (MSC) by Friednestein et al. [35-37]. In addition to this, subsequent researches have shown the capability of the MSC to auto-renew, differentiation, synthesis of extracellular matrix, intercellular

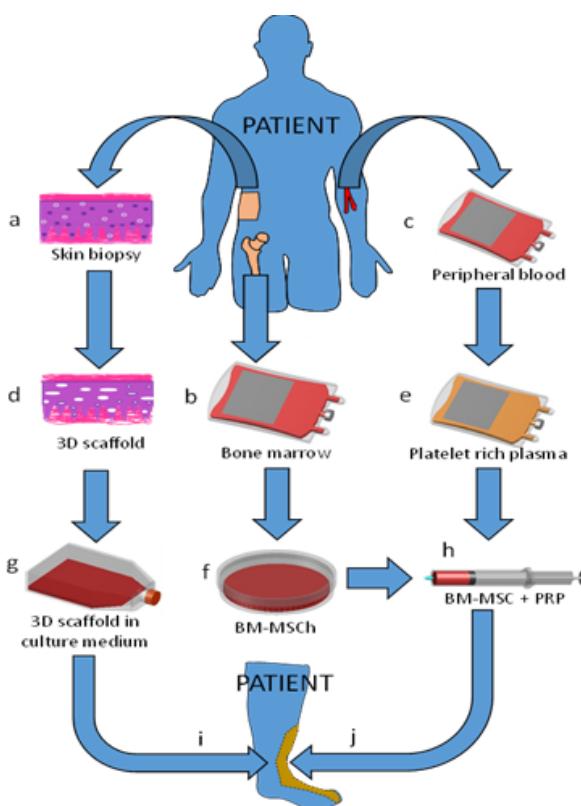
signaling, modulation of immune response and not to generation of rejection like others tissues [38-40]. All these characteristics have been crucial to employ the MSC to rebuild tissues and organs [38-53].

In the research made by Benítez-Arvíz et al. [54], strategies of medicine regenerative were implemented by the use of: a) growth factors of platelets [55,56], b) 3D scaffold of skin [57], and c) mesenchymal stem cells of bone marrow [54,58] (Figure 1). This therapy was possible because other researches have demonstrated the benefit of this kind of treatment in similar wounds [12,34,59]. At the same way, after several months of treatment, they could see completely incorporation of the 3D, this without side effects were seen.

In many researches have been demonstrated that medicine regenerative strategies in patients were best than conventional therapies, without collateral effects have been seen [30,60-65]. This becomes to RM an important element of support to the treatment in the case of cutaneous wounds with small possibilities of healing [66,67]. It is important to highlight that a good handling of DFUs could avoid more than half of amputations and, of course, this could represented a great save of money and improvements of patients quality life [68-73].

## Conclusions

Even though, there are a lot of information about the mesenchymal stem cells biology, there is still very limit the knowledge of the regenerative mechanisms induced by them in patients [74-77]. However, the increasing of clinic trials based in MSC could let us understand better the effect of them *in vivo* and this will open new scenes to strengthen and valid clinic trials of medicine regenerative a great scale [65,78-81]. This could be a solution by the world health problems that DM2, its complications and other kinds of disease do [82]. Finally, although our expectations about what medicine regenerative can do are huge, there are still a lot of things to do.



**Figure 1:** A schema about the implementation of medicine regenerative in the patient; firstly, there was necessary to get a skin biopsy (a), bone marrow (b), and peripheral blood (c) of the patient. After these, the elements were processed to obtain; a 3D scaffold (d), plasma rich platelet (e) and bone marrow mesenchymal stem cells (BM-MSCs) (f). As the BM-MSCs, the 3D scaffold was kept in culture conditions on Carrel's Flask at 37°C, 5% of CO<sub>2</sub> and saturated humidity until its use (g). Finally, in completely asepsis at operating room and previously surgical scrubbing, the 3D scaffold was fixed by suture at wound area (i) and the BM-MSCs into the PRP were placed (j).

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