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LETTERS TO THE EDITOR

Use of Bone Marrow-Derived Mesenchymal Stem Cells in Prostate Cancer Could Increase the Risk of Cancer Progression

We read an interesting article published by Schweizer et al. [1] titled "A Phase I Study to Assess the Safety and Cancer-Homing Ability of Allogeneic Bone Marrow-Derived Mesenchymal Stem Cells in Men with Localized Prostate Cancer." The aim of their study was to determine the homing ability of allogenic bone marrow-derived mesenchymal stem cells (BM-MSCs). The BM-MSCs were systemically infused into the patient with prostate cancer. Four days later, the patients were subjected to radical prostatectomy. The resected samples were examined for the presence of the BM-MSCs. None of the tissue samples showed detectable levels of BM-MSCs. Based on the results, the authors concluded that although there was no adverse immune reaction to the BM-MSC, modification in the form of genetic engineering, cell surface modifications, or preconditioning regimens may be needed for enhancing the homing ability of BM-MSCs. The basis of the above study was to exploit the tropism shown by MSCs to cancer for targeted drug delivery. We agree with the authors that MSCs show tropism toward pathological tissues, including cancer, and have immunomodulatory properties; thus, it could be introduced into a host without eliciting an adverse immune response [2–4]. Despite the tropism and immunomodulation, the major limitation in using MSCs as a drug delivery vehicle in cancer is the differential effect (inhibition/proliferation) the MSCs have on cancer cells depending on several factors, including tissue of origin of the MSCs, the individual variations in the genetic profile of the patients, and the typology of cancer [5]. Luo et al. [6] used animal models to study the effect of BM-MSCs on prostate cancer. The study showed that BM-MSCs resulted in prostate cancer progression through cell fusion. Similar results were shown by the Yang et al. [7] study wherein tumor necrosis factor-α and interferon-γ treated MSCs were shown to promote prostate tumor growth in a syngeneic mouse model. The prostate tumor and tumor stroma secreted transforming growth factor-β1 have shown to induce transdifferentiation of the BM-MSCs into cancer-associated fibroblast aiding in the progression of cancer [8, 9]. In the Mognetti et al. study [10], in vitro transwell coculture of BM-MSCs and prostate cancer cells showed secretion of stromal cell-derived factor-1α by BM-MSCs which promoted the motility of the cancer cells and activated several pro-survival kinases including AKT and ERK 1/2.

Based on the above data, it is evident that BM-MSC has an inherent potential to aid in the progression of prostate cancer either directly through cell fusion or indirectly through the secretory factors (Fig. 1). Use of an MSC with natural proclination to proliferate cancer cells for drug delivery, as in the case of BM-MSCs and prostate cancer, could potentially lead to detrimental effects. Thus, future studies investigating the potential use of an MSC as a drug delivery vehicle for cancer must first establish the type of effect (inhibition or proliferation) that the MSC of a specific tissue origin has on the cancer cell of a specific lineage using both in vitro cell cultures and in vivo animal models.

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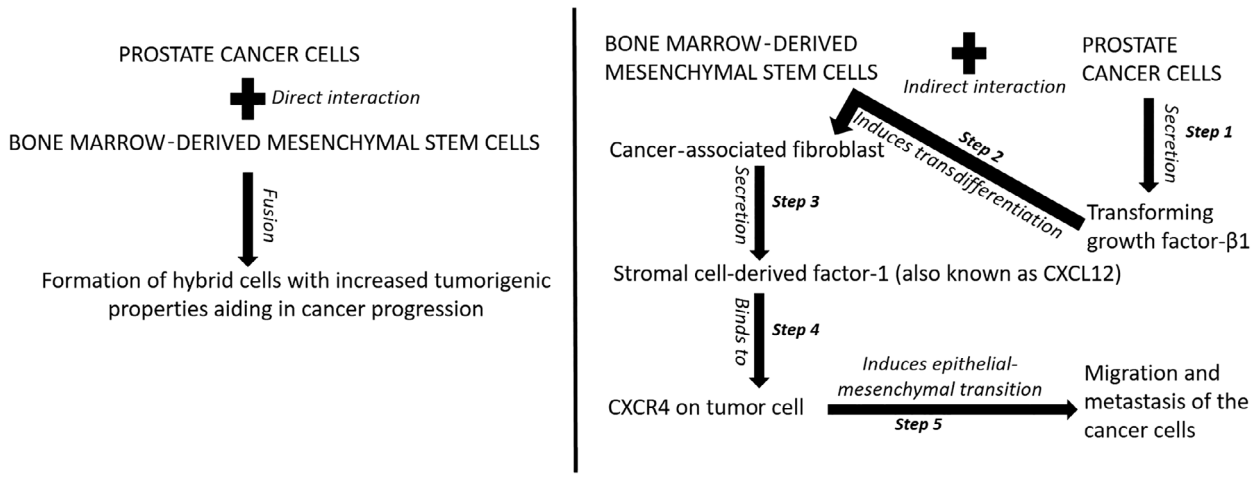

Figure 1. Bone marrow-derived mesenchymal stem cell-mediated progression of prostate cancer.

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Disclosure of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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