

Epithelial-Mesenchymal Interactions in Cancer; Edited by I.D. Goldberg and E.M. Rosen; Birkhäuser, Basel-Boston-Berlin, 1995. xii + 298 pp (hc). ISBN 3 7643 5117 9

Epithelial-mesenchymal/stromal interactions are crucial for embryogenesis, development, and maintenance of tissue organization as well as controlled tissue remodeling such as that of wound healing processes. It has long been known that the finely tuned balance between epithelium and stroma is perturbed in cancer. However, only within the latest decade have major steps forward in the understanding of the underlying processes been taken. The editorial introduction to this book (pp. ix–xii) promises to present highlights of the molecular mechanisms through which tumor cells interact with stroma.

The book contains fourteen chapters each comprising 10 to 34 pages including 36 to 190 references up to 1994. Many of the chapters include tables, line-drawings and micrographs, which are very helpful both to provide overview as well as to emphasize on details. The chapters: 'The Met-HGF/SF autocrine signaling mechanism is involved in sarcomagenesis' by Cortner et al. and 'Angiogenesis as a component of epithelial-mesenchymal interactions' by Grant et al. are presented as original papers, whereas the other chapters are reviews including data from some of the authors' own previously published papers. Although some consistency in the composition of the chapters would have given the book a more coherent appearance, both ways of presentation provide the reader with an insight into the extensive knowledge that the authors have in their respective fields of research. If used as a reference book for the different subjects discussed, the chapters can indeed stand alone. However, if the intention is to read the book as a whole to get an overview of the rapidly expanding area of epithelial-stromal interaction in cancer, one should be prepared for some difficulty. It is beyond any doubt that scatter factor (SF) is a topical mediator of epithelial-stromal interaction, but still, SF is probably not the answer to all our questions regarding tumor development and progression as one might be led to believe since six out of fourteen chapters focus mainly on SF. Consequently, the introductory sections of these chapters overlap somewhat, and references to the other chapters could to some extent have prevented this. Also, it would help the reader if the same terminology for scatter factor (SF/HGF) and its receptor (HGF-receptor/*c-met*/*Met*/*c-met* proto-oncogene) were used throughout. Nevertheless, each of the six chapters adds new information about SF.

Based on their own work on targeted mutation in the mouse, Birchmeier and Birchmeier (pp. 1–15) describe what is currently known about the role of SF in embryonic development, and the so-called epithelial-mesenchymal transition as defined by morphology. The role of E-cadherin in experimentally induced transition and in metastasis formation is reviewed. The molecular composition of intercellular junctions and how they are influenced by SF and E-cadherin is discussed in another chapter by Nusrat and Madara (pp. 69–87). Together, the two chapters make the point of the importance of intercellular junctions for correct tissue development and organization.

The following chapter by Rosen and Goldberg (pp. 17–31) provides data and hypotheses for the production of SF in tumors including the origin of SF-producing cells and how SF production might be regulated in culture. Normal breast fibroblasts as well as tumor-derived fibroblasts are tested in culture for their ability to produce SF in response to various cytokines. Based on the hypothesis of autocrine stimulation of SF in breast tumor fibroblasts, one would expect tumor fibroblasts to produce more SF than their normal breast counterparts, but this is unfortunately not addressed and the suggested models for SF-inducers and inducers of SF-inducers are somewhat speculative. Zarnegar (pp. 33–49) goes on to describe thoroughly what is currently known about the SF-gene and its promoter region as well as the SF-receptor (*c-met*) and its regulation by cytokines. Zarnegar also proposes a model for the coordinated expression of SF and SF-receptor, and here, some of the implicated SF- and *c-met*-inducers are known cytokines.

Polverini and Nickoloff (pp. 51–67) approach SF and its receptor from the point of angiogenesis. They give a good, brief and general

introduction to angiogenesis and an overview of known angiogenic mediators. SF as an inducer of angiogenesis both in vivo and in culture is discussed and the chapter is well illustrated. The paper by Cortner et al. (pp. 89–121) also deals with SF and its receptor, but more specifically as an autocrine signaling mechanism in sarcomagenesis. Data on SF and SF-receptor expression in cell strains and tissue sections are presented, and their significance in tumorigenesis in nude mice is implied.

At page 123, the book, and one is tempted to say finally, moves on to include a broader spectrum of epithelial-stromal interactions than those related to SF. Nicolson (pp. 123–156) very capably explains the heterogeneity and functional differentiation of endothelial cells, which are targets for angiogenic cytokines and basis for metastatic colonization. The cell-adhesion and extracellular matrix molecules involved are thoroughly discussed and contemporary references are given. In addition, growth factors for endothelium secreted by tumor cells and vice versa are reviewed. While angiogenesis is also discussed by Grant et al. (pp. 235–248), the two chapters are not redundant since the latter focuses on the significance of extracellular matrix and specific peptide sequences herein for endothelial tube formation. Levine et al. (pp. 157–179) also touch on the importance of extracellular matrix components and cell-adhesion molecules in invasion and metastasis, but emphasize their own work on 'autotaxin', which is an autocrine stimulator of motility in tumor cell lines. Thus, this and the following chapter by Kacinski (pp. 181–190) on cytokines influencing ovarian carcinoma cell lines are among the more specified chapters.

Another relatively recently discovered cytokine crucial for epithelial-stromal interactions is keratinocyte growth factor. Rubin et al. (pp. 191–214) excellently tell the story of keratinocyte growth factor including its physical and biological properties, expression patterns and possible involvement in cancer, and the presented figures nicely support the text.

In addition to dissemination and migration of tumor cells, proteolysis is instrumental for invasion and metastasis. A compact and well referenced review of proteolytic enzymes, with emphasis on type IV collagenase, in angiogenesis, invasion and metastasis is presented by Shi and Liu (pp. 215–234).

Finally, two chapters are devoted to the phenotypic characteristics and role of fibroblasts in tumor formation. Indeed at this point the reader is curious to learn more about the interacting fibroblasts. Whereas Hornby and Cullen (pp. 249–271) concentrate on the biological functions of stromal extracellular matrix components and cytokines implicated in breast cancer, Schor (pp. 273–296) considers the hypothesis that several subpopulations of fibroblasts exist, and some of these are accelerators of cancer progression. In these chapters, as well as in several of the others, the behavior of cultured cells is extrapolated to be true also for the tissue of origin. One could argue that current literature on both tumor cells and stromal cells suggests that this assumption should be stipulated: Cells derived from normal tissue have phenotypic traits induced that resemble those of the malignant tissue by the mere event of being placed in monolayer culture in the presence of serum. Thus, they may no longer be representative for the cells in situ. Nevertheless, it becomes clear to the reader that broadening of cancer research to encompass the role of stromal cells has provided additional clues as to how tumors develop and progress, and that this is certainly an important field of research to pursue.

To conclude, the editors have succeeded in putting together a book which indeed highlights some of the crucial mechanisms in epithelial-stromal interactions. The book is a very helpful tool as an introduction, and with the many literature references given, it is also suitable as a reference for further exploring of particular subjects of interest.

Lone Rønnov-Jessen