NEW VISTAS IN THERAPEUTICS
FROM DRUG DESIGN TO GENE THERAPY

Editors
SONIA I. SKARLATOS, PAUL VELLETRI, AND MARIANA MORRIS

Conference Organizers
MARIANA MORRIS, C. FRANK BENNET, PAUL A. VELLETRI, AMY TRAINOR,
SONIA SKARLATOS, AND VICTOR J. DZAU

DRUG-RESISTANT TUBERCULOSIS
FROM MOLECULES TO MACRO-ECONOMICS

Editor
PETER DAVIES

Advisory Board
PETER DAVIES, MARTY ADAIR, FRANCIS DREBNIEWSKI, JANE LEESE,
JOHN MOORE-GILLON, PETER ORMEROD, JOHN PORTER, ANTON POZNIAK,
AND JACK TINKER

[This volume is the result of two conferences: New Vistas in Therapeutics: From Drug Design to Gene Therapy, sponsored by the American Society for Biochemistry and Molecular Biology (ASBMB) and the American Society for Pharmacology and Experimental Therapeutics (ASPET) and held as a FASEB satellite meeting on June 3–4, 2000 in Boston, Massachusetts; and Tuberculosis Drug Resistance: From Molecules to Macro-Economics, sponsored by Royal Society of Medicine, Liverpool Medical Institution, and TB Focus and held on March 29–30, 2001 in London.]

CONTENTS

NEW VISTAS IN THERAPEUTICS: FROM DRUG DESIGN TO GENE THERAPY

Introduction. By SONIA I. SKARLATOS AND VICTOR DZAU .......................... 1
Medicinals for the Millennia: The Historical Record. By GORDON M. CRAGG
AND DAVID J. NEWMAN ................................................................. 3
Gene Therapy: A Brief Overview of the Past, Present, and Future. By ROLAND SCOLLAY ................................................................. 26


Retroviral Approaches to Gene Therapy of Cystic Fibrosis. By LARRY G. JOHNSON ................................................................. 43

Regulated Gene Expression in Gene Therapy. By PHILIP W. ZOLTICK AND JAMES M. WILSON ................................................................. 53

AAV-Mediated Gene Transfer for Hemophilia. By KATHERINE A. HIGH .. 64

Bone Marrow as a Source of Endothelial Cells for Natural and Iatrogenic Vascular Repair. By JEFFREY M. ISNER, CHRISTOPH KALKA, ATSUHIKO KAWAMOTO, AND TAKAYUKI ASAHIARA ............. 75

DRUG-RESISTANT TUBERCULOSIS: FROM MOLECULES TO MACRO-ECONOMICS

Introduction. By PETER DAVIES ................................................................. 87

Part I. The Scale of the Problem

The Burden of Drug-Resistant Tuberculosis and Mechanisms for Its Control. By MARIO C. RAVIGLIONE, RAJESH GUPTA, CHRISTOPHER M. DYE, AND MARCOS A. ESPINAL ................................................................. 88

India's Multidrug-Resistant Tuberculosis Crisis. By ZARIR F. UDWADIA .. 98

Drug-Resistant Tuberculosis in Africa. By A. MWINGA ................................................................. 106

Problems in Prisons Worldwide, with a Particular Focus on Russia. By VIVIEN STERN ................................................................. 113

The Impact of Worldwide Drug Resistance on the United Kingdom. By JOHN WATSON ................................................................. 120

Specific Features of the Spread of Tuberculosis in Russia at the End of the 20th Century. By MARGARITA V. SHILOVA ................................................................. 124

Tuberculosis in Russia and the Problem of Multiple Drug Resistance. By V.V. YEROKHIN, V.V. PUNGA, AND L.N. RYBKA ................................................................. 133

Part II. Scientific Basis of Drug-Resistant Tuberculosis

Molecular Techniques in the Diagnosis of Mycobacterium tuberculosis and the Detection of Drug Resistance. By M. CAWS AND F.A. DROBNIEWSKI ................................................................. 138

Letting the Genome Out of the Bottle: Prospects for New Drug Development. By DOUGLAS YOUNG ................................................................. 146

The Genetics of Host Resistance and Susceptibility to Tuberculosis. By PETER DAVIES AND JOHN GRANGE ................................................................. 151

Pharmacological Issues in the Treatment of Tuberculosis. By CHARLES A. PELOQUIN ................................................................. 157
Part III. Clinical Aspects of Drug Resistance

DOTS and DOTS-Plus: Not the Only Answer. By PAUL FARMER 165

Part IV. Practicalities of Prevention

The Clinical Management of the Drug-Resistant Patient. By PETER ORMERO 185
Multidrug-Resistant Tuberculosis and HIV Infection. By ANTON POZNIAK 192
Holding the Patient. By GINI WILLIAMS 199

Part V. Coercion or Commitment: Policies of Prevention

Moral Problems in the Use of Coercion in Dealing with Nonadherence in the Diagnosis and Treatment of Tuberculosis. By LEN DOYAL 208
Just Coercion? Detention of Nonadherent Tuberculosis Patients. By RICHARD COKER 216

Part VI. The Future

Multidrug-Resistant Tuberculosis: This Is the Cost. By JOHN MOORE-GILLON 233
Drug-Resistant Tuberculosis: Concluding Remarks. By PETER D.O. DAVIES 241

Index of Contributors 247
Subject Index 249

Financial assistance for New Vistas in Therapeutics: From Drug Design to Gene Therapy was received from:
- DUPONT PHARMACEUTICALS COMPANY
- ISIS PHARMACEUTICALS
- ASTRAZENECA
- VERTEX PHARMACEUTICALS INCORPORATED

Financial assistance for Drug-Resistant Tuberculosis: From Molecules to Macro-Economics was received from:
- DEPARTMENT FOR INTERNATIONAL DEVELOPMENT, UNITED KINGDOM
- DEPARTMENT OF HEALTH, UNITED KINGDOM
- ROCHE
- MERCK SHARP & DOHME
- SWEDISH ORPHAN
- BOEHRINGER ENGEIHEIM
- ORGANON
- 3M
- INTERMUNE PHARMACEUTICALS, INC.