Preface

During the past few decades, technical and conceptual breakthroughs have led to a virtual revolution in developmental biology. In part through cross-species comparisons and multidisciplinary approaches (combining, for example, classical embryology, genetics, molecular biology, and systems biology), major questions have often been redefined and examined from new angles and with innovative tools. Analyses using such model systems as *Drosophila*, *Xenopus*, zebrafish, chick, human, and mouse have underscored the remarkable extent to which molecular and genetic pathways are conserved across species and throughout embryonic, fetal, and adult development. What we learn from the embryo, then, is not only of fundamental interest, but may well have future practical applications in the clinic.

A number of excellent volumes, including several in this series (e.g., *Hematopoietic Stem Cell Protocols*, Klug and Jordan, eds., 2002), have surveyed methods used in the study of hematopoiesis—the processes by which the multiple lineages of the blood form from stem and progenitor cells during ontogeny and throughout the entire life of the animal. These collections of protocols have focused largely on the postnatal cells of mouse and human. Our understanding of hematopoietic development, however, has benefitted enormously from investigations in a variety of organisms at different stages of ontogeny. It is my hope that *Developmental Hematopoiesis* will serve as a starting point for students, postdocs, and more experienced investigators who have not previously studied hematopoietic development, as well as for those who wish to extend the scope of their work to another model organism. Several chapters depart from the standard format of this series, presenting an overview of useful approaches rather than a set of protocols. All of the chapters, however, contain a Notes section intended to provide practical advice not readily obtained from the standard literature.

Part I deals with genetic approaches to hematopoietic development. Each of these deals with the mouse, but the general approaches and concepts are broadly applicable to other systems. For more in-depth coverage of these areas, the reader may wish to consult *Mouse Genetics and Transgenics: A Practical Approach*, Jackson and Abbott eds., 2000. Part II covers two transplantation systems that can be used to follow the determination of cell fate following introduction of embryonic or fetal hematopoietic stem/progenitor cells into mice. Although these cells fail to effect long-term multilineage hematopoietic reconstitution of adult hosts, they do engraft in and reconstitute the hematopoietic systems of conditioned newborn recipients, indicating that they have the potential to function in adults and suggesting that they may need to mature (for example, to express certain homing receptors) during development.

Intrauterine transplantation has not yet been exploited for this purpose, but is likely to provide a second option for assessing developmental outcomes. Both transplantation approaches rely heavily on flow cytometric (FACS) methods for purification of

stem cell populations and analysis of cell fate outcomes, and a chapter on flow cytometric analysis of hematopoietic development has thus been included here. Transplantation approaches using adult mouse recipients are described in detail in *Hematopoietic Stem Cell Protocols*, Klug and Jordan eds., 2002.

Part III covers those model systems most widely used for investigating the formation of hematopoietic cells and tissues. The protocols include molecular and cellular assays; explant, organ, and cell culture; and whole animal approaches, including in vivo imaging. The developmental biology of hematopoiesis can be approached from numerous perspectives: ontogeny; cell fate specification [which lineage(s) will form from a given stem/progenitor cell]; signal transduction; gene regulation; cell migrations and interactions with other cells; changes that occur in stem cells (presumably allocated during embryogenesis) as the animal ages. From fruit flies to humans, blood cells form in several distinct phases during development. The earliest ("primitive") hematopoietic cell types are distinct from the later, "definitive" cells and, in general, arise in different (possibly multiple) regions within the developing animal. Maturation of stem and progenitor cells may occur in a location physically far removed from their site of origin. Each model system has unique advantages and limitations and is generally best suited to study certain types of biological problems. For more general information about the development of particular organisms, the reader is referred to well-known practical manuals published elsewhere, such as those from Cold Spring Harbor Press: *Manipulating the Mouse Embryo*, Third Edition, Nagy et al., 2003; *Early Development of Xenopus laevis: A Laboratory Manual*, Sive, Grainger, and Harland, eds., 2000; and *Drosophila: A Laboratory Handbook, Second Edition*, Ashburner, Hawley, and Golic, eds., 2004. *Zebrafish: A Practical Approach*, Nusslein-Volhard and Dahm, eds., 2002. Two other volumes from Humana Press cover the production of transgenic mice or frogs, and may be of interest to readers of *Developmental Hematopoiesis*; they are *Transgenic Mouse Methods and Protocols*, Hofker and van Deursen, 2002 and *Transgenic Xenopus: Microinjection Methods and Developmental Neurobiology*, Seidman and Soreq 1996.

Bioinformatics and functional genomics approaches for studying stem cells and their supporting stromal cells are outlined in Part IV. The Stem Cell Database (SCDb) has been discussed in a number of recent reviews, and a new, expanded version will be released shortly. The chapter included here touches briefly on SCDb, but focuses on the Stromal Cell Database (StroCDB). However, these approaches are generally applicable to any developing system. Global genomics technologies are particularly exciting: they hold the promise of eventually permitting the assembly of molecular components of the cell into pathways and networks that should afford an understanding of the regulation of cell fate specification at the "systems" level.

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