Preface

Cells are social entities. As such, they need to interact and communicate with each other, in order to be able to build organized structures of tissues, organs, and organisms or to ensure functional and physiological coordination. Cells dedicate considerable energy and various mechanisms to ensure cell-cell communication, because it is important for their survival, behavior, and fate within their environment. For cells, communicating is vital not only because they are part of organs and tissues of which they maintain the integrity and function but also because many of their functions need to be coordinated, fine-tuned, and limited spatiotemporally. Furthermore, cells use communication to minimize the energetic and signaling burden, whereas a single minimal signal could be amplified and propagated. The diversity of the types of intercellular communications emphasizes the need for cells to communicate in different ways and for different purposes, transfer of small molecules, signaling, establishment of barriers/polarity, paracellular permeability, and transmission of cytoskeleton-generated forces, all of which play critical roles in normal physiology and pathological development such as in cancer. As in many other diseases, an essential part of tumor genesis and progression is the deregulation of the ability of cells to communicate and transmit information to and receive signaling input from neighboring cells.

Communication as a basic cellular need uses different modes. A classical mode involves growth factors and other signaling molecules released by cells to act either locally as autocrine or paracrine moieties or to be systemically transported via the body fluids to affect the biology of remote target cells. However, the subject of this book on *Intercellular Communication in Cancer* is another mode of cell-cell communication that involves a direct contact between cell membranes.

First, we review junctional modes of intercellular communication. These modes are associated with the building of elaborate protein complexes, arranged to form specialized junctions between cells. Chapter 1 by Talhouk and colleagues shows an example of how the so-called gap junctions and their building blocks the connexin proteins regulate normal and malignant processes, i.e., in the mammary gland. Connexins can also be important in the communication of cancer cells with cellular components of their microenvironment, a process discussed in Chap. 2 by Lathia and colleagues in the context of brain tumors. Gap junctions have been classically known to ensure the transfer of ions and other small moieties. More recently, they have been shown as conduits for the transfer of important nucleic acid molecules such as microRNAs. As explained by Rameshwar and colleagues in Chap. 3, this mechanism could have an important impact on cellular therapy of glioblastomas.

The next chapters will introduce examples of other types of junctional intercellular communication. In Chap. 4, we can read from Jacquier-Sarlin and colleagues about how adherens junctions are regulated to play an essential function in cell differentiation and what the impact is on tumor development. In Chap. 5, Sen and colleagues, after introducing cadherins, the major component of adherens junctions, explain different computational and mathematical approaches used to explore different aspects of cadherin-mediated cell-cell adhesions. Furthermore, Al-Moustafa and colleagues, in Chap. 6, provide an overview of the role of E-cadherin/catenin complex modulations in human oral cancer and shed light on how the high-risk human papillomaviruses (HPVs) interfere with this complex to promote oral cancer progression.

In addition to junction-based interactions, we are also witnessing a growing interest in the role of non-junctional modes of cell-cell communication. First, Alaoui-Jamali and colleagues discuss the role of small cell-derived membranous vesicles released by cancer cells called exosomes, in metastatic signaling. They describe in Chap. 7 the use of exosomes as tumor biomarkers and their therapeutic impact. Another mode of cell-cell communication, introduced by Lou and colleagues in Chap. 8, addresses another type of membranous structures called tunneling nanotubes, which are made of elongated intercellular conduits that form bridges between cells. In other respects, in Chap. 9, Parris discusses the concept of cell-cell fusion between abnormal cells with "task force" cells of the immune system and its role in cancer progression. In line with these chapters, as Kandouz and colleagues explain in Chap. 10, cell-cell communication can be achieved without necessarily involving junctional structures, via Eph receptors and ephrin ligands, which constitute the largest family of receptor tyrosine kinases.

This book would have been incomplete if no chapters were dedicated to viewing cell-cell communication in the context of a community dynamic. Komurov in Chap. 11 describes computational approaches to modeling of molecular interactions in multicellular systems, while Goldberg and colleagues describe in Chap. 12 a process called contact normalization of tumor cells by communicating with neighboring normal cells. Last but not least, in Chap. 13, Nelson and colleagues provide an overview of intercellular communication within the tumor microenvironment.

We believe that the chapters presented in this volume provide a global overview of different modes of membrane-to-membrane intercellular communication. They are intended to update researchers in the field about novel developments and also to constitute an important knowledge base for researchers contemplating to engage in this exciting and rich research area. Nevertheless, it should be noted that this book is not an exhaustive repertoire of all known types of cell-cell communication. Rather, we made admittedly subjective choices to illustrate the diversity of these modes and their instrumental role in cancer.

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http://www.springer.com/978-94-017-7379-9

Intercellular Communication in Cancer
Kandouz, M. (Ed.)
2015, VIII, 366 p. 37 illus., 34 illus. in color., Hardcover
ISBN: 978-94-017-7379-9