This book was conceived to celebrate the fifteenth anniversary of the discovery of prominin-1, also known in the medical field as CD133. Since its original description in 1997 in the murine system by Anja Weigmann, myself, Andrea Hellwig and Wieland B. Huttner (Proc Natl Acad Sci USA, 94; 12425–12430), and independently in the human system by David W. Buck and his team (Blood, 90; 5002–5012; 5013–5021), this cholesterol-binding pentaspan membrane glycoprotein has emerged as the object of great attention worldwide. This coincides with the identification and isolation of stem cells from different types of tissue and organ for which prominin-1 has become one of the most valuable cell surface markers with clinical value. Expectations for the development of novel therapies through the replacement and regeneration of damaged or diseased tissues based on isolated stem cells has made this field one of the leading edges on the frontiers of modern medicine. The expression of prominin-1 by putative cancer stem cells has also brought new horizon in cancer treatments, and this molecule may be regarded as a potential target in the eradication of cancers. The medical significance of prominin-1 is also highlighted in the visual system where mutations in the PROM1 gene cause retinal degeneration.

As a biochemist, my long-standing interest in prominin-1 has brought me in the field of tissue engineering and cellular regeneration to understand the biological basis of tissue formation. The study of the molecular cell biology of prominin-1 in diverse cell types, e.g., epithelial cells, stem cells, and photoreceptors, which reflects by itself the broad tissue distribution of prominin-1, has emphasized divers’ phenomena including the organization, remodeling, and dynamics of the plasma membrane as important factors regulating specific properties of the cells. Remarkably, these mechanisms appear conserved despite the considerable difference in cellular function of the cells in question (e.g., stem cell versus photoreceptor). The budding of membrane vesicles containing prominin-1 from the tip of microvilli of polarized epithelial cells and their release during the process of stem cell differentiation, and the organization of photoreceptor cell outer segment are good examples. I believe that the exploration of prominin’s function(s) in various model organisms such as
mice, zebra fish, axolotls, and flies would bring more insights, not only for cell biological trends, but also in organogenesis and tissue regeneration.

This book is composed of 15 chapters that will describe, on one hand, the molecular and cellular biology of prominin-1 and other members of the prominin family and, on the other hand, the importance of this molecule in the medical field as a valuable marker of stem and cancer stem cells. The opening chapter by my coworkers and myself presents an overview of the identification of prominin-1, its relation to the widely used AC133 epitope, and the general interest of this molecule in regenerative medicine. This chapter is intended as an introduction to the book and provides molecular details of prominin-1 across species including splice variants, tissue distribution, and certain biochemical properties including its specific subcellular localization in plasma membrane protrusions. It connects directly with the topics elaborated in the subsequent chapters of the initial section constructed as a knowledge base essential to the grasp of the physiological function(s) of this glycoprotein with a particular medical interest: CD133. My colleague Christine A. Fargeas presents prominin-2, the prominin-1 paralog, and the evolution of the prominin family of proteins among the animal kingdom. Then, as prominin-1 is not only tightly associated with plasma membrane protrusions, but also released in association with membrane particles into different body fluids, Anne-Marie Marzesco describes such singularity not only from a cell biology aspect, but also clinically, as prominin-1-containing membrane vesicles might be recognized as potential biomarkers in certain diseases. In the fourth chapter, Elisabeth Knust and her colleagues describe the eminent role of prominin in the retina, which demonstrates not only the significance of prominin-1 in the vision but also its evolutionary conserved function in the maintenance of photoreceptive membranes from humans to flies. Kouichi Tabu and his colleagues present in the next chapter the complex gene regulation of PROM1 in normal and cancerous tissues. In the following 10 chapters, my colleagues describe new aspects of prominin-1-positive cells and the utility of this molecule as a marker of stem cells and cancer stem cells. Numerous tissues and organs are thus virtually dissected with regards to the expression of prominin-1 and the normal and cancerous cells harboring stem cell properties, i.e., self-renewal and multipotential differentiation capacities. In Chap. 6, Wieland B. Huttner, whose laboratory discovered murine prominin-1, presents with his coworker Alex M. Sykes novel features of neuroepithelial cells, precursors of all neurons of the central nervous system, including the asymmetric cell division. Rupert Handgretinger and Selim Küci present in great detail the importance of human prominin-1 (CD133) in the hematopoietic system and bring an update on the use of CD133+ cells in autologous and allogeneic hematopoietic stem cell transplantation. In humans, the clinical relevance of CD133+ cells is not limited to blood system; Benedetta Bussolati and Giovanni Camussi describe, for instance, the expression of CD133 in kidney under normal and pathological conditions. Although the possible use of CD133+ progenitors in human studies presents obvious limitations due to immunological barriers, the in vivo experiments reported in mice suggest a potential role of progenitors in renal regeneration. Mariusz Z. Ratajczak and colleagues present the expression of CD133 by very small embryonic/epiblast-like stem cells (VSELs), and its use for their
prospective immunoisolation. VSELs could provide a therapeutic alternative to the controversial use of human embryonic stem cells. Afterward, three clinically important organs are reviewed. Alessandro Sgambato and colleagues present the current knowledge on CD133 expression in normal and cancer colon tissues, both in humans and mice, and discuss the apparently conflicting data reported. Moreover, the authors devote great attention to the available information about the functional role of CD133 in colon cancer cells. Likewise, Norman J. Maitland and colleagues dissect the current literature regarding prostate cancer stem cells, with specific reference to the expression of CD133 as a stem cell marker to identify and purify stem cells in normal prostate epithelium and prostate cancer. In Chap. 12, Yuichi Hori reveals new facets of pancreatic progenitor cells and cancer stem cells by studying CD133 expression. Because it is also associated with melanoma stem cells, Aurelio Lorico and colleagues elegantly present the importance of CD133 as a therapeutic target. The two final chapters describe the diverse origins and utilizations of CD133+ cells. Peter Donndorf and Gustav Steinhoff give a thorough account of cardiac stem cell therapy, and Yvan Torrente and colleagues discuss potential therapeutic applications of CD133+ cells for degenerative diseases including muscular dystrophies.

Taken as a whole, I have attempted to gather almost all topics of significance to the prominin-1 research field and to its medical weight as a cell surface marker of stem and cancer stem cells. I have been greatly encouraged in this project by positive feedback from worldwide-recognized scientists and physicians working in these fields. Finally, it is my privilege to have the opportunity to edit these chapters and, also on behalf of all coauthors, to thank everyone who has helped us to produce this book.

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