

# Preface

Cancer is a term used for diseases that affect any organ in the body, in which abnormal cells divide in an uncontrolled manner and in some instances are able to invade other tissues. Cancer is not just one disease, but many diseases with origins in multiple different organ systems. The defining abnormality in cancer is an imbalance between cell proliferation and death and is caused by mutations in DNA that code for proteins that regulate these cellular processes. Genes that promote cell growth in tumors are called proto-oncogenes, while tumor suppressor genes code for proteins that mediate antiproliferation signals and suppress mitosis and cell growth. Upregulation of proto-oncogenes and/or downregulation of tumor suppressor genes are a common event in cancer.

Cells do not exist in isolation and require interactions with extracellular matrix (ECM) components in order to undergo normal morphogenesis with respect to organogenesis. ECM, which is composed of large macromolecules (e.g., collagens, fibronectin, laminins) and polysaccharides (e.g., glycosaminoglycans such as hyaluronan), plays a significant role in regulating numerous cellular functions including cell shape, adhesion, migration, proliferation, polarity, differentiation, and apoptosis. In physiological conditions, ECM levels are tightly regulated by a fine balance between synthesis and degradation. However, in pathological conditions, such as cancer, both increased synthesis of certain ECM components (i.e., collagens, fibronectin, and laminins) and/or increased breakdown with consequent generation of ECM cleavage products (i.e., laminin- or collagen-cleavage products) can contribute to cancer growth and progression. Finally, the observation that many growth factors (i.e., FGF, VEGF) are stored in the ECM milieu and released upon protease-dependent cleavage further confirms the importance of ECM in regulating cell functions.

Cells interact with ECM via a family of transmembrane receptors, known as integrins. These receptors are not only important for cells to adhere on ECM, but are also important regulators of cell signaling that controls cell processes such as proliferation, apoptosis, and migration. These signals are either transduced via the integrins upon binding to ECM components or by a crosstalk between integrins and

growth factor receptors. Both integrins and growth factor receptors have been shown to bind either directly and/or indirectly with numerous signaling and scaffolding molecules that have been linked to oncogenesis.

The overall goal of this book is to describe how ECM creates a niche for tumor formation and the contribution of ECM components and their respective receptors in the development and spread of cancer.

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