

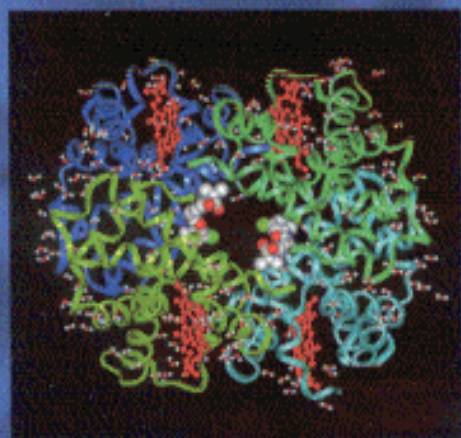
BURGER'S

Sixth Edition

# Medicinal & Chemistry Drug Discovery

Edited by

Donald J. Abraham



VOLUME 2  
Drug Discovery  
and Drug Development

# CONTENTS

---

**1 COMBINATORIAL CHEMISTRY  
AND MULTIPLE PARALLEL  
SYNTHESIS, 1**

Lester A. Mitscher  
Apurba Dutta  
*Kansas University  
Department of Medicinal Chemistry  
Lawrence, Kansas*

**2 HIGH-THROUGHPUT  
SCREENING FOR LEAD  
DISCOVERY, 37**

John G. Houston  
Martyn N. Banks  
*Pharmaceutical Research Institute  
Bristol-Myers Squibb  
Wallingford, Connecticut*

**3 HIGH-THROUGHPUT  
PHARMACOLOGY, 71**

Steven J. Brown  
Imran B. Clark  
Bala Pandi  
*Axiom Biotechnologies, Inc.  
San Diego, California*

**4 APPLICATION OF  
RECOMBINANT DNA  
TECHNOLOGY IN MEDICINAL  
CHEMISTRY AND DRUG  
DISCOVERY, 81**

Soumitra Basu  
*University of Pittsburgh  
Center for Pharmacogenetics  
Department of Pharmaceutical  
Sciences  
Pittsburgh, Pennsylvania*

Adegboyega K. Oyelere  
*Rib-X Pharmaceuticals, Inc.  
New Haven, Connecticut*

**5 OLIGONUCLEOTIDE  
THERAPEUTICS, 115**

Stanley T. Crooke  
*Isis Pharmaceuticals, Inc.  
Carlsbad, California*

**6 THERAPEUTIC AGENTS  
ACTING ON RNA TARGETS, 167**

Jason P. Rife  
*Virginia Commonwealth University  
Richmond, Virginia*

**7 CARBOHYDRATE-BASED  
THERAPEUTICS, 203**

John H. Musser  
*Pharmagenesis, Inc.*  
*Palo Alto, California*

**8 MEMBRANE TRANSPORT  
PROTEINS AND DRUG  
TRANSPORT, 249**

Peter W. Swaan  
*Division of Pharmaceutics*  
*Ohio State Biophysics Program*  
*OSU Heart & Lung Institute Core*  
*Laboratory for Bioinformatics and*  
*Computational Biology*  
*The Ohio State University*  
*Columbus, Ohio*

**9 ALLOSTERIC PROTEINS AND  
DRUG DISCOVERY, 295**

J. Ellis Bell  
*Department of Chemistry*  
*Gottwald Science Center*  
*University of Richmond*  
*Richmond, Virginia*

James C. Burnett  
*School of Pharmacy and*  
*Department of Medicinal Chemistry*  
*Institute for Structural Biology and*  
*Drug Discovery*  
*Virginia Commonwealth University*  
*Richmond, Virginia*

Jessica K. Bell  
*Department of Pharmaceutical*  
*Chemistry*  
*University of California at San*  
*Francisco*  
*San Francisco, California*

Peter S. Galatin  
Donald J. Abraham  
*School of Pharmacy and*  
*Department of Medicinal Chemistry*  
*Institute for Structural Biology and*  
*Drug Discovery*  
*Virginia Commonwealth University*  
*Richmond, Virginia*

**10 RECEPTOR TARGETS IN DRUG  
DISCOVERY AND  
DEVELOPMENT, 319**

Michael Williams  
*Department of Molecular*  
*Pharmacology and Biological*  
*Chemistry*  
*Northwestern University Medical*  
*School*  
*Chicago, Illinois*

Christopher Mehlin  
*Molecumetics Inc.*  
*Bellevue, Washington*

David J. Triggle  
*State University of New York*  
*Buffalo, New York*

**11 NICOTINIC ACETYLCHOLINE  
RECEPTORS, 357**

David Colquhoun  
Chris Shelley  
Chris Hatton  
*Department of Pharmacology*  
*University College London*  
*London, United Kingdom*

Nigel Unwin  
*Neurobiology Division*  
*MRC Laboratory of Molecular*  
*Biology*  
*Cambridge, United Kingdom*

Lucia Sivilotti  
*Department of Pharmacology*  
*The School of Pharmacy*  
*London, United Kingdom*

**12 LARGE-SCALE SYNTHESIS, 407**

Frank Gupton  
*Boehringer Ingelheim Chemicals,*  
*Inc.*  
*Ridgefield, Connecticut*

Karl Grozinger  
*Boehringer Ingelheim*  
*Pharmaceuticals, Inc.*  
*Ridgefield, Connecticut*

# 13 PRINCIPLES OF DRUG METABOLISM, 431

Bernard Testa

*School of Pharmacy*

*University of Lausanne*

*Institute of Medicinal Chemistry*

*Lausanne, Switzerland*

William Soine

*Virginia Commonwealth University*

*Department of Medicinal Chemistry*

*Richmond, Virginia*

# 14 METABOLIC CONSIDERATIONS IN PRODRUG DESIGN, 499

Luc P. Balant

*University Hospitals of Geneva*

*Clinical Research Unit*

*Department of Psychiatry*

*Geneva, Switzerland*

# 15 RETROMETABOLISM-BASED DRUG DESIGN AND TARGETING, 533

Nicholas Bodor

*Center for Drug Discovery*

*University of Florida*

*Gainesville, Florida*

*and*

*IVAX Research, Inc.*

*Miami, Florida*

Peter Buchwald

*IVAX Research, Inc.*

*Miami, Florida*

# 16 DRUG DISCOVERY: THE ROLE OF TOXICOLOGY, 609

James B. Moe

James M. McKim, Jr.

*Pharmacia Corporation*

*Kalamazoo, Michigan*

# 17 DRUG ABSORPTION, DISTRIBUTION, AND ELIMINATION, 633

Leslie Z. Benet

Beatrice Y. T. Perotti

*University of California*

*Department of Pharmacy*

*San Francisco, California*

Larry Hardy

*Aurigene Discovery Technologies*

*Lexington, Massachusetts*

# 18 PHYSICOCHEMICAL CHARACTERIZATION AND PRINCIPLES OF ORAL DOSAGE FORM SELECTION, 649

Gregory E. Amidon

Xiaorong He

Michael J. Hageman

*Pharmacia Corporation*

*Kalamazoo, Michigan*

# 19 THE FDA AND REGULATORY ISSUES, 683

W. Janusz Rzeszutarski

*Food and Drug Administration*

*Rockville, Maryland*

# 20 INTELLECTUAL PROPERTY IN DRUG DISCOVERY AND BIOTECHNOLOGY, 703

Richard A. Kaba

Timothy P. Maloney

James P. Krueger

Rudy Kratz

Julius Tabin

*Fitch, Even, Tabin & Flannery*

*Chicago, Illinois*

INDEX, 783