either the O or P teloblast was ablated, those peripheral dopaminergic neurons that are part of the "O" patterns in direct lineage tracing experiments are always missing, whereas those associated with the "P" pattern are always present. In sum, these findings are consistent with the notion that the O and P teloblasts are of equal developmental potential and that the fates of their progeny are assigned hierarchically on the basis of bandlet position within the germinal band or germinal plate, with "P" fate taking precedence over "O" in the hierarchy.

Conclusion

It may be useful to think of cell lineage in the leech as comprising three classes of cell divisions. Firstly, cleavage of the egg into large, yolky blastomeres in early embryogenesis may limit the developmental potential of different cell lines by segregating inherited factors in the cytoplasm, cytoskeleton, or cell surface. This class of division (and the next as well) seems to have been drastically modified or replaced in insects by a syncytial blastoderm. There, any determinants might be divided among a much greater number of progeny, and neighboring cells in the blastoderm may be of equal developmental potential.

A second class of cell division in leech embryogenesis is the stem cell-like divisions of laterally arrayed teloblasts, each of which generates a longitudinally arrayed set of segmental precursor cells, the primary blast cells. In the leech, less than 10 primary blast cells on each side generate a segmental complement of ectodermal and mesodermal tissues. By understanding the mechanisms controlling the generation of the primary blast cells, we may eventually understand how the precise enumeration of segments in the leech is achieved.

Finally, the subsequent divisions of the primary blast cells are analogous to those of the nematode P cells and the insect neuroblasts, in that they give rise to serially homologous progeny in each cell line. But, whereas the insect neuroblasts, true to their name, give rise to exclusively neural progeny, each ectoteloblast cell line in the leech generates both neural and epidermal progeny, thereby contradicting the very suppositions on which Whitman based his concepts of cell lineage! Why are four pairs of laterally arrayed ectoteloblasts produced during cleavage, a process thought to result in the segregation of developmental potential, if each is then to contribute progeny to the segmental ganglion of the ventral nerve cord? One explanation of this paradox lies in the evolution of the annelids.

The teloblast mode of development described here is a form of modified spiral cleavage, which serves as the basis for embryogenesis throughout the annelid phylum. The annelids are presumed to have arisen from organisms having a distributed nervous system, consisting of a ladderlike array of nerves, along which cell bodies were continuously distributed (Bullock et al., 1977); indeed, in some archiannelids and polychaetes, this primitive organization persists in the form of bilateral nerve cords linked by segmental commissures (Bullock and Horridge, 1965). An ontogenetic mode in which each of a laterally distributed set of precursors gives rise to both neural and epidermal cells in its locale would be entirely suited to produce an organism with a distributed nervous system. But in a distributed nervous system only a limited number of neuronal interconnections are possible without invoking cumbersome conduction delays. This restricts the behavioral sophistication of such organisms. A more sophisticated nervous system might be had by concentrating neurons medially and longitudinally to reduce conduction delays and increase the richness of possible intercellular connections. This improvement might evolve gradually by "tinkering" (Jacob, 1982) with the preexisting annelid mode of development so that neuronal progeny of the lateral blast cells migrated medially to form a central nervous system. But the complexity of the nervous system attainable by this patchwork developmental system might itself be limited by problems of orchestrating the differential migrations of various cell types. In addition, only small numbers of neurons could be made by less than 20 blast cells per segment, each of which is also committed, by the annelid developmental mode, to generating nonneural tissue as well. The leech is exceptional among annelids in the degree to which its neurons are organized into discrete ganglia (Bullock and Horridge, 1965), and thus may represent the acme of annelid neurogenesis (Sawyer, 1981). The next significant increase in the complexity of the nervous system was reached only by the embryological revolution leading to the syncytial blastoderm, which generated large numbers of centrally located neuron-specific blast cells, and with them a new animal phylum.

COMPARTMENTS, SEGMENTS, AND CELL LINEAGES IN INSECT EPIDERMIS*:

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What can we learn from cell lineage studies about the processes governing the construction of the central nervous system? Most of our examples of cell lineage using clonal analysis come from studies

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on the insect epidermis. However, since the epidermis and nervous system both arise from the ectoderm, the principles of construction and of genetic strategy might be similar.

Methods of indelibly marking embryonic cells have allowed studies of cell lineage to be made in developing insects. In the insect epidermis, most cell lineage studies have made use of somatic recombination with mutations that change the structure or color of the cuticle in specific ways. For example, on the wing of normal flies each cell secretes a single hair, whereas in flies with mutations, called *multiple wing hairs*, each cell secretes a group of hairs. Because the mutation is recessive (and is expressed only when a cell is homozygous), flies that are heterozygous for the mutation appear normal. By exposing a *Drosophila* embryo to X-rays, we cause breaks in some chromosomes, and occasionally obtain a "cross-over" during cell division (somatic recombination) that leads to one cell's becoming homozygous for the mutation. As the "marked" cell divides, it generates a clone of daughter cells, all of which bear the marker mutation and therefore express the mutant characteristic. Clonal analysis involves irradiating hundreds of embryos or larvae and examining the patches of marked cells in the adult. In addition, it has proved useful to make the marked cells grow more rapidly than all the other cells in the insect, as will be discussed later.

There are two contrasting modes of cell lineage: fixed and indeterminate. If cell lineage is fixed, then each cell in the embryo would always develop to form a specific part of the adult. If cell lineage is indeterminate, then any cell could develop to form any part of the adult. Analysis of cell lineage in the epidermis of *Drosophila* shows that neither of these extreme models is correct. When clones produced by somatic recombination are compared, they are found to overlap. This means that cell lineage is not fixed. However, cell lineage is not indeterminate, either. When clones of marked and normally growing cells are produced in a background of unmarked cells that divide particularly slowly (using the *Minute* mutant), then the marked cells have enough time to outgrow the unmarked cells and fill the entire epidermal area. Yet they never do. In the wing, for example, the marked cells in many such clones never fill more than half the wing and respect exactly the same boundary line. No individual clone ever crosses the boundary.

We now know that insects are constructed piecemeal. The large clones define precise regions, i.e., developmental compartments, in the cuticle. Each compartment develops from a small group of founder cells (a polyclone) that is set aside in the embryo (e.g., García-Bellido et al., 1973, 1979; Crick and Lawrence, 1975). The polyclone has a

precisely defined destiny, but the individual cells in the polyclone are not individually determined in that their progenies can intermingle and ultimately acquire their role by their position within the compartment. Compartments have been identified in many epidermal parts of the fly (because they can be easily labeled with genetic marker mutations), including, for example, all three thoracic segments and their appendages, the abdomen, and the genital organs. It is likely that other tissues like the CNS are also subdivided into compartments, but this is not yet known. Sometimes the lines demarcating compartments fall in surprising places, as in the case of the wing. At other times the lines fall more as expected, as with the line between segments. We imagine that the development of polyclones is under the control of specific genes that are activated in cells according to their location. The state of activity of these genes may, in combination, provide the basis for a binary code specifying the part constructed (García-Bellido, 1975; Morata and Lawrence, 1975). Consequently, the domain affected by mutation in these genes coincides with a compartment as defined by cell lineage.

Each segment is subdivided into an anterior and posterior compartment. These units are probably further subdivided into dorsal and ventral compartments. These polyclones are established progressively during development by the sequential subdivision of a polyclone into daughter polyclones.

The peripheral sensory neurons of insects develop directly from epidermal cells and so must belong to particular compartments as defined by cell lineage. Further, it is possible that the neuroblasts that generate the CNS of insects might separate from a defined polyclone and thus would have the determined state characteristic of that polyclone. It is possible that the separation of neuroblasts from epidermal cells may yet form another compartment (discussed in Lawrence, 1981a). It is also possible that the CNS is subdivided into further compartmental units, but this is not yet known. In both *Oncopeltus* (Lawrence, 1973a) and *Drosophila* (Wieschaus and Gehring, 1976), the segmental polyclones are established at, or soon after, blastoderm formation; i.e., possibly before the divisions that generate the neuroblasts. New methods of cell marking in *Drosophila* (Lawrence, 1981b) may allow a direct study of the cell lineage of the nervous system. This may define compartments there and also discover the degree of common precursors shared by the epidermis and CNS.

In *Oncopeltus,* axons of peripheral sensory neurons respect the compartment boundary that separates segmental polyclones (Lawrence, 1975). However, they do not respect the compartment