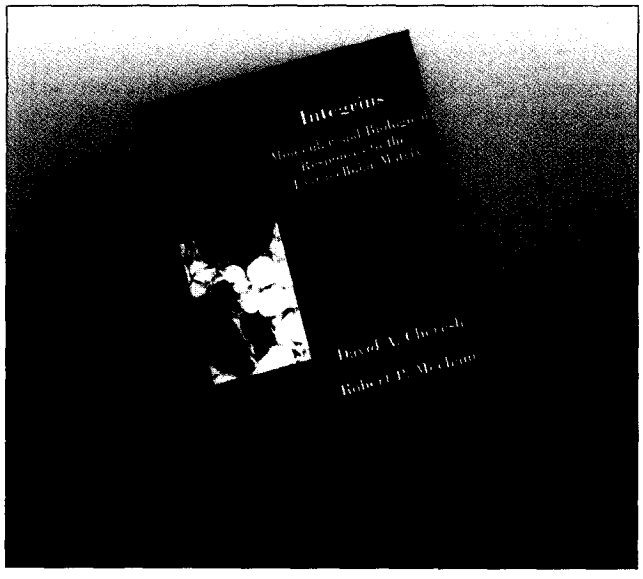
The ins and outs of integrins

Chemistry & Biology August 1995, **2**:515–516

Integrins: Molecular and Biological Responses to the Extracellular Matrix edited by David A Cheresh and Robert P Mecham. Academic Press, 1994, 278 pages. $89.95 hardcover (ISBN 0-12-171160-9).



If, like me, you are new to the field of integrin biology, you may have been looking for a slim volume that covers most of the main topics of this rapidly expanding field; this may be the book for you. This *vade-mecum* describes in depth most of the important aspects of integrin structure, function and biology, a field that has attracted scientists engaged in basic, applied and clinical aspects of medical research. Each chapter is a stand-alone review written by experts in the field, and is fully referenced with titles. A textbook of current research is, of course, an oxymoron, and this book covers the field until the end of 1993. The organization is such that many topics get touched on more than once, and I found the multiple points of view very useful.

Integrins are heterodimeric proteins that span the plasma membrane; they have a large extracellular portion, a transmembrane helix and a short but very important cytoplasmic tail. They promote both cell–cell and cell–matrix interactions, and while their extracellular domains are sticking to other proteins, their cytoplasmic tails are doing all sorts of interesting things, including reorganizing the cytoskeleton. Sometimes the tails can trigger the activation of the binding domains (inside-out signaling). On the other hand, sometimes it is binding to the outside that triggers intracellular signal transduction pathways (outside-in signaling). If integrins represent a connection between the extracellular environment and the intracellular compartment, then the corollary is that whenever the environment of a cell influences its activity (i.e. most of the time) integrins have an obligatory and maybe essential role. This means that they are going to be implicated in the whole gamut of cell biology and disease; they are important in cell differentiation, proliferation and migration, so they are involved in embryogenesis, wound healing, inflammation, cancer, and so on. There are so far 21 members of the integrin family, defined by the pairing of distinct α and β subunits, expressed on different cell types with very different or sometimes very similar specificities. With a family of this size, one feels it should one day be possible to know them all on a first-name basis. In the meantime this book has a very handy index so you need not worry about confusing $\alpha^6\beta_4$ and $\alpha^v\beta_6$ ever again.

The book kicks off with a stimulating chapter on the structural basis of integrin–ligand interactions, providing a nice introduction and background to the rest of the book. Of course there was no three-dimensional information available on integrins when this chapter was written, so some of the speculation is rather fanciful. The importance of the I domain in ligand binding had not been demonstrated when Chapter 1 was written, but luckily by the time we get to Chapter 7, the role of the I domain has been established. The author makes one mistake in proposing that Asp is preferred to Glu because Asp is longer than Glu; Asp is shorter.

The next four chapters discuss the big topics. Covered first is the role of integrins in signaling. This chapter is necessarily short, because although integrins are unambiguously involved in a variety of signal transduction pathways, the field is still at the stage of 'what gets phosphorylated when and where', without being able to distinguish between deliberate targets and innocent bystanders. It is also short so as not to preempt the next chapter on interactions with the cytoskeleton. The chapter is long enough, however, to make clear how fascinating it is that these short and innocuous-looking cytoplasmic domains can do so much, and raise the question of how does transmembrane signaling work? Chapter 3 reviews the expanding database on focal adhesion: again, lots of interesting data, lots of unanswered questions. Next comes a chapter on interactions with the extracellular matrix, presenting evidence for the involvement of integrins in both the induction and the recognition of changes in the composition of the extracellular matrix. These intersecting events presumably regulate morphogenesis, differentiation, tissue regeneration, and, in pathogenic situations, tumor growth and metastasis. Chapter 5 has one of those apparently profound titles: 'Integrins in development'.

But, as the authors note, most of the studies focus on the question of when and where integrins appear during development; no big answers here yet. Still, the chapter provides a useful compendium of data.

Chapters 6–8 focus on particular cell types and/or particular integrins. We get a rather personal account of epithelial cell integrins, focussing on the somewhat obscure $\alpha^6\beta_4$, and this is followed by a well written and comprehensive account of the more familiar leukocyte integrins, and the dynamic regulation of integrin adhesiveness in trafficking. Next, there is a very complete account of the doyen of the integrin class, $\alpha^{IIb}\beta_3$ (the 'platelet integrin').

Finally, there is a discussion of the therapeutic potential of integrin antagonists. These have applications in the treatment of thrombosis, inflammation, tissue remodeling and cancer. The focus is on drug design to treat osteoporosis and thrombosis, but the chapter illustrates general principles that may be applicable to other diseases.

In conclusion, a handy volume that makes good bedtime reading; light in weight, but not a lightweight.

Robert Liddington, Room D1040, Dana–Farber Cancer Institute and Harvard Medical School, 44 Binney Street, Boston, MA 02115, USA.