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Perspective Article

Hylonome

Principles of developmental biology

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Abstract

The field of developmental biology has a history that spans the last 500 years. Within the last 10 years, our understanding of developmental mechanisms has grown exponentially by employing modern techniques of genetics and molecular biology, frequently combined with experimental embryology and the use of molecular markers, rather than solely morphology, to identify critical populations of cells and their state of differentiation. Three main principles have emerged. First, mechanisms of development are highly conserved, both among developing rudiments of a variety of organ systems and among diverse organisms. This conservation occurs both at the level of tissue and cellular mechanisms, and at the molecular level. Second, the development of organ rudiments is influenced by surrounding tissues through interactions called inductive interactions. Such interactions are mediated by highly conserved growth factors and signaling systems. Third, development is a life-long process and can be reawakened in events such as wound healing and regeneration, and in certain diseases. Advances in understanding normal development provide hope that diseases in which development runs amuck, such as cancer, may soon be preventable and fully treatable. Supported by NS 18112 and DC 04185 from the NIH.

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The field of developmental biology is founded on a 500 year history of descriptive comparative embryology[1,2,3]. Over the last 100 years, mechanisms of development have been elucidated by utilizing the techniques of experimental embryology in which developmental rudiments are ablated, eliminating circumscribed populations of cells, or transplanted, often to ectopic sites (i.e., heterotopically) or to older or younger embryos (i.e., heterochronically). In the last 10 years, our understanding of developmental mechanisms has grown exponentially by employing modern techniques of genetics and molecular biology, frequently combined with experimental embryology and the use of molecular markers, rather than solely morphology, to identify critical populations of cells and their state of differentiation.

Recent advances in developmental biology have resulted mainly from the use of new technology and our realization that mechanisms of development are highly conserved, both among developing rudiments of a variety of organ systems and among diverse organisms. This conservation occurs both at the level of tissue and cellular mechanisms, and at the molecular level.

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The realization that developmental mechanisms are highly conserved has led to two important approaches. First, a small number of laboratory species, consisting of both invertebrate and vertebrate embryos, has been chosen as model organisms for most studies in developmental biology. Thus two invertebrates, *Caenorhabditis elegans* (the round worm) and *Drosophila melanogaster* (the fruit fly), are used as "simple" systems, and four vertebrates, *Danio rerio* (the Zebrafish), *Xenopus laevis* (the South African Clawed toad), *Gallus gallus domesticus* (the domestic chicken), and *Mus musculus* (the mouse), are used as representative of human embryos. This has facilitated our progress by providing standard models that allow us to build a critical mass of information and to take advantage of the particular strengths offered by each of the models for different experimental approaches. Aside from the validity of using model systems for the majority of studies, there is considerable value in surveying mechanisms of development in a wide variety of species, for example, to ascertain new insight into evolutionary solutions within particular developmental contexts, so a renaissance has occurred in the last few years in comparative embryology, as studied at the molecular level.

The second approach resulting from the realization that developmental mechanisms are conserved, involves the

cloning of genes based on their homology with genes present in other organisms. Thus, developmental control genes can be identified in organisms in which they can be readily mutated (e.g., C. *elegans or Drosophila*), thereby revealing their function in development, and subsequently cloned. Then, their orthologs can be cloned in more complex organisms (e.g., mouse or chick), where their relevance to vertebrate development (and presumably human development) can be assessed.

These studies have revealed that a small number of signaling pathways control tissue patterning during embryogenesis. However, although only about 20 such pathways exist, considerable complexity underlies each of their components. For example, although *Drosophila* has only one FGF (Branchless), 22 or 23 members of the FGF family have been identified in mammals. Additionally, although *Drosophila* has only one receptor for FGF (Breathless), four FGF receptors are present in mammals, and three of these four receptors, each have two alternative splice forms that affect ligand binding, resulting in a total of seven receptor isoforms. Further complexity exists in the intracellular signaling transduction proteins and the resulting transcription factors and target genes activated or suppressed by these transduction proteins.

The development of organ rudiments is influenced by surrounding tissues. This influence, which can evoke the attainment of a new cell fate, or can suppress the formation of a default cell fate, is called an inductive interaction; it is mediated by diffusible growth factors and signaling molecules. Thus during inductive interactions, families of growth factors are secreted from inducing cells to interact with their receptors on responding cells. This leads to the activation of intracellular signal transduction machinery and changes in the expression of transcription factors. Growth factors, their receptors, intracellular signal transduction proteins, and transcription factors are highly conserved, both among developing rudiments of a variety of organ systems and among diverse organisms.

An often under-appreciated feature of development is that it is a lifetime process, not just a prenatal event. Development is reawakened and recapitulated in such processes as wounding, healing and regeneration. Moreover, disease results when developmental events go awry, such as the mutation of a tumor suppressor gene or the conversion of a proto-oncogene to an oncogene, both of which lead to cancer. Aging also is believed to involve adverse changes in developmental processes.

In summary, studies in developmental biology have revealed the enormous complexity underlying developmental systems. Although such complexity will tax our ability to synthesize a global understanding of development, our tremendous progress in the last ten years justifies our having real hope for the first time that the elucidation of the mechanisms underlying many serious birth defects is truly at hand.

References

1. Wolpert L, Beddington R, Brockes J, Jessell T, Lawrence P, Meyerowitz E. “Principles of Development”. Current Biology Ltd., London; 1998.
2. Gilbert SF. “Developmental Biology”. Sixth Edition. Sinauer Associates, Inc., Sunderland, Massachusetts; 2000.
3. Kalthoff K. “Analysis of Biological Development”. Second Edition. McGraw-Hall, New York; 2001.