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LETTER TO THE EDITOR

Mesenchymal stem cells and psoriasis: State of the art and future perspectives

Dear Editor

Mesenchymal stem cells (MSCs) are a subset of pluripotent cells present in tissues of mesenchymal origin and responsible for their regeneration. MSCs include many different cell types, probably the most widely studied being the bone marrow stromal stem cells (BMSCs). Other types of MSCs are, for example, umbilical cord mesenchymal stem cells (UCMSCs), amniotic fluid stem cells (Amn-MSC), and adipose-derived stem cells (ADSCs). MSCs are currently widely studied not only for their regenerative capacity but also for their immunomodulating properties, thus giving reason to their use in clinical trials for autoimmune and autoinflammatory disorders. In this setting, several authors have investigated the role of MSCs as a possible therapeutic strategy for the treatment of psoriasis in both clinical and preclinical models.

Previous studies already confirmed the involvement of MSCs in the pathogenesis of the disease and, therefore, designated MSCs as important potential therapeutic targets in the setting of psoriasis (Niu & Zhang, 2016). Liu and coworkers stated that lymphocyte inhibition is compromised in psoriatic skin, mainly because of MSCs in psoriatic lesions leading to abnormalities in cytokine secretion (Liu, Yang, Yan, & Zhang, 2013). MSCs from skin lesions of psoriatic patients also promote keratinocyte proliferation, resulting in abnormal thickening of the epidermis (Figure 1). Moreover, several papers reported on the central role played by MSCs in response to biologic therapies: MSCs in fact seem to be key players in mediating the pleiotropic effects of those drugs on both keratinocytes and T cells. Campanati and coauthors in particular demonstrated that the effects of TNF-alpha inhibitors take place at the level of dermal MSCs, which probably represent the cells primarily involved in the "psoriatic march" (Campanati et al., 2017).

To date, only few anecdotal reports of patients treated with MSC-based regimens have been published. A total of six patients

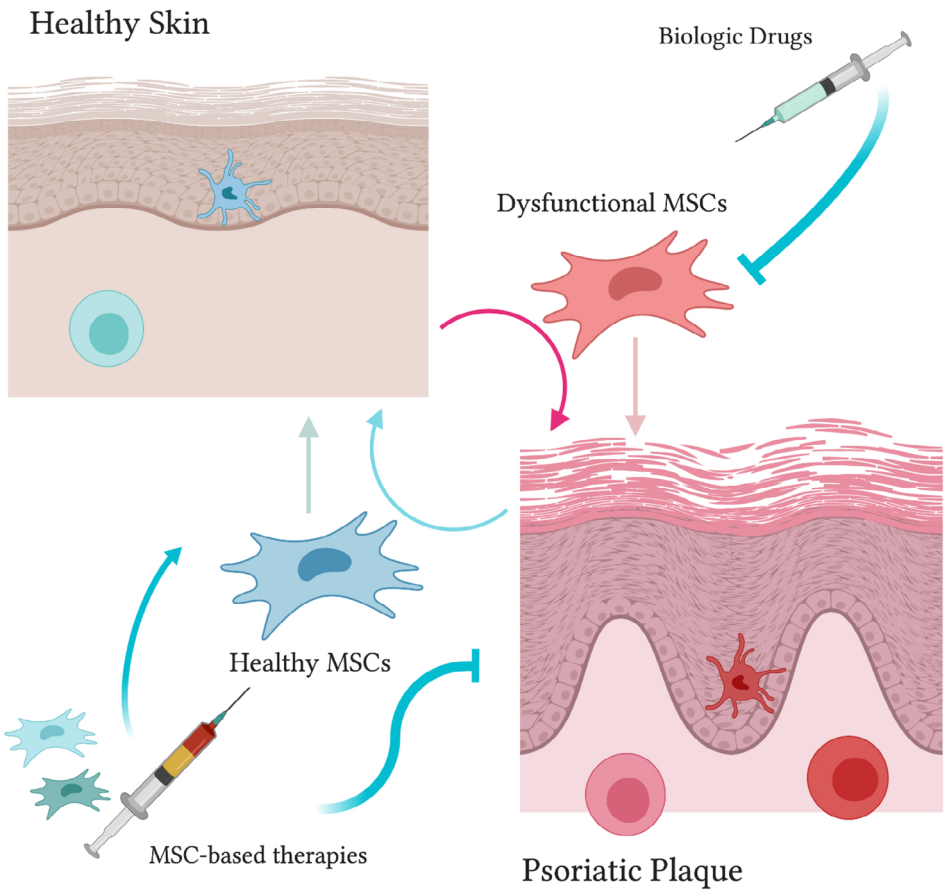

FIGURE 1 Schematic representation of the role of mesenchymal stem cell in psoriasis. Under physiological conditions, skin-resident T lymphocytes and Langerhans cells are in a quiescent state and epithelial renewal is finely controlled. On the contrary, MSC dysfunction results in secretion of proinflammatory cytokines and local recruitment of activated Th1 and Th17 lymphocytes, responsible for the hyperkeratosis, parakeratosis, and papillomatosis typical of psoriatic plaques. Although therapies of conventional immunosuppressants for psoriasis only act on lymphocyte modulation, biologic therapies have a combined action on both cytokine and MSC modulation. The aim of MSC-based therapeutic regimens is to restore a physiological nondysfunctional MSC population (created with BioRender.com)

affected by psoriasis have been described in four clinical studies. Of them, two patients received intravenous injection of UCMSCs and three of ADSCs, while only one patient was treated with topical application of ADSC-conditioned medium. So far, MSC-based therapies proved their efficacy in all described cases (Chen et al., 2016).

However, most of the research is today still limited to the bench side. Preclinical studies, mainly using imiquimod-induced murine models of psoriasis, have in fact recently stressed the potential therapeutic efficacy of MSCs, with surprisingly promising results (Chen et al., 2019). However, no standardized experimental models are currently available, since huge differences both in the type of MSC used (dermal MSCs, ADSCs, UCMSCs, and embryonic stem cell-derived MSCs) and the administration route (intravenous, intralesional, and topical) can be found in the literature. The effects of MSC administration are certainly mediated by their well-known immunomodulating action on both T cells and dendritic cells through cytokine secretion. However, the possibility of a direct interaction between MSCs and keratinocytes remains unknown and should be clarified. Another important point for future research is the possibility of obtaining efficient MSC from psoriatic patients: since dermal MSCs in psoriatic plaques have been shown to be altered, also other MSCs could be impaired in terms of function and it is therefore imperative to check whether autologous MSCs can be efficiently used for psoriasis treatment.

CONFLICTS OF INTEREST

The authors have no conflict of interest to declare.

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