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Half the Secret of Life Is outside the Cell

Extracellular Matrix–Cell Interaction: Molecules to Diseases
Edited by Yoshifumi Ninomiya, Bjorn R. Olsen, and Toshiro Ooyama
Basel, Switzerland: S. Karger AG (1998). 382 pp. $255.75

Matrix Metalloproteinases
Edited by William C. Parks, and Robert P. Mecham
San Diego, CA: Academic Press (1998). 362 pp. $89.00

In the nineteenth century, the extracellular matrix (ECM) was viewed as an amorphous "ground substance" embedded with various types of fibers, providing support for cells in tissues. Early in this century, the scientific investigation of the structure and biochemistry of the ECM grew out of the needs of the leather, tanning, and glue industries, because the collagen-rich connective tissue ECM forms the major component of skin. "Twenty years ago . . . when we asked . . . students what extracellular matrix was they answered, 'It is abundant and exists on the outside of cells. It is inert, does not change much but builds up a complex architecture. . . .' Today they would answer, 'Extracellular matrix plays an important role in development, cell differentiation, cancer metastasis, and pathogenesis of various disorders'" (*Extracellular Matrix–Cell Interactions*, p. v).

How and why has there been such a remarkable change in the perception of the ECM? After half a century of toil on ECM structure, scientists realized only recently that the biologic unit of function is a cell and its ECM. As such, ECM is fundamental to the most important concepts in cell and molecular biology. Without ECM and ECM adhesion, cells fail to polarize, respond to growth factors or migrate. They are miscued, and either die or misbehave. The cell cycle, apoptosis, signal transduction, cytoarchitecture, and differentiation of individual cells in isolation all require inputs from ECM. The development and morphogenesis of multicellular tissues require ECM for signaling, as well as for structural and mechanical support. Genetic mutations and acquired alterations of the ECM and its remodeling contribute significantly to major human disease processes including arthritis, atherosclerosis, and tumor progression.

The concept of ECM degradation was pioneered in 1962 by Gross and Lapiere, who found that collagenase, the first eukaryotic matrix metalloproteinase (MMP), was produced by cultures of resorbing tails of tadpoles undergoing metamorphosis. Subsequently more than 20 MMPs have been found in organisms as diverse as plants and man, and in many tissues during development, repair, and disease. It is only in the last five years that the importance of proteolysis of the ECM and cell surface proteins as a mechanism for extracellular signal transduction has come to the fore (Werb, 1997). The consequences of proteolysis are signals for life or death, altered bioavailability of growth or differentiation factors, and altered cellular adhesion and organization.

What both *Extracellular Matrix–Cell Interaction: Molecules to Diseases* and *Matrix Metalloproteinases* promise to deliver is a wealth of information about ECM macromolecules and their remodeling. However what both books fail to convey is why ECM is so topical, why the cell and molecular biology of ECM–cell interaction and extracellular proteolysis are hot areas of research (with more than 2000 papers per year added to the literature) or why newcomers may wish to enter these fields. The now dated second edition of *Cell Biology of the Extracellular Matrix* edited by Elizabeth Hay (1991) did this more successfully. Perhaps the excitement in this rapidly advancing field can be captured only in research articles and journal reviews. The most seminal advances in ECM and MMP mechanisms have come from the genetic analysis of human and mouse diseases, and from phenotypic analysis of induced mutations in mice. An emerging concept in this field is that common polymorphisms that alter transcription of ECM and MMP genes may be risk factors for human diseases. Very recently common genetic variants of the stromelysin-1 (MMP3) and collagenase-1 (MMP1) gene promoters have been found that alter gene expression and are associated with progression of atherosclerosis (Ye et al., 1996) and tumors (Rutter et al., 1998).

Still, books should be able to capture the basic concepts underlying critical questions that remain to be answered. With the exceptions of the chapters by Krane and Zhou (p. 1) in *Extracellular Matrix–Cell Interaction* on the collagenase cleavage site mutation in type I collagen, and the overview of *Matrix Metalloproteinases* by Woessner (p. 1), both books lack the critical analysis and speculation as to what the key questions are, or what mechanisms govern the biologic effects. The chapters tend to be lists of experiments done, substrates degraded, sequences mutated, often exclusively from the authors' own laboratories. Inherent to all multiauthor books is some redundancy and inconsistency in quality. However, the multiplicity of proteins and the complexity of the field are such that there is little overlap among chapters in these two volumes.

Overall, *Matrix Metalloproteinases* is the more successful book. It is an encyclopedic and up-to-date compendium of the minute details of the literature on all the characterized MMPs for specialists in this field. Unlike the earlier *Matrix Metalloproteinases and Inhibitors* edited by Birkedal-Hansen et al. (1992), it is not comprehensive. The editors' decision not to include a chapter on the tissue inhibitors of metalloproteinases (TIMPs) is unfortunate, but can be overcome by reading recent reviews (Willenbrock and Murphy, 1994). The book would also have benefited from inclusion of a chapter on the structurally related ADAMs (the adamalysin-related transmembrane metalloproteinases with disintegrin domains), which have important functions in modification

and shedding of ectodomains of cell surface proteins (Blobel, 1997; Werb and Yan, 1998). Similarly, given the importance of structural considerations in MMP activation and substrate choice, it is remarkable that not a single X-ray crystallographic structure of an MMP (e.g., Fernandez-Catalan et al., 1998) appears in *Matrix Metalloproteinases*. The book is also impoverished of illustrations. The half-tone pictures are truly dreadful. The inclusion of more diagrams and color photographs would have made the presentations clearer and more accessible. Yet the high quality of the authors means that the material presented is accurate and not overinterpreted, and the separation of the chapters into individual MMPs provides a foundation for further studies. But, would I buy it? Yes. Even with these faults, it is useful to have one place where detailed information and primary citations on MMPs are available.

Extracellular Matrix–Cell Interactions is less successful, with chapters of uneven quality both in content and style. Overall this book suffers from being primarily a meeting report. The title of the book is an unfortunate choice because cell adhesion, the major form of cell interaction, is completely ignored. However, the emphasis on ECM genetics, structure, and diseases is timely. The book is neither comprehensive nor basic. Still, it covers material not readily available elsewhere. Selected articles are useful reading for researchers who study the genetics and biochemistry of ECM, because of treatment of subjects rarely reviewed and inclusion of many unpublished results. I found the chapters on effects of mutation of the collagenase substrate (p. 1), laminin assembly (p. 41), tenascin-C in cancer (p. 87), type IV collagen genes (p. 235), and the genetics of cartilage collagens (p. 323) particularly enlightening. There is also a scholarly coverage of the genetic basis of connective tissue diseases. However, this information is readily available in recent review articles (Gorski and Olsen, 1998; Lukashev and Werb, 1998). The beginner will find these papers and related review series in *Trends in Cell Biology* and *Current Opinion in Cell Biology* more accessible.

Are books published on ECM useful? Yes. For specialists several of the other volumes in the *Biology of Extracellular Matrix Series*, edited by Robert P. Mecham have a more comprehensive coverage of the structure, function, and assembly of ECM and adhesion molecules, such as proteoglycans, fibronectin, collagens, and integrins. But no one book or review article can fast-track a novice on the history, conceptual framework, jargon, and multiplicity of components of ECM. For the less scientifically sophisticated reader, a comprehensive but brief and basic overview of ECM proteins, adhesion molecules, and proteases is far more useful. The second edition of *Guidebook to the Extracellular Matrix and Adhesion Molecules* edited by the late Thomas Kreis, and Ron Vale (Oxford University Press, due out March 1999) will fill this niche nicely.

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Means to Ends: Establishing Cell Polarity

Advances in Molecular and Cell Biology: Volume 26, Cell Polarity
Edited by James R. Bartles and E. Edward Bittar
Stamford, CT: JAI Press (1998). $128.50

Because so many biological functions—motility, tissue communication and architecture, differentiation, and more—rely upon the polarity of cells, mechanistic analyses frequently require addressing such basic questions as how asymmetry is specified, constructed, and maintained. The field began as descriptions at the level of microscopy of morphologically differentiated domains; it has benefited enormously in recent years from applications of molecular biology, genetics, and biochemistry. The identification of molecules displaying a restricted pattern of localization, and of mutations that affect those patterns, has provided high-resolution markers of individual steps in the expression of polarity as well as an evolving picture of the underlying machinery. Arguably the most striking and important consequence of this work is an appreciation of the extent to which homologous markers and mechanisms are common to otherwise disparate systems. For example, the details of yeast bud site selection often parallel those associated with compartmentalization of animal cell domains. Although the lists of components are continuing to expand, and the nominally simplifying diagrams at the ends of papers are in fact growing more complex, the data promise syntheses to come.

All of which would make this time ideal for a book that explicitly makes the case for areas of convergence and divergence. *Cell Polarity*, the 1998 number of the *Advances in Molecular and Cell Biology* series, is only partly the book called for. It contains six essays, each dealing with a cell type. The editors' choices include some of the standards in this area—yeast, epithelia, neurons, and cultured fibroblasts—along with two systems—the early mouse embryo and skeletal muscle—