Editorial

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Invasion and Metastasis in the Viewpoint of Cell Adhesive Molecules

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The cell membrane may face a luminal surface, a matrix, or attached adjacent cells. It not only protects the cell from its surroundings, but is also involved in a variety of cellular processes, such as cell adhesion or attachment, ion conductivity, endocytosis or exocytosis, cell signaling, etc. It is not a simple structure, but a very delicate and detailed one. Inevitably, a cell receives outside information through its membrane, which acts like a messenger by way of receptors or molecules like receptors. So far, numerous receptors and membrane molecules have been named and their functions have been revealed by studies. Nevertheless, many parts and functions of the cell membrane remain to be unveiled [1].

Integrin is one of the numerous membrane molecules and transmembrane receptors that mediate the attachment between a cell and its surroundings, such as other cells or the extracellular matrix (ECM). Integrins work alongside other proteins, such as cadherins, immunoglobulin superfamily cell adhesion molecules, selectins, and syndecans, to mediate cell-cell and cell-matrix interactions and communication. Integrin also binds the cell's surface to ECM components such as fibronectin, vitronectin, collagen, and laminin. Many types of integrin molecules exist, and many cells have multiple types on their surfaces. Integrins are of vital importance to all animals and have been found in all animals [2].

Integrin has two main functions: attachment of the cell to the ECM and signal transduction from the ECM to the cell. In signal transduction, integrins pass information about the chemical composition and mechanical status of the ECM into the cell. That is to say, they play an important role in cell signaling by modulating the cell signaling pathways of transmembrane protein kinases such as receptor tyrosine kinase. However, they are also known to be involved in a wide range of other biological activities, including immune patrolling, cell migration, and binding of certain viruses to cells [3].

Invasion and metastasis are two distinguishing characteristics of cancer. These distort or disjoint the stable cell-cell and cell-matrix relation. Thus, the number of free or circulating integrins can be presumed to be larger during cancerous changes. As the author mentioned, these types of integrins might be correlated with circulating tumor cells away from the primary tumor site. In this point, we should consider integrins' roles again. Although they are an important structure of the cell membrane and are related to its stability, as adhesive molecules, they might contrarily play certain roles in the process of tissue invasion and metastasis: for example, the guiding, arrival and seeding of cancer cells at new sites. In this process, many of their roles have been reported via signaling interactions with surrounding cells, the ECM, or vessels [4, 5].

As above, we only considered the aspect of integrin; what about the invading or metastasizing cells themselves? As we know, cancer cells arise from the epithelium. Once they start to invade or metastasize, they are no longer epithelial cells. They begin to change their character to that of a mesenchymal cell. We name this process or phenomenon as the epithelial-mesenchymal transition (EMT). This not only is an important step through which epithelial cells transform into mesenchymal cells, as during embryonic development, but also is characterized by loss of cell polarity, decreased cell-to-cell adhesion, increased migratory ability, and increased invasiveness [6, 7]. According to recent studies, certain cancer cells even seem to be able to obtain a stem-cell-like phenotype during the EMT process. In this process, integrins, depending upon available ligands and their interactions with membrane receptors, seem to be able to transduce bi-directional signals to regulate cancer-cell migration and invasion-facilitating mechanisms such as the EMT [8, 9].

Especially, integrin α9β1 is expressed in human cancers and appears to correlate with a higher grade of malignancy. It also seems to play a role in angiogenesis and lymphangiogenesis, thus facilitating metastasis [10, 11]. Like the author suggested [12], integrin

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may be a potential factor or marker that can be used for determining a prognosis and for monitoring the progress of the disease. Moreover, by controlling the EMT process, we may be able to use integrins to target biologic therapy.

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