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Exosomes from human adipose-derived mesenchymal stem cells promote migration through Wnt signaling pathway in a breast cancer cell model

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Abstract Human mesenchymal stem cell (MSC)-conditioned medium (CM) was previously reported to affect the biology of tumor cells; however, the precise mechanisms remain unclear. Here, we show that MSCs secreted 40–100 nm particles, which have the typical characteristics of exosomes, and these MSC-derived exosomes promoted migration of the breast cancer cell line MCF7. Global gene expression profiling revealed that several cancer-related signaling pathways were upregulated after exosome treatment in MCF7, and the Wnt signaling pathway was further confirmed to be activated. Our findings demonstrated a new mechanism through which MSC-CM may contribute to tumor cell migration.

Keywords Exosome · Mesenchymal stem cell · MCF7 · Wnt · Migration

Ruizhu Lin and Shihua Wang have contributed equally to this study.

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Introduction

MSCs are a heterogeneous population of adult stem cells derived from a variety of tissues such as bone marrow and adipose tissue. Under the appropriate conditions, MSCs can give rise to cells of various lineages, including bone, muscle, fat, and cartilage. They also have unique immunological properties that allow their survival in a xenogeneic environment [1]. Therefore, MSCs present an intriguing model for the investigation of cell and gene therapy. However, there are studies reporting that MSCs could contribute to the formation of a tumor microenvironment and affect tumor cell biology. For example, Karnoub et al. [2] found that bone marrow-derived human MSCs, when mixed with otherwise weakly metastatic human breast carcinoma cells, could cause a substantial increase in the metastatic potency of the cancer cells. The possible mechanisms by which MSCs affect tumor initiation and progression have been explored. One mechanism is paracrine factors secreted by MSCs. De Boeck A et al. [3] reported that MSCs promote colorectal cancer progression through paracrine neuregulin 1/HER3 signaling.

In addition to diffusible factors such as cytokines and growth factors, cell-derived exosomes have recently been described as a new type of cell-to-cell communication [4]. Exosomes are small membrane vesicles (30–100 nm) derived from the luminal membranes of multivesicular bodies and are constitutively released by fusion with the cell membrane [5]. Exosomes transfer not only membrane components but also nucleic acids between different cells, emphasizing their role in intercellular communication [6]. Exosomes derived from MSCs have been reported to alleviate live fibrosis [7] and reduce myocardial ischemia/reperfusion injury [8]. Exosomes may also play a role in the crosstalk between tumors and MSCs. Therefore, the