Preface

The ability of tissue cells to be attached to each other and to the surrounding solid substance (extracellular matrix) is a pivotal regulator of major cellular functions such as proliferation, responses to growth-stimulating factors, cell survival, differentiation, and migration of cells in an organism.

Therefore, the cellular adhesive interactions play a critical role in basic biological processes such as formation of tissues and organs in embryonic development, maintenance of structural integrity of all tissues in an adult organism, and tissue regeneration and remodeling. The adhesive interactions are also involved in inflammation and degeneration processes, which are at the basis of many diseases.

As a result of oncogenic transformation, the adhesive interactions of transformed cells are significantly altered. In the pathological behavior of malignant tumor cells, significant weakening of their ability to adhere to each other, to normal cells, and to the extracellular matrix, plays a key role. Alterations in these adhesive interactions form the basis of invasion and metastasis of malignant tumors.

Therefore, the understanding of mechanisms of cellular adhesive interactions and their alterations in malignant tumors is very important in both biological and medical aspects.

Adhesive Interactions in Normal and Transformed Cells starts with the description of molecular composition of *the extracellular matrix,* which tissue cells adhere to. The matrix proteins that are bound with the specific cell surface receptors resulting in the cell-matrix adhesion are also discussed.

Several sections are devoted to the *cytoskeleton systems*. Particular attention is given to the actin filaments and microtubules that play a pivotal role in cell-extracellular matrix and cell–cell adhesive interactions, and also in cell migration. The formation, regulation, and dynamics of these cytoskeleton systems are examined.

Different types of *pseudopodia* that are formed and used by cells as "driving organs" during cell spreading and cell migration are described.

Various types of *specific adhesion structures* formed by cells in order to attach to the extracellular matrix are considered. Attention is given to focal adhesions (focal contacts), to their structure, regulation, and dynamics, which play a critical role in cell migration.

Several sections are devoted to the intracellular *signal transduction pathways*. The signaling pathways are triggered by the extracellular molecules (ligands) that bind to specialized cell surface receptor proteins. Different types of cell surface receptors are characterized. Particular attention is given to integrin receptors, which as components of focal adhesions play a key role in cell-matrix attachment and also fulfill functions of transducers of intracellular signals. Different integrin receptor-mediated signaling pathways that determine and control cell morphology, proliferation, survival, and locomotion are considered. Also, the growth factor receptor-mediated mitogenic and morphogenic signaling pathways are examined.

Special attention is given to significant *alterations in the integrin mediated cell-matrix adhesion* caused by *oncogenic transformation* of the cells. The consequences of these alterations manifested in such typical traits of transformed cells as weakening of the cell-matrix adhesion, "anchorage independence", constitutive mitogenic activation, escape from anoikis, and high locomotory activity are considered.

The *movement of fibroblastic cells* and different factors involved in the cell locomotion machinery are considered. These factors include actin cytoskeleton reorganizations and microtubule dynamics, the phenomenon of "contact inhibition of cell locomotion", and dynamic regulation of focal adhesions during cell locomotion. The morphogenic action of soluble growth factors resulting in cell locomotion is also examined.

Several sections are devoted to fundamental *alterations in cell locomotion machinery* caused by *oncogenic transformation* of the cells. These alterations apply to the pseudopodial activity and focal adhesion formation in transformed cells, and also their sensitivity to growth factors.

The ability of cells to respond to the *adhesion heterogeneity* or various *geometrical configurations (topography) of the extracellular matrix surfaces* is discussed in detail. The topographic cell responses to cylindrical surfaces of high curvatures or the surface reliefs of various kinds (such as nanoscale or microscale linear grooves, holes, or vertical rods) are examined. These responses apply to the cell shape, locomotion, and other cellular functions. The mechanisms of these cell responses are discussed.

The *alterations in the topographic cell responses* caused by *oncogenic transformation* of cells are considered. In particular, alterations of the cell shape, changes in the direction of cell migration, and alterations in the functional activities as a result of oncogenic transformation are described.

Last chapter of the book is devoted to the *intercellular adhesive interactions.* The compositions of several types of the intercellular adhesion structures are described. Particular attention is paid to the adherens junctions, their structure and dynamic regulation, which is the basis of cell rearrangement and tissue integrity maintenance.

A critical contribution of cadherin receptors and local actin cytoskeleton to the regulation of cell–cell adhesion is examined. Signaling pathways coupling cadherin-mediated intercellular contacts to cell proliferation are considered.

The *cell–cell adhesion alterations* caused by *oncogenic transformation* of the cells are further examined. These alterations result in uncontrolled proliferation of malignant tumor cells, their inability to form orderly tissue structures, cancer invasion, and metastasis.

Adhesive Interactions in Normal and Transformed Cells is based on modern scientific data and includes the results of the author's long-term research. It is intended for researchers, postdocs, undergraduate, and graduate students, whose scientific interests are in the fields of cell biology, cancer biology, cancer research, and developmental biology.

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