Meetings

Morphogenetic Tissue Interactions

Margaret Mead and Paul Byers view the small substantive conference as a new form of communication—a new social invention (*1*). Mead closed her discussion of the conference process with a Japanese characterization of it: conference as Sukiyaki. "There is no single recipe—it is a kind of group cooking. The taste must be different according to each group. . . . Quite often it takes a little while to know the impact of the meal. . . ."

A month now has elapsed since I attended the Workshop on Morphogenetic Tissue Interactions, sufficient time for me to assess the "recipe" of the workshop and its impact. These questions are important, for the workshop was the first of several to be mounted by the International Society of Developmental Biologists. Should it be the prototype?

Scientific organizations must evolve, along with the scientific approaches and sophistication of their constituents. Thus at its congress in Paris in 1968, the ISDB (formerly the International Institute of Embryology) decided to embark upon a program of small conferences, each designed to explore some aspect of the field in depth. The first of these was held in Nokkala, Finland, near Helsinki, 1–4 September 1969, sponsored by the ISDB and the Finnish Ministry of Education. I don't know whether the organizers, led by Alberto Monroy of Palermo, president of the ISDB, and Lauri Saxén of Helsinki, chairman of the local committee, had read the Mead-Byers book. However, in almost all essential features, the workshop was a model of the successful small conference. Invited participants numbered about 30 (from 13 countries) to which were added about 15 key members of the host institution. Emphasis was successfully placed on discussions. Holding the meeting at the secluded Savings Bank Institute, where everyone could be accommodated, enabled the participants to live and work together.

According to the ISDB's guidelines, the topics of its workshops should, whenever possible, be related to the competence of the host institution. The Finnish embryologists, under the leadership of Professors Toivonen and Saxén, have long been committed to the study of inductive tissue interactions. Thus they could be knowledgeable in the selection of participants. Moreover they brought to the discussions not only an awareness of the difficulties of the subject but also the intensity of their own drive toward its solutions.

I consider the workshop a success because I think new understandings emerged from it; ultimately there will be tangible results. It was a success, especially because one conflict was aired—not a conflict of individuals, but of ideas. Mead and Byers had written (*1*, p. 22) "Conferences may also release very deep-seated and unacknowledged ambivalences and deeply buried and disallowed attitudes." It became clear at the very beginning of the workshop that the idea that induction may be an "instructional" event, which Waddington recently stated (*2*) had disappeared on his side of the Atlantic almost a third of a century ago, was still very much alive to some Europeans as well as to some Americans. Do both Europeans and Americans enjoy flogging dead horses? Or did Waddington *et al.* fail to deliver the *coup de grâce* in 1936? Are inductive interactions all permissive, or may some involve instructive mechanisms? The former implies that, as a result of an interaction, one or another gene or sequence of genes is selected and expressed. It falls completely within the framework of the modern theory of development. The latter, however, says that the inductive tissue imparts new "information" at some level, that is, it "instructs." One group including John Paul (United Kingdom) and Leo Sachs (Israel), among others, objected to the latter designation, partly because the word *information*, as it is used today ordinarily implies genetic (nucleic acid) information, for which there is no consistent body of supporting evidence in inductive systems studied thus far. Moreover they stressed that all of the systems described could possibly be explained by the "permissive" (selective) model. It is not easy, however.

It was agreed that at one extreme, primary embryonic induction [as reviewed by Nieuwkoop (Holland)] falls into the permissive category. A number of additional examples of this category were discussed by F. Dieterlen-Lievre (France), N. Le Douarin (France), M. Doskocil (Czechoslovakia), and K. Kratochwil (Austria). However, even from a given experimental system, evidence for both kinds of mechanisms is said to emerge. For example, Dieterlen-Lievre concludes from the study of the chick pancreas (in agreement with Rutter, Wessells, and others) that determination of the pancreatic epithelium is an early event. Various heterologous mesenchymes, but not all, are permissive for differentiation of this epithelium. Moreover, pancreatic epithelium induces granulopoiesis in associated heterologous mesenchymes, but whether the mechanism is permissive or instructive is not clear. The most extreme example said to fall into the instructive category was the following. E. Wolff (France) described recent experiments conducted in Gomot's laboratory (France) by Alain Propper (*3*). Embryo epidermis from 7-day-old chicks was combined in vitro with mammary mesenchyme from the 14-day-old rabbit embryo. It induced the production in the epidermis of structures having the histological appearance of spherical and elongated mammary buds. It is possible, of course, to argue that cells in the chick epidermis might contain nucleotide sequences, normally never expressed, controlling the formation of mammary structures, or possibly some closely related or homologous structures. And there are ways of examining that possibility, before concluding that the rabbit mesenchyme has "instructed" the chick epidermis. Before doing either, however, it might be well to ask whether the system can be better defined and simplified. Can a controlled, clonally derived culture of epidermal cells be made to form mammary structures? Can the "mammary structures" be defined more precisely, in, say, the synthesis of a readily identifiable product? Indeed one of the questions most frequently raised was

whether it might be possible for students of the subject to agree to focus on one experimental system, for it is impossible to subscribe to any view, as long as the evidence is in its current state.

A concerted attack on one of the presumed instructive systems might be in order. Some additional features of the development of the mammary gland make it an attractive target, especially its sensitivity to hormones. For example, in the male mouse the gland begins to regress at 13.5 days as a consequence of the secretion of androgens of the fetal testes. This regression is also observed in vitro when 13-day-old mammary gland rudiments are combined with 13-day-old testes. However, according to Kratochwil the regression of the epithelium requires its combination with homologous mesenchyme. Neither mouse mammary epithelium combined with salivary mesenchyme nor salivary, lung, or pancreatic epithelium combined with mammary mesenchyme respond to male hormone.

Other speakers, notably Elsdale (United Kingdom), Weston (United States), and Sachs (Israel), emphasized that even in clonal and other simplified experimental systems, phenotypic expression may be influenced by contact-mediated interactions between cells. For example, Elsdale described interactions between fibroblasts and epithelial cells in vitro which suggest that the acquisition of polarity by epithelial cells may serve to restrict the possibilities for morphogenesis in mixed epithelial-mesenchymal systems. Finally, Ringertz (Sweden) described evidence from model experiments with hen erythrocyte ghosts which suggested that chromatin activation may be triggered by changes in the state of the cell membrane. His observations, coupled with other evidence on the possible importance of association between chromosomes and the nuclear membrane on the one hand, and on the occurrence of nucleic acids in cell membranes on the other, may enable us to begin to understand how a cell's genome may be influenced by contact with another cell.

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References

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