

*Methods in Enzymology*

*Volume 292*

*ABC Transporters:  
Biochemical, Cellular, and  
Molecular Aspects*

EDITED BY

*Suresh V. Ambudkar*

NATIONAL CANCER INSTITUTE  
NATIONAL INSTITUTES OF HEALTH  
BETHESDA, MARYLAND

*Michael M. Gottesman*

NATIONAL CANCER INSTITUTE  
NATIONAL INSTITUTES OF HEALTH  
BETHESDA, MARYLAND



ACADEMIC PRESS

San Diego London Boston New York Sydney Tokyo Toronto

## Table of Contents

CONTRIBUTORS TO VOLUME 292. . . . .	xi
PREFACE. . . . .	xvii
VOLUMES IN SERIES . . . . .	xix

### Section I. Prokaryotic ABC Transporters

1. Overview of Bacterial ABC Transporters	HIROSHI NIKAIIDO AND JASON A. HALL	3
2. Preparation and Reconstitution of Membrane-Associated Maltose Transporter Complex of <i>Escherichia coli</i>	JASON A. HALL, AMY L. DAVIDSON, AND HIROSHI NIKAIIDO	20
3. Maltose Transport in <i>Escherichia coli</i> : Mutations That Uncouple ATP Hydrolysis from Transport	CYNTHIA H. PANAGIOTIDIS AND HOWARD A. SHUMAN	30
4. Binding Protein-Dependent ABC Transport System for Glycerol 3-Phosphate of <i>Escherichia coli</i>	WINFRIED BOOS	40
5. Structure-Function Analysis of Hemolysin B	FANG ZHANG, JONATHAN A. SHEPS, AND VICTOR LING	51
6. <i>Erwinia</i> Metalloprotease Permease: Aspects of Secretion Pathway and Secretion Functions	PHILIPPE DELEPELAIRE	67
7. Arsenical Pumps in Prokaryotes and Eukaryotes	MASAYUKI KURODA, HIRANMOY BHATTACHARJEE, AND BARRY P. ROSEN	82

### Section II. Eukaryotic ABC Transporters

8. Evolutionary Relationships among ABC Transporters	JAMES M. CROOP	101
9. Cloning of Novel ABC Transporter Genes	RANDO ALLIKMETS AND MICHAEL DEAN	116
10. <i>Saccharomyces cerevisiae</i> ABC Proteins and Their Relevance to Human Health and Disease	DANIEL TAGLIGHT AND SUSAN MICHAELIS	130

#### A. Nonmammalian ABC Transport Systems

11. <i>Arabidopsis</i> MDR Genes: Molecular Cloning and Protein Chemical Aspects	ROBERT DUDLER AND MICHAEL SIDLER	162
--	-------------------------------------	-----

12. Functional Analysis of <i>pfmdr1</i> Gene of <i>Plasmodium falciparum</i>	SARAH VOLKMAN AND DYANN WIRTH	174
13. Amplification of ABC Transporter Gene <i>pgpA</i> and of Other Heavy Metal Resistance Genes in <i>Leishmania tarentolae</i> and Their Study by Gene Transfection and Gene Disruption	MARC OUELLETTE, ANASS HAIMEUR, KATHERINE GRONDIN, DANIELLE LÉGARÉ, AND BARBARA PAPADOPOULOU	182
14. Functional Assay for Analysis of Yeast <i>ste6</i> Mutants	GABY L. NIJBROEK AND SUSAN MICHAELIS	193
15. ABC Transporters Involved in Transport of Eye Pigment Precursors in <i>Drosophila melanogaster</i>	GARY D. EWART AND ANTHONY J. HOWELLS	213

### B. Mammalian P-Glycoproteins

16. Isolation of Altered-Function Mutants and Genetic Suppressor Elements of Multidrug Transporter P-Glycoprotein by Expression Selection from Retroviral Libraries	IGOR B. RONINSON, DONALD ZUHN, ADAM RUTH, AND DAVID DE GRAAF	225
17. Selection and Maintenance of Multidrug-Resistant Cells	MICHAEL M. GOTTESMAN, CAROL CARDARELLI, SARAH GOLDENBERG, THOMAS LICHT, AND IRA PASTAN	248
18. Monoclonal Antibodies to P-Glycoprotein: Preparation and Applications to Basic and Clinical Research	MIKIHICO NAITO AND TAKASHI TSURUO	258
19. Topology of P-Glycoproteins	WILLIAM R. SKACH	265
20. Use of Cell-Free Systems to Determine P-Glycoprotein Transmembrane Topology	JIAN-TING ZHANG	279
21. Photoaffinity Labels for Characterizing Drug Interaction Sites of P-Glycoprotein	AHMAD R. SAFA	289
22. Identification of Drug Interaction Sites in P-Glycoprotein	LEE M. GREENBERGER	307
23. Photoaffinity Labeling of Human P-Glycoprotein: Effect of Modulator Interaction and ATP Hydrolysis on Substrate Binding	SAIBAL DEY, MURALIDHARA RAMACHANDRA, IRA PASTAN, MICHAEL M. GOTTESMAN, AND SURESH V. AMBUDKAR	318
24. Identification of Phosphorylation Sites in Human MDR1 P-Glycoprotein	TIMOTHY C. CHAMBERS	328

25. Identification of <i>in Vivo</i> Phosphorylation Sites for Basic-Directed Kinases in Murine <i>mdr1b</i> P-Glycoprotein by Combination of Mass Spectrometry and Site-Directed Mutagenesis	J. S. GLAVY, M. WOLFSON, E. NIEVES, E.-K. HAN, C.-P. H. YANG, S. B. HORWITZ, AND G. A. ORR	342
26. P-Glycoprotein and Swelling-Activated Chloride Channels	TAMARA D. BOND, CHRISTOPHER F. HIGGINS, AND MIGUEL A. VALVERDE	359
27. Functional Expression of <i>mdr</i> and <i>mdr</i> -like cDNAs in <i>Escherichia coli</i>	EITAN BIBI, ROTEM EDGAR, AND ODED BÉJÀ	370
28. Yeast Secretory Vesicle System for Expression and Functional Characterization of P-Glycoproteins	STEPHAN RUETZ	382
29. High-Level Expression of Mouse Mdr3 P-Glycoprotein in Yeast <i>Pichia pastoris</i> and Characterization of ATPase Activity	LUCILLE BEAUDET, INA L. URBATSCH, AND PHILIPPE GROS	397
30. Mutational Analysis of P-Glycoprotein in Yeast <i>Saccharomyces cerevisiae</i>	LUCILLE BEAUDET AND PHILIPPE GROS	414
31. Baculovirus-Mediated Expression of Human Multi-drug Resistance cDNA in Insect Cells and Functional Analysis of Recombinant P-Glycoprotein	URSULA A. GERMANN	427
32. Recombinant Vaccinia Virus Vectors for Functional Expression of P-Glycoprotein in Mammalian Cells	MURALIDHARA RAMACHANDRA, MICHAEL M. GOTTESMAN, AND IRA PASTAN	441
33. Functional Expression of Human P-Glycoprotein from Plasmids Using Vaccinia Virus-Bacteriophage T7 RNA Polymerase System	CHRISTINE A. HRYCYNIA, MURALIDHARA RAMACHANDRA, IRA PASTAN, AND MICHAEL M. GOTTESMAN	456
34. pHaMDR-DHFR Bicistronic Expression System for Mutation Analysis of P-Glycoprotein	SHUDONG ZHANG, YOSHIKAZU SUGIMOTO, TZIPORA SHOSHANI, IRA PASTAN, AND MICHAEL M. GOTTESMAN	474
35. Mutational Analysis of Human P-Glycoprotein	TIP W. LOO AND DAVID M. CLARKE	480
36. Purification and Reconstitution of Human P-Glycoprotein	SURESH V. AMBUDKAR, ISABELLE H. LELONG, JIAPING ZHANG, AND CAROL CARDARELLI	492

37. Drug-Stimulatable ATPase Activity in Crude Membranes of Human <i>MDRI</i> -Transfected Mammalian Cells	SURESH V. AMBUDKAR	504
38. ATPase Activity of Chinese Hamster P-Glycoprotein	ALAN E. SENIOR, MARWAN K. AL-SHAWI, AND INA L. URBATSCH	514
39. Construction of <i>MDRI</i> Vectors for Gene Therapy	YOSHIKAZU SUGIMOTO, MICHAEL M. GOTTESMAN, IRA PASTAN, AND TAKASHI TSURUO	523
40. Construction of <i>MDRI</i> Adeno-Associated Virus Vectors for Gene Therapy	MARION BAUDARD	538
41. Retroviral Transfer of Multidrug Transporter to Murine Hematopoietic Stem Cells	THOMAS LICHT, MICHAEL M. GOTTESMAN, AND IRA PASTAN	546
42. Retroviral Transfer of Human <i>MDRI</i> Gene into Human T Lymphocytes	CAROLINE G. L. LEE, IRA PASTAN, AND MICHAEL M. GOTTESMAN	557
43. Construction and Analysis of Multidrug Resistance Transgenic Mice	GREGORY L. EVANS	572

### C. Multidrug Resistance Associated Protein

44. Cloning, Transfer, and Characterization of Multidrug Resistance Protein	CAROLINE E. GRANT, GABU BHARDWAJ, SUSAN P. C. COLE, AND ROGER G. DEELEY	594
45. Transport Function and Substrate Specificity of Multidrug Resistance Protein	DIETRICH KEPPLER, GABRIELE JEDLITSCHKY, AND INKA LEIER	607

### D. Cystic Fibrosis Transmembrane Conductance Regulator

46. Heterologous Expression Systems for Study of Cystic Fibrosis Transmembrane Conductance Regulator	XIU-BAO CHANG, NORBERT KARTNER, FABIAN S. SEIBERT, ANDREI A. ALEKSANDROV, ANDREW W. KLOSER, GRETCHEN L. KISER, AND JOHN R. RIORDAN	616
47. Characterization of Polyclonal and Monoclonal Antibodies to Cystic Fibrosis Transmembrane Conductance Regulator	NORBERT KARTNER AND JOHN R. RIORDAN	629

48. Identification of Cystic Fibrosis Transmembrane Conductance Regulator in Renal Endosomes	ISABELLE T. CRAWFORD AND PETER C. MALONEY	652
49. Assays of Dynamics, Mechanisms, and Regulation of ATP Transport and Release: Implications for Study of ABC Transporter Function	ERIK M. SCHWIEBERT, MARIE E. EGAN, AND WILLIAM B. GUGGINO	664
50. Overexpression, Purification, and Function of First Nucleotide-Binding Fold of Cystic Fibrosis Transmembrane Conductance Regulator	YOUNG HEE KO AND PETER L. PEDERSEN	675
51. Recombinant Synthesis of Cystic Fibrosis Transmembrane Conductance Regulator and Functional Nucleotide-Binding Domains	SCOTT A. KING AND ERIC J. SORSCHER	686
52. Cationic Lipid Formulations for Intracellular Gene Delivery of Cystic Fibrosis Transmembrane Conductance Regulator to Airway Epithelia	SENG HING CHENG, JOHN MARSHALL, RONALD K. SCHEULE, AND ALAN E. SMITH	697
53. Adeno-Associated Virus Vectors for Gene Therapy of Cystic Fibrosis	TERENCE R. FLOTTE AND BARRIE J. CARTER	717

#### E. Sulfonylurea Receptor

54. Sulfonylurea Receptors and ATP-Sensitive Potassium Ion Channels	LYDIA AGUILAR-BRYAN, JOHN P. CLEMENT IV, AND DANIEL A. NELSON	732
---	---	-----

#### F. Intracellular ABC Transporters

55. Peptide Transport Assay for TAP Function	YE WANG, DAVID S. GUTTOH, AND MATTHEW J. ANDROLEWICZ	745
56. Peroxisomal ABC Transporters	NOAM SHANI AND DAVID VALLE	753
57. Mitochondrial ABC Transporters	JONATHAN LEIGHTON	776
AUTHOR INDEX . . . . .		789
SUBJECT INDEX . . . . .		833