

> This book is a unique overview of cardiovascular development from the cellular to the organ level across a broad range of species. Leading experts in the fields of anatomy, embryology, experimental and molecular biology, comparative physiology, pediatric cardiology, and fetal heart surgery have contributed to this integrated text. The book is divided into three parts. The first focuses on the molecular, cellular, and integrative mechanisms that determine cardiovascular development. It discusses the molecular biology, intracellular and extracellular environment, functional maturation, vasculogenesis, and regulation of developing cardiovascular systems. The second part summarizes cardiovascular development in invertebrate and vertebrate systems. The third provides an overview of environmental factors and the effects of disease on cardiovascular development with discussions of the effects of environmental and morphogenetic influences on nonmammalian and mammalian development. It offers strategies for the management of congenital cardiovascular malformations in utero and postnatally.

> The book will interest those who work in the fields of developmental biology, physiology, and molecular and pediatric cardiology.





DEVELOPMENT OF CARDIOVASCULAR SYSTEMS





# DEVELOPMENT OF CARDIOVASCULAR SYSTEMS

MOLECULES TO ORGANISMS

Edited by

WARREN W. BURGGREN

University of Nevada, Las Vegas

BRADLEY B. KELLER

University of Rochester





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## **Contributors**

Thomas K. Borg
Department of Developmental Biology and
Anatomy
University of South Carolina School of
Medicine
Columbia, SC 29208
USA

George B. Bourne Department of Biology University of Calgary Calgary, Alberta T2V 1N4 Canada

Warren W. Burggren Department of Biological Sciences University of Nevada, Las Vegas 4505 Maryland Parkway Las Vegas, NV 89154-4004 USA

Wayne Carver
Department of Developmental Biology and
Anatomy
University of South Carolina School of
Medicine
Columbia, SC 29208
USA

Jau-Nian Chen Cardiovascular Research Center Massachusetts General Hospital–East 149 13th Street Charlestown, MA 02129 USA

Ka Hou Chu Department of Biology Chinese University of Hong Kong Hong Kong

Edward B. Clark
Department of Pediatrics
Medical Director's Office
Primary Children's Medical Center

100 North Medical Drive Salt Lake City, UT 84113 USA

Anthony P. Farrell Department of Biological Sciences Simon Fraser University Burnaby, BC V5A 1S6 Canada

Mark C. Fishman
Developmental Biology Laboratory and
Cardiovascular Research Center
Massachusetts General Hospital–East
149 13th Street
Charlestown, MA 02129
USA

Regina Fritsche University of Göteborg Department of Zoophysiology Medicinaregatan 18A 41390 Göteborg Sweden

George D. Giraud
Departments of Physiology, Medicine, and
Pediatrics and the Congenital Heart
Research Center
Oregon Health Sciences University
3181 SW Sam Jackson Park Road
Portland, OR 97201
USA

Adriana C. Gittenberger–de Groot University of Leiden P.O. Box 9602 2300 RC Leiden The Netherlands

Frank L. Hanley Department of Surgery University of California, San Francisco 505 Parnassus Avenue, Box 0118

X



Contributors

San Francisco, CA 94143-0118

**USA** 

Ping-Chun Lucy Hou Department of Biology

National Cheng Kung University

Tainan, Taiwan **ROC 700** 

José M. Icardo

Department of Anatomy and Cell Biology

Faculty of Medicine University of Cantabrai Poligono de Cazona, s/n 39011 Santander

Spain

Fusae Kajio

Division of Pediatric Cardiology The Heart Institute of Japan Tokyo Women's Medical College 8-1 Kawada-cho, Shinjuku-ku

Tokyo 162 Japan

Bradley B. Keller

NIH Specialized Center of Research in Pediatric Cardiovascular Diseases

Department of Pediatrics

University of Rochester School of Medicine

601 Elmwood Avenue, Box 631

Rochester, NY 14642

USA

Lynn Mahony

Department of Pediatrics

University of Texas Southwestern Medical

Center at Dallas

5323 Harry Hines Boulevard Dallas, TX 75235-9063

USA

Brian R. McMahon Department of Biology University of Calgary Calgary, Alberta T2V 1N4

Canada

Mark J. Morton

Departments of Physiology, Medicine, and Pediatrics and the Congenital Heart Research

Center

Oregon Health Sciences University 3181 SW Sam Jackson Park Road

Portland, OR 97201

USA

Anne M. Murphy Ross Laboratories 1144

The Johns Hopkins University School of

Medicine

хi

720 Rutland Ave Baltimore MD 21205

**USA** 

Makoto Nakazawa

Division of Pediatric Cardiology The Heart Institute of Japan Tokyo Women's Medical College 8-1 Kawada-cho, Shinjuku-ku

Tokyo 162 Japan

Bernd Pelster Institut für Zoologie

Leopold-Franzens-Universität

A-6020 Innsbruck

Austria

Alan W. Pinder Department of Biology Dalhousie University Halifax, NS B3H 4H7

Canada

Robert E. Poelmann University of Leiden P.O. Box 9602 2300 RC Leiden The Netherlands

Anna Ratajska

Department of Anatomy and The Cardiovascular Center

Bowen Science Building University of Iowa Iowa City, IA 52242-1109

**USA** 

V. Mohan Reddy

Division of Cardiothoracic Surgery University of California, San Francisco 505 Parnassus Avenue, M593 San Francisco, CA 94143-0118

**USA** 

Mark D. Reller

Departments of Physiology, Medicine, and Pediatrics and the Congenital Heart Research

Center

Oregon Health Sciences University 3181 SW Sam Jackson Park Road

Portland, OR 97201

Peter J. Rombough Department of Zoology **Brandon University** Brandon, MB R7A 6A9

Canada

Hiroshi Tazawa

Department of Electronic Engineering



#### xii Contributors

Muroran Institute of Technology 27-1 Mizumoto Muroran Japan

Louis Terracio
Department of Developmental Biology and
Anatomy
University of South Carolina School of
Medicine
Columbia, SC 29208
USA

Kent L. Thornburg Department of Physiology School of Medicine Oregon Health Sciences University Portland, OR 97201 USA

Robert J. Tomanek Department of Anatomy University of Iowa 1402 Bowen Science Building Iowa City, IA 52242-1109 USA

Stephen J. Warburton Department of Biology New Mexico State University Las Cruces, NM 88003 USA

Constance Weinstein
National Institutes of Health
National Heart, Lung, and Blood Institute
Two Rockledge Center, Suite 9044
6701 Rockledge Drive, MSC 7940
Bethesda, MD 20892-7940
LISA

Jackson Wong Pediatrix Medical Group, Inc. Broward General Medical Center 1455 Northpark Drive Fort Lauderdale, FL 33326 USA



### Foreword

**CONSTANCE WEINSTEIN** 

Several features distinguish this book from others on development of the cardiovascular system and therefore establish it as an important contribution to literature on the subject. Among these features is the careful description of the anatomy and physiology of various animal models of development commonly used in genetic and molecular biological studies of the heart and vascular system. Understanding the differences among species is crucial to proper interpretation of findings, particularly when those findings form the basis for inferences on their significance for human malformations and diseases.

A laudable emphasis on the physiology of the developing cardiovascular system appears throughout the book. This draws attention to the fact that, although form and function are closely related, function may be perturbed without visible perturbations of form, and because the physiology of the embryo and fetus differs from that of the postnatal organism, malformations may have deleterious physiological effects only after birth. The text sets out clearly that among species there are important functional differences that are reflected in the expression of proteins characteristic of the individual species and that change with maturation of the cardiovascular system. All these factors must be taken into account when considering the significance of experimental results.

To my knowledge, this is the first book to cover comparative embryology of the cardiovascular system in invertebrates and vertebrates in a text that is intended to attract readers engaged in biomedical research, closing as it does with chapters on human disease and treatment strategies. Comparative embryology is an important branch of science, and its inclusion in this book may inspire investigators to explore less commonly used models for answers to difficult questions about more complex physiological systems. For example, scientists have long been puzzled by the fact that mature cardiomyocytes appear to be terminally differentiated; that is, they are unable to reenter the cell cycle and replace dead cells after injury to the heart. If the controls that govern the cardiomyocyte cell cycle were understood, it might be possible to treat myocardial infarction by stimulating cellular proliferation to replace dead muscle tissue. Despite the eagerness of investigators to overcome the obstacle of terminal differentiation, few have paid attention to the observation made by the Oberprillers more than 20 years ago (Oberpriller & Oberpriller, 1974) that cells of adult newt and frog hearts are able to reenter the cell cycle and undergo complete mitosis with cytokinesis in response to injury. Over the years they have identified a number of molecules that enhance or inhibit replication of cardiac myocytes in amphibians (Oberpriller et al., 1995). Such information provides a strong background for cell-cycle experts to initiate new studies of mammalian cardiac cells.

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#### xiv Constance Weinstein

This book provides interesting reading but, more important, it will be a source of ideas for new approaches to the problems of perturbed cardiovascular development and treatment of acquired disease.