

# Is it Safe to Use Mesenchymal Stem Cells in Cancer Patients?

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*World Journal of Dentistry* (2019); 10.5005/jp-journals-10015-1688

Cancer patients, postsurgical intervention, often present with minimal residual disease (MRD), which is treated either through radiotherapy or chemotherapy or a combination of both.<sup>1</sup> The resurgence of these MRDs into an active neoplastic lesion depends on several factors including the presence of a tumor-promoting stimulus and a sustainable microenvironment. Several studies have shown the role of mesenchymal stem cells (MSCs) in cancer initiation and progression either through direct interaction (cell fusion) or through their secretory factors.<sup>2,3</sup> On the contrary, there are few studies wherein the MSCs have shown to inhibit cancer.<sup>4</sup> The type of effect (inhibition/progression) the MSCs would have on cancer depends on several factors including the tissue of origin of the MSCs, cancer cell lineage, and the genetic profile of the individual.<sup>5</sup>

Surgical interventions in cancer often involve the removal of a large portion of tissues, which leads to a significantly reduced quality of life. The advent of regenerative medicine has allowed the regeneration of a wide variety of tissues. The application of such regenerated tissues to replace the surgically resected sites would aid in improving the patient's quality of life. Mesenchymal stem cells are one of the most commonly explored agents in regenerative medicine due to their potential for multilineage differentiation and their immunomodulatory properties. The immunomodulatory property of the MSCs allows it to be introduced into a host without eliciting any adverse reaction.

Despite their regenerative potential and compatible nature, introducing MSCs into the postsurgical sites of cancer patients would require caution, due to the dual role of MSC (inhibition/proliferation) toward cancer. If MSCs that have shown to induce progression against specific tumors lineage are introduced into patients with similar tumor lineage, MSCs could potentially induce the MRD to proliferate and establish a recurrence.<sup>3</sup> In addition to MSCs influencing the MRD, the cancer cells may, in turn, induce the MSCs to differentiate into cancer-associated stromal cells as evidenced by Barcellos-de-Souza et al.'s observation of the interaction between prostate cancer and bone marrow-derived MSCs.<sup>6</sup> In such cases, the MSC-derived stroma would provide the ideal microenvironment for the MRD to establish and progress.

In addition to being used as a regenerative agent, MSCs are being assessed for potential application as a drug delivery vehicle due to their natural tropism toward pathological tissues, including cancer.<sup>7</sup> As mentioned earlier, irrespective of the application (as drug delivery vehicles or regenerative agents), when MSCs are introduced into a cancer patient, there is a constant risk of tumor recurrence. The precaution in such cases would be to study the natural proclination the MSC of a specific origin has on cancer of a specific lineage using *in vitro* cell culture and *in vivo* animal model

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**How to cite this article:** Raj AT, Kheur S, Gupta AA. Is it Safe to Use Mesenchymal Stem Cells in Cancer Patients? *World J Dent* 2019;10(6):407.

**Source of support:** Nil

**Conflict of interest:** None

studies. Unless there is sufficient evidence that MSC of a specific tissue origin has an inhibitory or at least lacks any pro-carcinogenic effect on the cancer of a specific lineage, the use of the specific MSC must be restricted.

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