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## Correspondence

### By the skin of our teeth: potential applications of dental pulp stem cells to cutaneous disease

Dear Editor,

As the search for novel therapeutics and new treatments continues in dermatology, a recent discovery in regenerative medicine has shown increased potential. Dental pulp stem cells (DPSCs), first isolated by Gronthos & colleagues in 2002, represent a novel adult stem cell population with considerable ability to proliferate, self-renew, and differentiate into multiple lineages.<sup>1</sup> Notably, DPSCs have demonstrated superior growth potential compared to stem cells harvested from bone marrow.<sup>2</sup> Not only do these stem cells have the ability to differentiate into cell types such as osteoblasts, adipocytes, and chondrocytes but their proliferation and differentiation can be induced *in vitro* such that a small number of DPSCs can be engineered to produce a large variety of cell types in sufficient amounts for clinical application.<sup>3</sup>

Currently, the therapeutic potential of DPSCs in humans is high, with numerous *in vivo* studies confirming the effects of DPSCs following transplantation. DPSCs have been used to treat spinal cord injury, repair infarcted myocardium, modulate autoimmune conditions, and treat diseases of the pancreas, liver, and oral cavity.<sup>4</sup> However, the clinical applicability of DPSCs remains limited in humans at this time, with only a handful of human studies being published in the literature. These pilot studies have been limited to the treatment of pulpitis and pulp necrosis, finding the implantation of DPSCs to be safe and effective albeit in small sample sizes.<sup>4-5</sup>

One potential dermatological application of DPSCs may be to treat psoriasis. For years, serious adverse events have been reported from biologic drugs in psoriatic clinical trials. Meng et al. sought to provide another means of treatment while avoiding the use of biologics. Thus, the authors found that the immunomodulatory effects of DPSCs could be amplified with overexpression of hepatocyte growth factor (HGF) *in vivo*.<sup>6</sup> Topical imiquimod was used to induce psoriatic symptoms on the backs of mice. An intravenous injection of DPSC suspension was injected, and the skin lesions were subsequently collected for histological and immunohistochemical analysis. The researchers discovered that HGF-expressed DPSCs downregulated critical pathophysiological mediators of psoriasis, such as Th1 and Th17 cells, and their downstream cytokines including IL-17A, IL-17F, IL-23, TNF- $\alpha$ , and IFN- $\gamma$ . They were also found to upregulate Treg cells and decrease the production of proinflammatory cytokines such as cytokerin 6 and 17. Ultimately, the overexpression of HGF in DPSCs improved the erythema, scaling, and hyperkeratinization associated with psoriatic lesions in a mouse model.

DPSCs may also have the potential as an anti-aging treatment. According to Li et al., DPSCs, if co-cultured with skin fibroblasts, significantly decreased proliferation of the fibroblasts.<sup>7</sup> This reduction in dermal fibroblast proliferation appears to be mediated by effects on the cell cycle. Fibroblasts decreased in the G1 phase but increased in the S and G2 phases. In addition, fibroblasts co-cultured with DPSCs expressed increased amounts of pRb and decreased amounts of p53 and p21.

Although DPSCs were first isolated nearly two decades ago, the potential therapeutic applications of these stem cells to cutaneous conditions have not been explored until recently.

The aforementioned studies suggest that DPSCs may have clinical value in psoriasis treatment and anti-aging via immunomodulation and alteration of dermal fibroblasts, respectively. Additional studies of DPSCs are needed before human trials can begin, including additional research to determine the potential for harmful side effects. Therefore, the use of DPSCs in dermatological conditions remains in the nascent phases. In fact, the coming years may reveal additional novel applications of DPSCs to cutaneous disease.

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