

Preface

During the last century cancer research was mainly focussed on the tumor cells alone which could be easily propagated in cell culture. During this time many important findings were obtained clearly demonstrating that cancer is a genetic disease, controlled by the activation and/or inactivation of critical control genes.

However during the last two decades it has become increasingly clear that genetic alterations alone are not the sole driving force behind tumor development but that tumor growth and progression are rather intimately controlled by the microenvironment. One could almost speak of a “rediscovery” of the tumor as a highly complex tissue composed of carcinoma cells and surrounding stroma. Studies in different areas of biology including tumour biology have demonstrated that tissue structure, function and dysfunction are highly intertwined with the microenvironment and that during the development of cancer tissue biology and host physiology are subverted to drive malignant progression. It is now clear that the context is crucial and that the status of the cellular microenvironment plays a significant role in determining whether cells within a tissue retain their normal architecture or undergo tumor progression.

The tumor stroma or microenvironment is made up of multiple non-malignant cell populations, including fibroblasts, adipocytes, endothelial and inflammatory cells that are embedded in a tumour specific extracellular matrix (ECM). Nowadays, there is a huge interest in tumor stroma research, and in understanding the contributions of the different stromal cell types to tumor growth and progression. One of the key components of the tumor microenvironment in carcinomas are activated fibroblasts termed cancer associated fibroblasts (CAFs). In the meantime our knowledge of CAFs has changed from being viewed as a passive bystander to becoming an important co-mediator of cancer progression.

In response to cancer growth, host stromal fibroblasts undergo a dramatic morphologic and biochemical transition to form “reactive stroma” in a desmoplastic reaction much like the granulation tissues found at the site of wound healing. While the malignant cells activate fibroblasts in the tumor stroma by various stimuli, including growth factors and cytokines, cancer associated fibroblasts secrete growth factors and build a permissive soil in which the cancer cells thrive. CAFs are responsible for the elaboration of most of the connective tissue and ECM components

as well as, proteolytic enzymes and their inhibitors. The composition and structure of the ECM in the tumor microenvironment is essential for promoting tumor development and metastasis. The constituents of the ECM include collagens, laminins, fibronectin and several proteoglycans. They provide mechanical support for cells, facilitate cell communication and serve as substrates for cell migration. Changes in the composition or architecture of the extracellular matrix within tumors can alter integrin expression and function and promote metastatic progression, angiogenesis and lymphangiogenesis.

In this unique textbook world leading experts of the area of tumor microenvironment review the most recent knowledge of the still growing complexity of the tumor microenvironment focussing on tumor associated stromal cells and the most important extracellular matrix components and summarize the role of these players in tumor progression. Moreover, novel therapeutic targets are discussed that have been discovered in the tumor microenvironment and are increasingly used in experimental and clinical tumor therapy. The message from their contributions is clear: the tumor microenvironment and its components are important and essential players in tumor progression and interesting targets for novel therapeutic strategies. However there are still many white areas on the map and we are just beginning to understand the complex interplay between tumor and stromal cells.

We express our deepest gratitude to all our colleagues who have made this book the first comprehensive anthology covering all major aspects of the role of the tumor microenvironment and its extracellular matrix components.

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