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Bone marrow-derived fibrocytes promote stem cell-like properties of lung cancer cells

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Abstract

Cancer stem cells (CSCs) represent a minor population that have clonal tumor initiation and self-renewal capacity and are responsible for tumor initiation, metastasis, and therapeutic resistance. CSCs reside in niches, which are composed of diverse types of stromal cells and extracellular matrix components. These stromal cells regulate CSC-like properties by providing secreted factors or by physical contact. Fibrocytes are differentiated from bone marrow-derived $CD14^+$ monocytes and have features of both macrophages and fibroblasts. Accumulating evidence has suggested that stromal fibrocytes might promote cancer progression. However, the role of fibrocytes in the CSC niches has not been revealed. We herein report that human fibrocytes enhanced the CSC-like properties of lung cancer cells through secreted factors, including osteopontin, CC-chemokine ligand 18, and plasminogen activator inhibitor-1. The PIK3K/AKT pathway was critical for fibrocytes to mediate the CSC-like functions of lung cancer cells. In human lung cancer specimens, the number of tumor-infiltrated fibrocytes was correlated with high expression of CSC-associated protein in cancer cells. These results suggest that fibrocytes may be a novel cell population that regulates the CSC-like properties of lung cancer cells in the CSC niches.