Developmental Biology

FOURTH EDITION

SCOTT F. GILBERT

SCOTT F. GILBERT *Swarthmore College*

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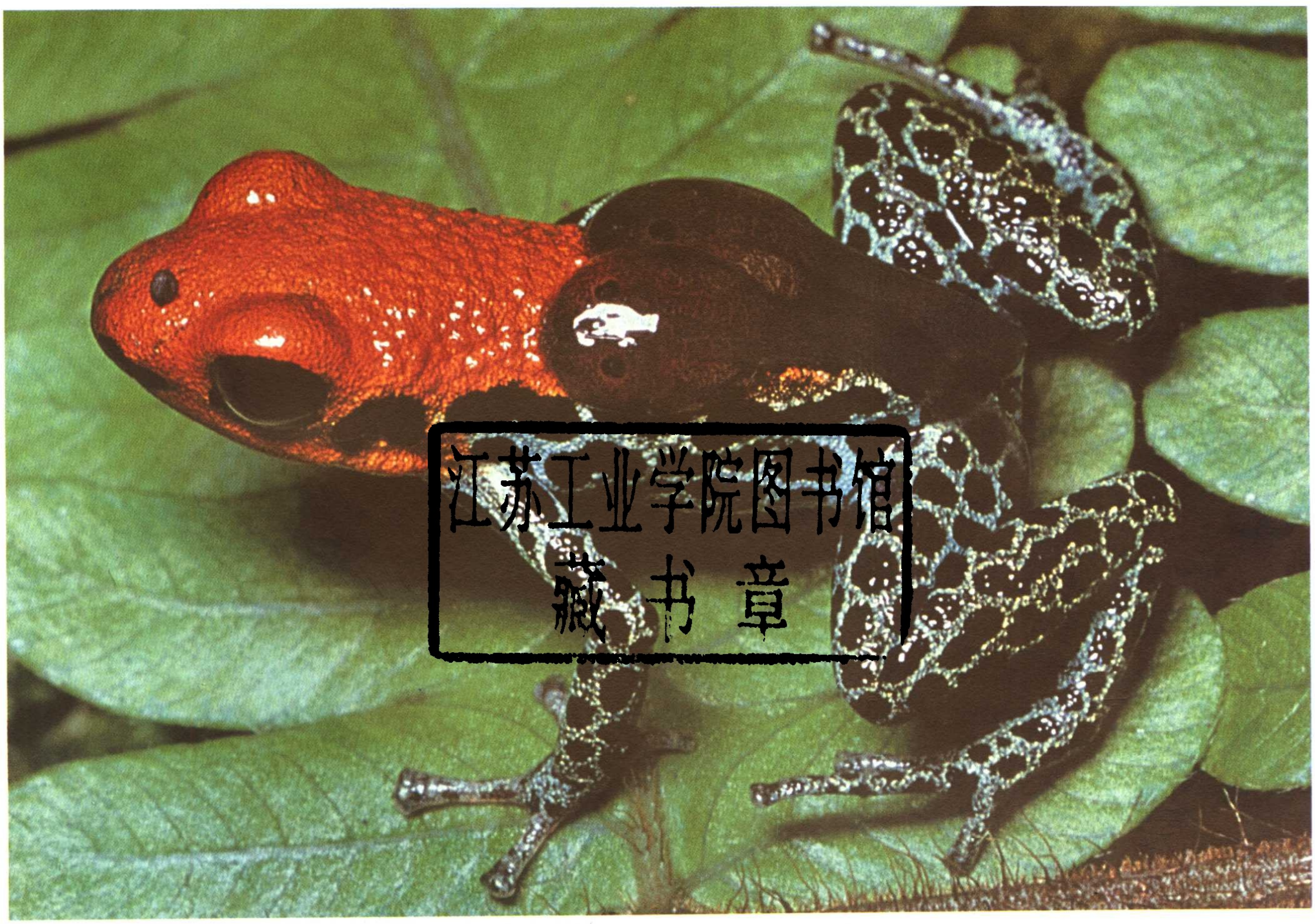

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THE COVER

The Myf-5 protein is expressed in muscle cell precursors and plays a role in their becoming skeletal muscle cells. The genetic elements regulating the temporal and spatial expression of the *Myf-5* gene can be discerned by fusing a β-galactosidase gene to the sequences surrounding the *Myf-5* locus. This newly constructed gene is inserted into a pronucleus of a newly fertilized mouse egg, and the β-galactosidase protein can be stained when it appears in the embryo. Here a particular sequence upstream from the *Myf-5* gene causes the expression of the gene (black stain) in the neck muscles, pharyngeal arches, ocular muscles, forelimb muscles, and segmented myotomes of a 13.5-day mouse embryo. The gene family to which *Myf-5* belongs is discussed in Chapters 9 and 10. (Photograph courtesy of A. Patapoutian, G. Lyons, J. Miner, and B. Wold.)

THE TITLE PAGES

Left page: Diffusible signals from the notochord (green tube at bottom) induce the formation of the floor plate at the ventral side of the neural tube (green). The floor plate cells induce the formation of the two regions of motor neurons (gold) on the ventrolateral sides. The notochord also restricts the expression of dorsalin protein (needed for neural crest cell development) to the most dorsal region of the neural tube (blue). See Chapter 16. (Photograph courtesy of T. M. Jessell.)

Right page: Tadpoles of the reticulated poison-dart frog are carried on their parents' backs to small pools of water at the base of bromeliad leaves in the rain forest canopy. The female of this Peruvian Amazon species will then supply unfertilized eggs as food for the developing tadpoles. See Chapter 20. (Photograph by M. Fogden/DRK Photo.)

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Preface

In 1894, three publications changed the rationale for studying development and charted new paths for embryological investigations. In that year, Wilhelm Roux founded the journal *Archiv fur Entwicklungsmechanik der Organismen* (*Archives for the Developmental Mechanics of Organisms*) and announced a new program for embryological research that would be based on experimentation. Roux exhorted young biologists to intervene experimentally in the developmental process in order to find the laws that underlie the differentiation and organization of bodily cells, tissues, and organs. Also in 1894, Hans Driesch published his *Analytische Theorie der Organischen Entwicklung* (*Analytical Theory of the Development of Organisms*) wherein, among other things, he proposed a relationship between chromosomes and cytoplasm in which the chromosomes directed the formation of new materials in the cytoplasm and the cytoplasm reciprocated by directing the chromosomes to synthesize different materials than they had before. Also that year, Oscar Hertwig's *Präformation oder Epigenese* (*Preformation and Epigenesis*) directed the attention of embryologists to the interactions between cells that cause each cell to become defined in relationship to its neighbors within the embryo. These three visionary treatises shifted the emphasis of embryology from comparative anatomy to experimentation.

A hundred years later, developmental biology is in the middle of another major revolution. The ability to introduce new genes into embryos, to activate specific genes in particular cells, and to suppress specific gene expression in cells has given us insights unimaginable even a decade ago. The structures that once were useful for presenting animal development no longer do it justice. The ability to discuss developmental anatomy as something separate from developmental genetics is gone. Similarly, the usefulness of separating vertebrate from invertebrate development has vanished with the uncovering of developmental pathways that are fundamentally the same in nematodes, flies, and humans.

This revolution of content has caused a dramatic restructuring of this book. First, there are now three introductory chapters that bring material on genetic analysis and cell membranes to the front of the book. This enables us to discuss the cellular and molecular bases of the anatomical changes seen in subsequent chapters. Second, the chapters on developmental genetics have been moved to precede the chapters that discuss the specification of the body axes and the determination of the first cell types. This was done because our understanding of the genetic bases for cell specification has expanded enormously over the past three years, and we have a much richer account when these incredible events can be approached from both embryological and genetic studies. These changes seem to reflect the way developmental biology is now being taught.

Elements present in the first three editions of this book have been strengthened. Modern developmental biology demands that both the organismal and molecular approaches to biology be respected (indeed, celebrated). The most interesting areas of the field are probably those where these approaches intersect, and I have tried to integrate them. I have also attempted to blur some of the artificial boundaries that have divided developmental biology from its sibling disciplines of evolutionary biology and genetics. However, I extend apologies to my colleagues and friends (I think I still have some) in plant developmental biology for writing a book that is all meat and no vegetables. This book would be far too long were it to do justice to the plant kingdom, and I feel strongly that plant development deserves its own course and textbook.

As the field continues to expand and deepen, a word of warning is called for: Developmental biology cannot be taught—or learned—in a single semester. This text is an attempt to provide each person with sufficient material for their course, but a teacher need not feel guilty for not assigning every chapter, and students need not feel deprived if they have not read every chapter. This is the beginning of the path, not its conclusion.

I tell my students that studying developmental biology is their reward for doing well in cell biology and genetics. Now they can have fun asking the important questions and, perhaps, finding a problem to study that is worthy of their talents. The problems are among the most important in all science: How do the egg and sperm interact to create a new organism? How does a single cell give rise to the diverse cell types of the adult body? How do neurons make their specific connections with other neurons and with peripheral tissues? How do organs form?

It was Roux's vision that developmental biology would "sometime constitute the common basis of all other biological disciplines and, in continued symbiosis with these disciplines, play a prominent part in the solutions of the problems of life." These were bold, even arrogant words one hundred years ago; today, they express a widely held assumption. Development integrates all areas of biology and plays the crucial role of relating genotype to phenotype. Development can be studied using any organism and at any level of organization, from molecules to phyla.

A final caveat: At the Marine Biology Laboratory at Woods Hole, Massachusetts (scene of some of the most important embryological investigations in the United States), there hangs a handwritten banner that reads, "Study Nature, Not Books." This sign hangs over the main entrance to the *library* as a reminder that we come to study organisms, not the history of how they are studied. This book is successful to the point that it stimulates one to relinquish it and to study the organism.

Acknowledgments

This book has benefitted enormously from the comments and criticisms of several investigators who took the time to read drafts of these chapters. These stalwarts include: R. and L. Angerer, M. Bronner-Fraser, D. D. Brown, S. Carroll, E. DeRobertis, B. A. Edgar, J. Fallon, A. Fausto-Sterling, G. Guild, R. Grainger, G. Grunwald, Z. Hall, V. Henrich, L. A. Jaffe, R. E. Keller, K. J. Kemphues, J. Kimble, W. Loomis, W. McGinnis, J. Opitz, D. Page, C. Phillips, R. Raff, L. Saxén, I. Thesleff, R. Tuan, H. Weintraub, and M. Wormington. Moreover, this book could not have been completed without the considerable effort from the scores of researchers who sent me photographs that appear herein and preprints for the Fourth Edition. This edition was substantially improved by those scientists who sent me critiques of the Third Edition, including M. Benecke, J. Koevenig, J. B. Morrill, J. E. Rebers, and F. Schwalm. Thanks also to R. Dratman for computer help when it was of crucial importance.

This edition, like its earlier incarnations, owes a great deal to the suggestions and criticisms of the students in my developmental biology

and developmental genetics classes. The extremely supportive staff and faculty of Swarthmore College have also played major roles in producing this book, and science librarians E. Horikawa and M. Spencer are due special thanks for keeping recent volumes from being sent to the bindery while I was writing the book.

Andy Sinauer has yet again managed to gather the same remarkable people around this project, and it has been a privilege to work with them. My thanks to him and to editor Carol Wigg, production coordinator Chris Small, artist John Woolsey, designer Rodelinde Albrecht, copy editor Gretchen Becker, layout artist Janice Holabird, and Joe Vesely, art editor emeritus. Because publishing deadlines must be met and other work gets put aside, I have to thank my family for once again allowing me to get away with this. Especially, this book could never have been completed were it not for the encouragement of my wife, Anne Raunio, who, as an obstetrician, enjoys the more practical side of developmental biology. My thanks to you all.

SCOTT F. GILBERT

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AN INTRODUCTION TO DEVELOPMENTAL BIOLOGY