Book Reviews

Embryonic Cells

Epithelial-Mesenchymal Interactions. Eighteenth Hahnemann Symposium. RAUL FLEISCHMAJER and RUPERT E. BILLINGHAM, Eds. Williams and Wilkins, Baltimore, 1968. xiv + 326 pp., illus. $15.75.

A quarter of a century ago, Johannes Holtfreter—to whom *Epithelial-Mesenchymal Interactions* is dedicated—wrote a series of pioneering papers in which he explored the relations between the developmental behavior of embryonic cells and *Gewebeaffinität* (tissue affinities). In these investigations he emphasized the importance of cell-to-cell interactions in morphogenesis and differentiation and provided early evidence for such interactions, mediated via differential cell adhesiveness and the transfer of inductive agents.

Since that time, the evidence has become increasingly strong that communication between cells of dissimilar ontogenetic origin, often brought into association in the embryo by spatial reorganization or morphogenetic movements, may trigger the emergence of new cell types. However, it has become equally apparent in recent years that many of the classic terms and concepts applied to these phenomena by most investigators, such as *induction, determination, organizer, canalization,* and *competence,* are ambiguous or may no longer be meaningful in modern experimental terms. Many of the contributors to the 18th Hahnemann Symposium have taken it upon themselves to reevaluate and redefine some of these ideas. As a result, the proceedings volume has more of an element of scientific excitement about it than is found in most symposium volumes. In keeping with the title, most of the 20 chapters in this book emphasize work on the heterotypic interactions that occur between epithelia and mesenchymatous tissues.

Numerous questions are asked. First, what is an eipthelium? what is mesenchyme? are they really different tissue types? In an elegant and logically forceful analysis of the ultrastructure of early chick embryo tissues, Elizabeth Hay explores these questions and redefines the terms on the basis of presence or absence of basement laminae, polarity of cells, and types of intercellular junctions. Isolated in tissue culture, cells of mesenchymal or epithelial origin maintain important differences. Abercrombie and Middleton compare the locomotor behavior of and the effects of contact inhibition between the two cell types. McLoughlin analyzes the spreading behavior of epidermal epithelium in contact with a variety of mesenchymes.

A second question relates to the mechanisms that underlie the interactions between mesenchyme and epithelia. The interaction classically referred to as induction has generally been described as an instructive event in which, according to the traditional paradigm, an inducing tissue releases a unique macromolecule, which instructs "undifferentiated" naive responding cells to differentiate into specialized cells. From his study of the induction of somite epithelium to form chondrocytes, Holtzer is led to question these assumptions. Instead, he suggests that induction may often involve a sequence of *permissive* events influencing covertly differentiated cells. Rutter and his co-workers also take the position that the classic concept is highly oversimplified and probably misleading in many respects. By examining exhaustively the initiation of enzyme synthesis in the early pancreatic rudiment, these workers demonstrate that in the prepancreatic endoderm the synthesis of pancreatic proteins is essentially zero. Thus the cells are undifferentiated with respect to the pancreas, although, as is pointed out, they may be differentiated by other criteria. At approximately the 20-somite stage in the rat embryo, as a result of a presumed "primary regulatory event," the epithelium first enters a phase, termed the "protodifferentiated" state, in which a low level of specific protein synthesis is coupled with intense mitotic activity and preliminary morphological changes. Lash finds a similar partially differentiated state in somite tissue. As a result of a secondary regulatory event, cells are converted from a protodifferentiated to a differentiated state in which cell proliferation gradually ceases, specific enzyme activity increases dramatically, and cytodifferentiation occurs.

As is emphasized by Wessells, however, these regulatory events need not involve transmission of specific molecules from one tissue type to the other. Tissue mass effects, the influence of extracellular matrix, and secondary effects of mitotic regulation all may play crucial roles in inductive interactions. Whether a "critical cell division" (Holtzer) is required for an inductive interaction to result in a differentiative event is left for future results to decide. However, that there is a relation between the control of mitotic activity and of differentiation by the same or related inductive interactions is brought out by several contributors. The possibility that cell division may be controlled by specific glycosaminoglycans produced by mesenchymal cells (Lippman) may provide a means of analyzing such relations.

Other contributors discuss transfilter experiments (Grobstein; Saunders and Gasseling; Hilfer), disaggregation-reaggregation studies (Hilfer; Moscona and Garber), dermal-epidermal interactions (Billingham and Silvers; Oliver, Moscona, and Garber; Van Scott and Flaxman), trophoblast-host reactions (Kirby and Cowell), and the relation between induction and neoplasia (Dawe, Morgan, and Slatick).

This is a well-produced volume. Illustrations, especially the numerous electron micrographs, are carefully reproduced, and I found very few typographic errors.

Workers familiar with the current literature on tissue interactions will not find much new information in this volume which has not already appeared in the last year or so in research reports. However, for those readers interested in synthesizing a large body of data, for those philosophically minded who enjoy discussions longer and more speculative than are generally found in research journals, for students wishing an introduction to a scattered literature, and especially for those who agree that the greatest excitement in science comes from watching traditional ideas succumb to the force of new techniques and concepts, I recommend this book.

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