Cancer has become the global health, social, and economic burden that direly needs a revolutionized novel treatment for a broad spectrum of tumors. Among the innovative and promising therapeutic modalities, the use of mesenchymal stem cells (MSCs) as a tool for delivering an antitumorigenic activity via its inherent antiproliferative capability or transportation of proteins or genes that suppress tumor has created a new way to circumvent cancers. MSCs are one of the most studied adult stem cells in the field of regenerative medicine, gene therapy, and immunomodulation due to its unique biological characteristics. Upon an in vivo administration, MSCs are able to migrate and home to the tumor site and exert either stimulatory or inhibitory effects on tumor cell growth, invasion, and metastasis via regulating angiogenesis, altering immune surveillance, modifying signaling pathways, and regulating apoptosis. Nonetheless, the mechanisms involved in the reported inhibition or stimulation are still elusive. Therefore, a better understanding of the biological consequences of MSCs–tumor interaction, prior to a successful MSCs based therapy, should be warranted. In this chapter, a number of previous findings associated with mutual interplays between MSCs and tumor cells are summarized and highlighted.