Beyond the language of cell polarity

Cell Polarity

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Cellular asymmetry has been widely acknowledged as being fundamental to various aspects of cell and organism physiology. For example, yeast cells choose a single site at the cell surface to direct the formation of a new daughter cell. In addition, the propagation of a nervous impulse from dendrites to axon and the absorption of ions and fluid across an epithelium each depend on the differential distribution of membrane proteins. The anisotropic distribution of differentiation determinants has been shown to play a critical role in the cell-fate decisions of bacteria (for example, swarmer versus stalked cell in *Caulobacter crescentus*), nematodes (specification of founder blastomeres in *Caenorhabditis elegans*) and frogs (establishment of the dorsal/ventral axis in *Xenopus laevis*). As a graduate student in the field of epithelial polarity, I remember learning of these myriad examples of 'cell polarity' and wondering with some scepticism whether the single most unifying aspect of polarity was the language used to describe it, rather than the molecular mechanisms required to generate and maintain it. But, after ten years, ten chapters and a thoughtful preface to this volume, a general framework for polarity development has emerged, and it is clear that there is certainly more than language that is shared between cell division in budding yeast and apical/basolateral polarity in epithelia.

The examples of cell polarity presented in this volume cover a variety of cell types (bacteria, yeast, and plant and animal cells) that undergo diverse biological processes (division, differentiation, migration). Most chapters do a fine job of explaining how the asymmetries of a given system are critical to a particular aspect of cell/organism physiology. Fewer chapters discuss molecular mechanisms, and it is no surprise that the genetically tractable systems seem to have led the way in both identifying the molecules and providing the conceptual framework for discussion (that is, what is it

that initiates, interprets and reinforces the polarity cue?). It is unfortunate that the chapter on yeast polarity, arguably one of the leading systems in the field with regard to identifying proteins and mechanisms that generate polarity, is the least well communicated to the non-specialist — key concepts are overly burdened with molecular detail. Ironically, chapters covering genetically intractable systems (such as ciliates and brown algae), in which the authors are obliged to discuss mechanisms without an understanding of specific molecules, seem more conceptual. Perhaps when there are enough molecules implicated in a process, there is a tendency to focus on molecules, motifs and binding partners at the expense of the phenomenon they regulate.

The chapter on morphogenesis in skin epithelia, although certainly comprehensive (five pages are devoted to the expression and protein structure of keratin), contributes little to the discussion of polarity mechanisms, containing statements such as "the profound asymmetry that characterizes skin epithelia is mirrored by their patterns of keratin gene expression". Moreover, although there is little doubt that "the structural and functional polarity of [a tissue] goes hand-in-hand with the stage-specific expression of several regulatory genes", one may not agree with the authors' assertion that "the up-and-coming DNA chip technology" will provide us with a better understanding of tissue polarity. Cell/organism polarity is not a question of the mere presence of different gene products, but of how the cell generates these differences. In fact, most evidence implicates basic components of the secretory and cytoskeletal machinery as opposed to unique determinants. Together with the observation that inheritance of cortical structures in ciliates is an epigenetic phenomenon, it is hard to imagine how relative differences in gene expression will offer much mechanistic insight into cell polarity.

An excellent chapter by Piano and Kemphues on the genetic analysis of intrinsically asymmetric cell divisions raises a sobering point for those hoping to find strong molecular conservation between experimental systems. From mating-type switching in yeast to specification of cell fate in the nervous system of *Drosophila*, if coordination of segregation of cell-fate determinants with cell division is clearly conserved, the molecules and mechanisms are not (even when comparing asymmetric divisions within the same organism). This raises an interesting question for those studying polarity in systems that are not genetically tractable, such as epithelial polarity in mammalian cells. Although Nelson and colleagues demonstrate neatly that the proteins that regulate polarized secretion in yeast have structural and functional homologues that mediate basolateral targeting in epithelia (the Sec6/8 complex), how do we identify the mechanisms that do not fit into the conceptual or molecular template of yeast polarity? Also, although the authors provide a cogent argument for cadherin-based adhesion as the symmetry-breaking polarity cue in epithelia, attention should perhaps also be given to the proteins that have unexpectedly been revealed by *Drosophila* genetics to be important for epithelial polarity (such as Crumbs, Discs Lost, Discs Large and Lethal Giant Larvae).

Despite my obvious interests and biases, all of the chapters of this book are useful and should appeal to cell-polarity aficionados and beginners alike. What should a book offer that a stack of recent reviews by these very same contributors might not? The answer is an overarching synthesis. The editor, David Drubin, has written an excellent foreword, highlighting themes and variations, so that this volume achieves much more than the sum of its individual chapters. □

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