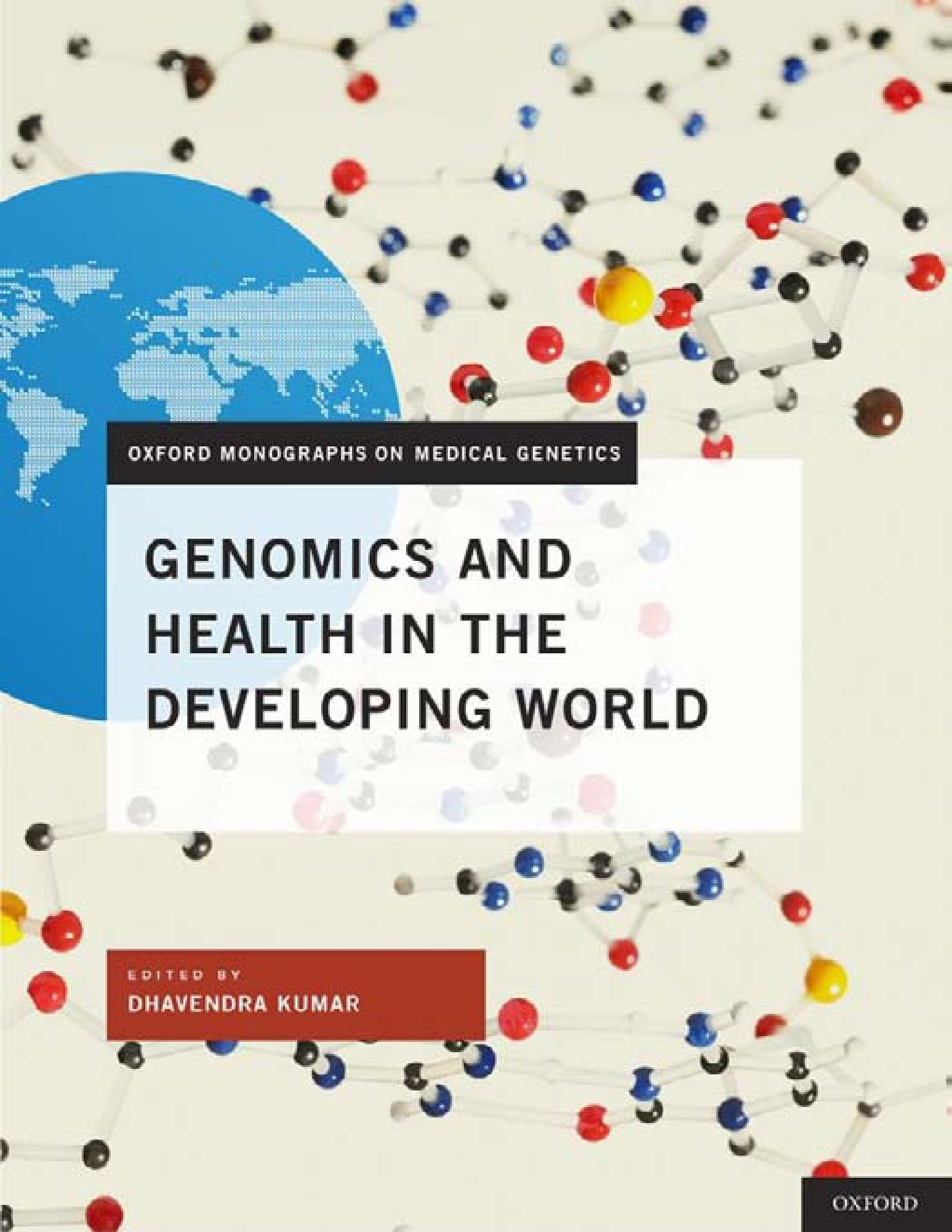

OXFORD MONOGRAPHS ON MEDICAL GENETICS

GENOMICS AND HEALTH IN THE DEVELOPING WORLD

EDITED BY
DHAVENDRA KUMAR

OXFORD

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GENOMICS AND HEALTH IN THE DEVELOPING WORLD

EDITED BY

Dhavendra Kumar, MD, FRCP, FRCPCH, FACMG

CONSULTANT IN CLINICAL GENETICS

UNIVERSITY HOSPITAL OF WALES, CARDIFF, WALES;

INSTITUTE OF MOLECULAR AND EXPERIMENTAL MEDICINE, SCHOOL OF MEDICINE

CARDIFF UNIVERSITY & GENOMIC POLICY RESEARCH UNIT, SCHOOL OF HEALTH

SPORT & SCIENCE, THE UNIVERSITY OF GLAMORGAN, PONTYPRIDD, WALES

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OXFORD
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Oxford University's objective of excellence
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Oxford New York
Auckland Cape Town Dar es Salaam Hong Kong Karachi
Kuala Lumpur Madrid Melbourne Mexico City Nairobi
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With offices in
Argentina Austria Brazil Chile Czech Republic France Greece
Guatemala Hungary Italy Japan Poland Portugal Singapore
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Published by Oxford University Press, Inc.
198 Madison Avenue, New York, New York 10016
www.oup.com

Oxford is a registered trademark of Oxford University Press

Library of Congress Cataloging-in-Publication Data
Genomics and health in the developing world / edited by Dhavendra Kumar.
p. ; cm. — (Oxford monographs on medical genetics ; no. 62)
Includes bibliographical references and index.
ISBN-13: 978–0–19–537475–9 (hardcover : alk. paper)
ISBN-10: 0–19–537475–4 (hardcover : alk. paper)
I. Kumar, Dhavendra. II. Series: Oxford monographs on medical genetics ; no. 62.
[DNLM: 1. Genetic Diseases, Inborn—epidemiology. 2. Developing Countries.
3. Genetics, Medical. 4. Genomics. QZ 50]
616'.042091724—dc23 2012002317

1 3 5 7 9 8 6 4 2
Printed in the United States of America
on acid-free paper

“To millions of people in the developing world who live with poverty, hunger and disease”

“Science to be science must afford the fullest scope for satisfying the hunger of body, mind and soul”

— Mahatma Gandhi

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PREFACE

Health of any nation depends upon its sound economic base, political stability, healthy agriculture (crops/animal stock), a safe environment (clean water, sanitation and climate control) and the general well-being of its peoples. Among several biological and ecological factors, the role of genetics and genomics is now widely accepted as a major determinant for the health of a nation. There are diverse and far reaching applications of genetics and genomics that we are beginning to utilize in all walks of life, including genetically engineered vaccines and biological products (insulin and growth hormone), new drugs (cancer and heart disease), genetically modified crops (enhanced produce and biofortification), developing bioengineered vectors for controlling malaria and other parasitic diseases, and the preservation of animal and plant life (rare and extinct species).

Most developed nations in the West have invested, and continue to do so, in harnessing the benefits of genetics and genomics. However, large populations in the less developed and least developed countries—comprising more than two-thirds of the world's population—continue to be deprived of potential health and socioeconomic applications (Figure 1). It is estimated that the current global population of around 7 billion will rise to around 10 billion by 2050 (Figure 2). There is concern that currently around 5 billion people are deprived of the benefits of modern science and technology, including genetics and genomics.

The clinical use of medical genetics and human genetic research is concentrated in the developed nations of Europe and North America that cover less than one billion people. In contrast, India alone has over 1 billion people equally at risk for being affected with a wide range of genetic diseases! The volume and burden of genetic disease afflicting those in other, developing or less developed or "low income" countries are beyond both imagination and comprehension. In addition to medicine and health, whole nations and peoples are being deprived of the socioeconomic benefits from investment and infrastructure developments in areas like biomedical and agriculture technology. The current and future applications of genome science and technology in pharmaceutical, bioengineering, and the food and agriculture industries hold great promise for the new emerging economies of the developing world (Juma and Yee-Cheong, 2005). This challenge offers new opportunities for promoting international cooperation in relevant biomedical research in developing countries as recommended by the United Nations' Millennium Project Task Force on Science, Technology and Innovation (UN Millennium Project Report, 2005). These recommendations are included in the UN Millennium Development Goals (Acharya et al., 2003).

Since the completion of mapping/sequencing of the human genome and other genomes, rapid progress has been made in a number of areas of biomedical research and biotechnology. Biotechnology has emerged as one of the methods that can be used to address health and other socioeconomic challenges in developing countries (Acharya et al., 2003). This largely depends upon the development of infrastructure and adopting a diverse set of policies aimed at translating scientific discoveries into goods and services. These technologies include molecular diagnostics, recombinant vaccines, techniques of vaccine and drug delivery, bioremediation (use of living organisms to degrade hazardous matter), sequencing pathogen genomes, female-controlled protection against sexually transmitted infections, bioinformatics, nutritionally enriched genetically modified crops, recombinant therapeutic proteins, and combinatorial chemistry (Daar et al., 2002).

While it is necessary to prioritize the current limited resources in dealing with the most common socioeconomic and health problems faced by developing countries, especially the least developed countries, resulting from poverty, malnutrition, unsafe water supply, poor sanitation, and communicable diseases, it is nevertheless important to invest in new science and technology to bridge the gap and prepare some ground for future developments. Unfortunately, geographic, economic, and political challenges in these countries often restrict investment and improvement in the infrastructure development necessary to sustain progress in any area. There is ample evidence to argue that genetic and genomic factors play an important role in the causation of the common health problems affecting developing and least-developed nations, and in their consequences for these populations. This issue was examined and highlighted in the WHO

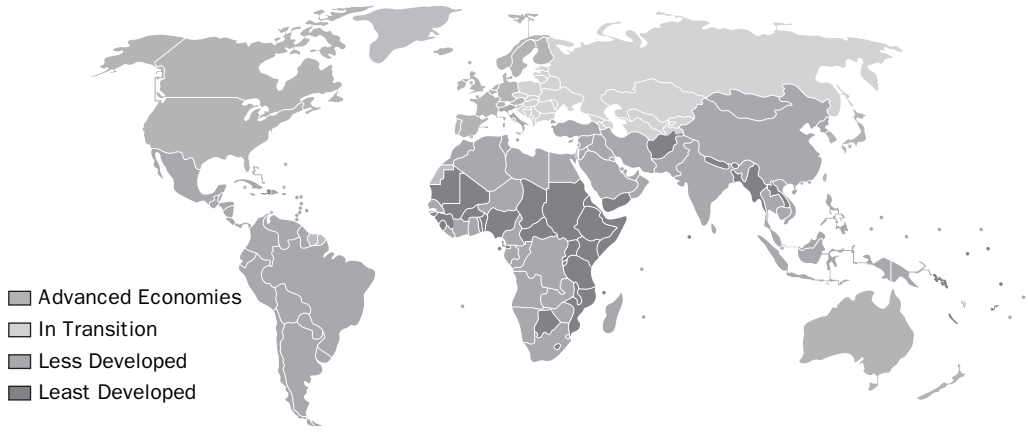

Figure 1 The world map showing least and less developed nations including those in transition.

expert committee report on role of genomics for global health (WHO, 2002). This has been followed by several reports and publications that lend further support to the view that the developing nations in Asia should not be left behind in acquiring relevant genetic and genomic technologies for the betterment of health. A recent editorial commentary (*Nature*, 2007) points to this subject and sets out an optimistic picture of the future of genetics and genomics in developing countries, particularly India, Latin America, the Arab world, and parts of Africa. The importance of genetics and genomics is acknowledged in the recent WHO statement on the global prevention of birth defects endorsed by the Sixty-Third World Assembly (WHO, April 2010). The WHO 'Grand Challenges' project on applications of genomics in the public health in the developing world (July 2011) is expected to identify potential areas and offer strategic guidance to member Nations in the developing world.

The practice of clinical medicine in public health is rapidly changing in the light of recent critical advances in genetics and genomics. This is largely based upon the sequencing of the human genome and a number of other genomes, including agricultural crops and other plants, as well as pathogens and important model organisms (microbes, worms, insects, and mammals). The true extent of the power of genomic science and technology in shaping and influencing medicine and the economy is difficult to describe but is likely to be vast. There are now several dedicated publications and on-line resources specifically reporting and discussing this subject. The publication of this book is timely, and we hope that the reader will find the insights presented throughout the volume to be exciting, challenging, and constructive. In addition, the book contains information that will be helpful beyond the confines of the profession of medicine, including the range of those with responsibility for making decisions on biotechnology development and health planning, and those concerned with related social, ethical, economic, and legal matters.

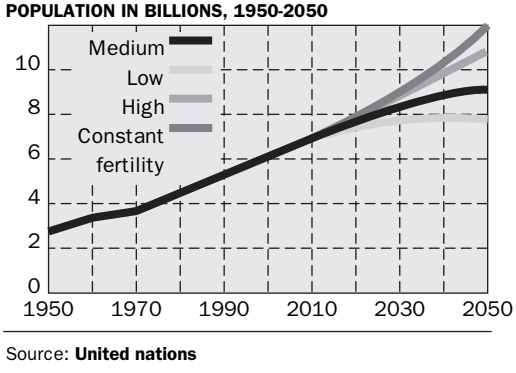

Figure 2 The United Nations projection of the global population.

There is no single book that deals with the issues and challenges for the emerging economies of the developing world in confronting the rapid advances of genome science and technology. This is probably the first book providing a detailed and comprehensive account of this extremely important field, and it is likely to have a major impact on healthcare and the economy in most countries in the developing and least-developed world. There are a few volumes currently available that cover selected population groups only, for example Jewish peoples (Abel, 2001) and peoples of African descent (Bowman and Murray Jr., 1998). There are only two books that cover in some detail the human genetics of the Arab world (Teebi and Farag, 1996) and the populations of the Indian subcontinent (Kumar, 2004). It is anticipated that the publication of this new book will fill a huge gap that currently exists in information and issues about human health in those countries that constitute the newly emerging and other developing economies of the world. It is now widely believed that the rapid development and inclusion of genetic and genomic technologies will be crucial to any nation's socioeconomic well-being, and the health of its population. It is important that this technology and expertise should not remain beyond the reach of the developing world, confined to the

global West and North. We hope that the structured presentation of factual information in this book will serve as a useful resource for a wide range of professionals in medicine, population health, the biotechnology industries, media, and public services.

The book is expected to be useful to a broad range of audiences including practicing and trainee medical practitioners, health professionals, human genetic scientists, medical geneticists, genetic counselors, public health physicians and consultants, experts in health economics, bioethics, sociology, anthropology, and others leading various projects at national and international levels. The book includes material that is also applicable to medical and related professionals about the minority migrant or resident ethnic populations working and living in the developed countries of Europe and North America, as well as Australasia.

This "multi-author" edited book includes several expertly written chapters providing a detailed and comprehensive account on most aspects of population and human genetics, with an emphasis on medical and health issues related to a defined geographic region and, as far as possible, covering all major ethnic groups. The book is set in two parts, each part with several chapters contributed by a panel of internationally renowned experts in the designated field or area of interest. The first part covers general aspects of population origin and heterogeneity, an introduction to basic genetics and genomics, and the principles of human genetics, the classification of human disease from genetic and genomic perspectives, the current and future health strategies in dealing with the common human genetic diseases affecting developing countries, social and cultural practices and legislation pertinent to human genetics and genomics, the impact of genomics on human health in the developing world, and the related social, ethical, economic, and legal issues. The second part gives an account of selected genetic disorders and the genetic services relevant to major geographic and population-specific regions. Chapters within each section are written and carefully edited with the advice of experts with specialist knowledge and understanding of the subject and related regional and ethnic issues.

This book is only a small effort by several dedicated professionals, who share the commitment and strong belief that the applications of genome science and technology are crucial for the socio-economic development and provision of modern healthcare to large heterogeneous populations in the developed and least-developed nations of the world. Hopefully, it will be a contribution, however small, to achieving the goals of the World Health Organization and that of emerging low- and middle-income economies across the world.

Dhavendra Kumar
University Hospital of Wales , Institute of Molecular and Experimental Medicine, School of Medicine, Cardiff University; Genomic Policy Research Unit, School of Health, Sport & Science The University of Galmorgan United Kingdom

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FOREWORD I

The past one hundred years has seen the remarkable rise of science and medicine in the West. The great public investments in biomedical research and technology by the developed economies have not only contributed to the vastly improved health of their citizens, but that knowledge and its practice has, in no small measure, contributed to the improved health of populations in the developing economies as well. It is now an expectation, of people and their governments, that investments in science and medicine should improve health in their lifetimes. For someone like myself, who started academic life merely interested in the mysteries that genes offered, and who has found himself in the rapidly advancing biomedical field of human genetics, this last statement is extraordinary but possibly realizable.

We are likely in the midst of another major revolution in medicine occasioned by the human genome sequence. The rise of genetics and genomics has not only produced a common intellectual (and intelligible) language for the biomedical sciences, but has raised huge expectations that we can rationally understand the molecular causes of any human disease, create efficient diagnostic tools, and invent rational chemical therapies. More importantly, genomics has added a new dimension to medical practice, raising the expectation that we might be able to "personalize" treatment to the individual patient. Will the transfer of this new science and health knowledge, from the developed to the developing countries, be the same as that in the past? There are many reasons to suspect that it will not, and this edited volume by Professor Dhavendra Kumar is an argument for this view. Three major underlying themes in his book deserve mention.

First, genetics explains our individuality and how our recent shared human ancestry affects the variation in our genomes. Consequently, there is no full understanding of a human disease, not even a purely single-gene Mendelian disorder, from studying patients in one geographical locale. Alternatively, a comparative study of the same disease across cultures, ecologies, and ancestries is more informative for all patients. Second, unique cultures often produce unique genetic outcomes not always observed elsewhere. This could include the occurrence of consanguinity, or unique diets and lifestyles, and have effects on the distribution of the types and nature of genetic mutations. If we are to understand gene–environmental interactions it is quite clear that we will need a global study. Third, modern genetic and genomic technologies, ever since the recombinant DNA days, are powerful primarily because they are "species-independent" and can be of great benefit not only to medicine but also to agriculture and veterinary applications. This has not escaped the notice of many governments who are now enthusiastic about their investments in "biotechnology." Consequently, and despite the differing magnitudes of investment, many developing nations think it in their self-interest to develop biotechnology for solving health problems unique to their lives.

Genomics and Health in the Developing World is a potpourri of chapters that attempts to educate us to the nature, magnitude, successes, and opportunities for genetic studies in the developing world. Individually, the chapters inform us about the current state of the art. Collectively, the chapters demonstrate that a true understanding of the problems of genetic disease and personalized genetics will require solid and persistent contributions from the developing world.

We all live in a remarkable time in biomedicine, where each human has something credible to contribute to humanity's understanding of health and disease, and the practice of medicine. Whether you are a student or teacher, geneticist or not, researcher or health professional, you will find this treasure exciting.

Aravinda Chakravarti, PhD
Baltimore, MD
December, 2011

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FOREWORD II

Because of the extremely high childhood mortality in the poorer countries of the world resulting from malnutrition, limited public health services, and the ravages of communicable disease, international health agencies have tended to ignore the growing importance of congenital malformation and genetic disease as an emerging global health problem. In 2006 the American charity, March of Dimes, in its *Global Report on Birth Defects* estimated that more than 7,000,000 babies are born each year with either a congenital abnormality or genetic disease, and that up to 90% of these births occur in low- or middle-income countries. Remarkably, over 25% of them consist of only five conditions: congenital heart defects, neural tube defects, inherited disorders of hemoglobin, Down syndrome, and glucose-6-phosphate dehydrogenase deficiency. Overall, however, over 7,000 birth defects of genetic or partial genetic origin have been identified.

There are several reasons why there is a higher frequency of births with these conditions in the poorer countries. They include natural selection, a high frequency of consanguineous marriages, increased maternal age, and the effects of the epidemiological transition whereby, as public health measures and improved standards of living reduce childhood mortality rates, many babies who would have died with genetic disorders are now surviving long enough to present for diagnosis and treatment.

It is clear, therefore, that genetic disease cannot continue to be ignored by governments of the developing countries or by the international health agencies. One of the major obstacles toward progress in this field is lack of accurate global data about the frequency of these conditions, and current facilities for their diagnosis and management. In this book, many aspects of the current background to the high frequency of genetic disease in the poorer countries are explored, together with representative accounts of the problems raised by genetic disease in many of these countries. It is hoped that information of this type will form the basis for educating governments and health agencies about the increasing problems that genetic disease will pose in the future, particularly in countries that are going through the epidemiological transition with falling childhood mortality rates. This is a critically important topic for the future of global healthcare, and I wish this book all the success it deserves.

D.J. Weatherall, FRS
Oxford
September 2011

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PART ONE: GENOMICS IN MEDICINE AND HEALTH—GENERAL

CONTRIBUTORS

Abdelhak, Sonia, PhD
Molecular Investigation of Genetic Orphan Diseases Research Unit
Institut Pasteur de Tunis
Tunis
Tunisia

Abu-Libdeh, Bassam, MD
Department of Pediatrics & Clinical Genetics
Al Makassad Arabic Hospital
East Jerusalem
Israel

Adib, Salim M, MD
Department of Social and Family Medicine
Faculty of Medicine
Saint Joseph University
Beirut
Lebanon

Agarwal, Neeraj
National Eye Institute
National Institutes of Health
Bethesda, MD
USA

Agrawal, Anurag, PhD
Institute of Genomics and Integrative Biology (IGIB-CSIR)
Mall Road
Delhi
India

Akhmetova, Vita L
Institute of Biochemistry and Genetics
Ufa Science Center
Russian Academy of Sciences
Prospekt Oktyabrya, 71
Ufa, Bashkortostan, 450054
Russia

Al-Aqeel, Aida I, MD, FACMG
Senior Consultant Pediatrics, Medical Genetics and Endocrinology
Department of Paediatrics
King Faisal Specialist Hospital and Research Centre
Riyadh Military Hospital
Kingdom of Saudi Arabia

Al Ali, Mahmoud Taleb
Centre for Arab Genomic Studies
Dubai
United Arab Emirates

Al-Arrayed, Shaikha Salim, PhD
Genetics Department
Salmaniya Medical Complex
Ministry of Health
Bahrain

Al-Gazali, Lihadh, MSc, FRCP
Professor of Clinical Genetics
Department of Paediatrics
Faculty of Medicine & Health Sciences
UAE University
Al-Ain
United Arab Emirates

Al Homssi, Mohamad
College of Medicine
University of Sharjah
Sharjah
United Arab Emirates

Al-Saud, Haya
Department of Genomics of Common Disease
School of Public Health
Imperial College London
London
UK

Alessandrini, Marco
ME Health Enterprises CC
Centurion
South Africa

Apte, Bal N
Formerly Head of Human Genetics Laboratory
Bombay Hospital
Mumbai
India

Arunkumar, Ganesh Prasad
Department of Immunology
Madurai Kamaraj University
Madurai-625021
Tamil Nadu
India

Arun, Varatharajan Santhakumari
Dept of Immunology
Madurai Kamaraj University
Madurai-625021
Tamil Nadu
India

Asfaha, Sahle M.
Departments of Immunology
Faculty of Health Science
University of Pretoria
South Africa

Balu, Sam
Department of Human Genetics
National Institute of Mental Health and Neurological Sciences (NIMHANS)
Bangalore, Karnataka
India

Baldo, Guilherme
Gene Therapy Center
Hospital de Clinicas de Porto Alegre
Rua Ramiro Barcelos
Porto Alegre, RS
Brazil

Beighton, Peter, PhD, FRCP
Emeritus Professor
Division of Human Genetics
Faculty of Health Sciences
University of Cape Town
South Africa

Bharadwaj, Dwaipayan, PhD
Genomics and Molecular Medicine Unit
Institute of Genomics and Integrative Biology (IGIB-CSIR)
Mall Road
Delhi
India

Bhardwaj, Minakshi, PhD
Centre for Economic and Social applications of Genomics (CESAGEN)
School of Social Sciences
Cardiff University
UK

Bhatt, Meenakshi, MD, MRCPI
Associate Professor/Consultant in Clinical Genetics
Centre for Human Genetics & Indira Gandhi Child Health Institute
Bangalore, Karnataka
India

Bhatnagar, Deepak, PhD, FRCP
Consultant/Senior Lecturer in Diabetes & Metabolism
The Royal Oldham Hospital
University of Manchester Cardiovascular Research Group/Diabetes Centre
Rochdale Road
Oldham OL1 2JH
UK

Bissar-Tadmouri, Nisrine, MD
Assistant Professor
University Of Sharjah
College of Medicine
Department of Basic Medical Sciences
Sharjah
United Arab Emirates

Bittles, Alan H, PhD
Professor, Centre for Comparative Genomics
Edith Cowan University & Murdoch University
South Street
Perth, WA
Australia

Black, Michael L.
Centre for Comparative Genomics
Murdoch University
South Street
Perth, WA
Australia

Blakemore, Alexandra, PhD
Department of Genomics of Common Disease
School of Public Health
Imperial College London
London
UK

Brahmachari, Samir K, PhD
Director-General & Secretary
Council of Scientific and Industrial Research
Government of India
New Delhi
India

Buxton, Jessica
Department of Genomics of Common Disease
School of Public Health
Imperial College London
London
UK

Campino, Susana G, D Phil
The Genome Campus
Wellcome Trust Sanger Centre
Hinxton
UK

Cerda-Flores, Ricardo M, PhD
School of Nursery and Center for Research
Development in Health Sciences
Universidad Autonoma de Nuevo Leon
Monterrey
Mexico

Chakrapani, Anupam, FRCPCH
Inherited Metabolic Disease Unit
Birmingham Children's Hospital
Birmingham
England
UK

Charfeddine, Cherine
Molecular Investigation of Genetic Orphan Diseases
Research Unit
Institut Pasteur de Tunis
Tunis
Tunisia

Chen, Chien-Hsiun
Institute of Biomedical Sciences
Academia Sinica Taipei
Taiwan
and
Graduate Institute of Chinese Medical Science
China Medical University
Taichung
Taiwan

Chen, Yuan-Tsong, MD, PhD
Institute of Biomedical Sciences
Academia Sinica, Taipei
Taiwan
and
Department of Pediatrics
Duke University Medical Center Durham, NC
USA

Chetan GK
Department of Human Genetics
National Institute of Mental Health and Neurosciences
(NIMHANS)
Bangalore, Karnataka
India

Clark, Taane G
London School of Hygiene and Tropical Medicine
Gower Street
The University of London
London
UK

Clarke, Angus J, DM, FRCPCH
Institute of Medical Genetics
School of Medicine
University Hospital of Wales
Cardiff
UK

Cleary, Maureen, MD, FRCPCH
Inherited Metabolic Disease Unit
Great Ormand Street Hospital for Sick Children
London WC1
UK

Cogliati, Tiziana
National Eye Institute
National Institutes of Health
Bethesda, MD
USA

Cohen, Joel I, PhD
International Food Policy Research Institute
Washington, DC
USA

Cotton, Richard GH, PhD, DSc
Genomic Disorders Research Centre
Howard Florey Institute and Convenor,
Human Variome Project
Faculty of Medicine, Dentistry and
Health Sciences
University of Melbourne
Parkville VIC 3010
Australia

Cutiongco-de la Paz, Eva Maria
Institute of Human Genetics
National Institutes of Health
Manilla
The Philippines

Daar, Abdallah S, MD, FRCS
The McLaughlin–Rotman Centre for
Global Health
Program on Life Sciences, Ethics and Policy
McLaughlin Centre for Molecular Medicine
The Faculty of Medicine
Medical Sciences Building
University of Toronto
Ontario
Canada

Dai, Ying
Department of Public Health and Epidemiology
Capital Medical University
Beijing
Republic of China

Das, Reena, MD
Thalassaemia and Haemoglobinopathy Laboratory
Department of Haematology
Post Graduate Institute of Medical Sciences
Chandigarh
India

de Silva, Deepthi, MRCP
Department of Physiology
Faculty of Medicine
University of Kelaniya
Ragama
Sri Lanka

de Wit, Erika
University of Wittwatersand
Johannesburg
South Africa

Dissanayake, Vajira HW, MBBS, PhD
Senior Lecturer/Medical Geneticist
Human Genetics Unit
Faculty of Medicine
University of Colombo
Kynsey Road, Colombo 00800
Sri Lanka

Dodgen, Tyren M.
Departments of Immunology and Pharmacology
Faculty of Health Science
University of Pretoria
South Africa

Elles, Robert George, PhD
Director of Genetic Laboratory
Department of Genetic Medicine
St Mary's Hospital
Central Manchester Hospitals Foundation
Manchester, England
UK

Eloff, Arinda
Departments of Immunology
Faculty of Health Science
University of Pretoria
South Africa

Faruq, Mohammed, PhD
Functional Genomics Unit
Institute of Genomics and Integrative Biology (IGIB-CSIR)
Mall Road, Delhi 110007
India

Faskhutdinova, G
Institute of Biochemistry and Genetics
Ufa Scientific Center
Russian Academy of Sciences
Prospekt Oktyabrya 71
Ufa 450054
Russia

Fedorova, Sardana A
Department of Molecular Genetics
Yakut Research Center of Complex
Medical Problems
Russian Academy of Medical Sciences
Sergelyakhskoe shosse 4, Yakutsk, 677010
Russia

Ferraz, Victor Evangelista de Faria
Department of Medical Genetics
Instituto Fernandes Figueira
Fundação Oswaldo Cruz
Rio de Janeiro—RJ
Brazil

Frenk, Julio
Dean of the School of Public Health
Harvard University
Boston, MS
USA

Friedman, James
National Eye Institute
National Institutes of Health
Bethesda, MD
USA

Fucharoen, Suthat, MD
Department of Health, Ministry of Public Health and Thalassemia Research Center
Institute of Molecular Biosciences
Mahidol University
Thailand

Gaysina D
Institute of Biochemistry and Genetics
Ufa Scientific Center
Russian Academy of Sciences
Ufa, 450054
Russia

Geerts, Lut, BSc (Hons.), MRCOG
Associate Professor in Obstetrics and Gynaecology
University of Stellenbosch and Tygerberg Hospital
Stellenbosch
South Africa

Ghosh, Balram
Institute of Genomics and Integrative Biology, (IGIB-CSIR)
Mall Road
Delhi
India

Gilliat-Ray, Sophie, PhD
Centre for the Study of Islam in the UK (Islam-UK)
Department of Religious Studies and Theology
School of History, Archaeology and Religion
Cardiff University
Cardiff
UK

Gilyazova, Irina R
Institute of Biochemistry and Genetics
Ufa Science Center
Russian Academy of Sciences
Prospekt Oktyabrya, 71
Ufa, Bashkortostan, 450054
Russia

Ginter, EK
Research Center for Medical Genetics
Russian Academy of Medical Sciences
Moskvorechje St., 1
Moscow
Russia

Giugliani, Roberto, MD
Gene Therapy Center
Hospital de Clinicas de Porto Alegre
Rua Ramiro Barcelos 2350—CEP 90035–903
Porto Alegre, RS
Brazil

Goodsaid, Federico
The Genomics Group
Office of Clinical Pharmacology, Office of Translational Science
Center for Drug Evaluation and Research, US Food and Drug Administration
Silver Spring, MD
USA

Gotoh, Norimoto
National Eye Institute
National Institutes of Health
Bethesda, MD
USA

Gouider-Khouja, Neziha, MD
Department of Neurology
Institut National de Neurologie
La Rabta 1007
Tunis
Tunisa

Greenberg, Jacquie, PhD
Professor, Genetic Counsellor
Department of Human Genetics
University of Cape Town
South Africa

Grimaji SC
Department of Psychiatry
National Institute of Mental Health and neurological Sciences (NIMHANS)
Bangalore, Karnataka
India

Gupta, Amrendra Kumar, PhD
Institute of Genomics and Integrative Biology (IGIB-CSIR)
Mall Road
Delhi 110007
India

Gupta, Neerja, DM
Genetics Division, Department of Pediatrics
All India Institute of Medical Sciences
New Delhi
India

Hamamy, Hanan, MD
Department of Genetic Medicine and Development
Geneva University Hospital
Geneva Foundation for Medical Education and Research
Geneva
Switzerland

Hardy, Billie-Jo, PhD
The McLaughlin–Rotman Centre for Global Health
McLaughlin Centre for Molecular Medicine
University of Toronto
College Street, Toronto, Ontario
Canada

He, Yan
School of Public Health and Family Medicine, Capital Medical University
College of life Sciences, Graduate University
Chinese Academy of Sciences
Beijing
China

Hoal, Eileen, PhD
Associate Professor in Molecular Biology
University of Stellenbosch
Cape Town Area
South Africa

Hochfeld, Warren E
Department of Medical Genetics
School of Clinical Medicine
Cambridge University
UK

Horovitz, Dafne Dain Gandelman, MD, PhD
Department of Medical Genetics
Instituto Fernandes Figueira
Fundação Oswaldo Cruz
Rio de Janeiro—RJ
Brazil

Hurst, Jane A, FRCP
Department of Clinical Genetics and Molecular Genetics
Great Ormond Street Hospital for Sick Children
Institute of Child Health
Guilford Street
London, WC1
UK

Hussain, Rafat, PhD
Associate Professor and Deputy Head of School
School of Rural Medicine
University of New England
Australia

Izhevskaya, VL
Institute of Biochemistry and Genetics of Ufa Science Center
Russian Academy of Sciences
Prospekt Oktyabrya, 71, Ufa, 450054
Russia

Ivanov, VI
Institute of Biochemistry and Genetics of Ufa Science Center
Russian Academy of Sciences
Prospekt Oktyabrya, 71, Ufa, 450054
Russia

Jayalakshmi, Mariakuttikan
Department of Immunology
Madurai Kamaraj University
Madurai-625021
Tamil Nadu
India

Jenkins, Trefor, PhD
Department of Human Genetics
University of the Witwatersrand
National Health Laboratory Service
Johannesburg
South Africa

Jiménez-Sánchez, Gerardo, MD, PhD
Formerly Executive Director-The National Institute of Genomic Medicine
Periferico Sur 4124, Torre Zafiro II
Piso 6 Col. Jardines del Pedregal, Mexico D.F. 01900
Mexico

Jones, Wendy, MRCP
Department of Clinical and Molecular Genetics
Great Ormond Street Hospital for Sick Children
Institute of Child Health
Guilford Street
London, WC1
London
UK

Johnson, Colin A, PhD
International Resource for Autozygosity Mapping
Division of Molecular & Translational Medicine
Leeds Institute of Molecular Medicine
University of Leeds
UK

Jorde, Lynn B, PhD
The Department of Human Genetics
University of Utah Health Sciences Center
Salt Lake City, Utah
USA

Kabra, Madhulika, MD
Genetics Division
Department of Pediatrics
All India Institute of Medical Sciences
New Delhi
India

Kalyanaraman, Narayanan
Dept of Immunology
Madurai Kamaraj University
Madurai-625 021
Tamil Nadu
India

Kaput, Jim, PhD
Division of Personalized Nutrition and Medicine
National Center for Toxicological Research
United States Food and Drug Administration
3900 NCTR Road
Jefferson, AR 72079
USA

Kaur, Gurvinder, PhD
Department of Immunology and Transplantation
All India Institute of Medical Sciences
New Delhi
India

Kavitha, Valampuri John Mary Selvam
Department of Immunology
Madurai Kamaraj University
Madurai-625021
India

Kazantseva, A
Institute of Biochemistry and Genetics
Ufa Scientific Center
Russian Academy of Sciences
Prospekt Oktyabrya 71, Ufa 450054
Russia

Kefi, Rym
Institut Pasteur de Tunis Laboratoire de séquençage et de typage génétique
UR: Exploration Moléculaire des maladies orphelines d'origine génétique
Tunis
Tunisia

Kent, Alastair, MA
Director
Genetic Alliance
London
UK

Khidiyatova, Irina M
Institute of Biochemistry and Genetics
Ufa Science Center
Russian Academy of Sciences
Prospekt Oktyabrya, 71
Ufa, Bashkortostan, 450054
Russia

Khneisser, Issam, MBA
Newborn Screening Laboratory Manager
Saint Joseph University
11–5076 Riad Elsolh, Beirut
Lebanon

Khusnutdinova, Elza K
Institute of Biochemistry and Genetics
Ufa Science Center
Russian Academy of Sciences
Prospekt Oktyabrya, 71, Ufa, 450054
Russia

Kononova, SK
Department of Molecular Genetics
The Yakut Research Center of Complex Medical Problems
Siberian Branch, Russian Academy of Medical Sciences
Sergelyakhskoe shosse 4
Yakutsk 677010
Russia

Kozlova, SI
Russian Medical Academy for Postgraduate study
Moscow
Russia

Krause, Amanda, MB, ChB, PhD
Department of Human Genetics
National Health Laboratory Service
University of Johannesburg
Johannesburg
South Africa

Kromberg, Jennifer GR, PhD
Department of Human Genetics
University of the Witwatersrand
National Health Laboratory Service
Johannesburg
South Africa

Kumar, Dhavendra, MD FRCP FACMG
Institute of Molecular and Experimental Medicine,
Cardiff University School of Medicine
University Hospital of Wales
Cardiff
UK
and
Genomic Policy Research Unit
School of Health, Sport and Science
University of Glamorgan
Pontypridd, Wales
UK

Kumaramanickavel, Govindasamy, PhD
Director of Research
Narayana Nethralaya, Health City
Bangalore
India
and
Aditya Jyot Eye Hospital
Mumbai
India

Kutuev, IA
Institute of Biochemistry and Genetics
Ufa Science Center
Russian Academy of Sciences
Prospekt Oktyabrya, 71, Ufa, 450054
Russia

Laffita-Mesa, José Miguel, BSc
Centre for the Research and Rehabilitation of Hereditary Ataxias
Holguín
Cuba

Lee, Ming Ta Michael
Institute of Biomedical Sciences,
Academia Sinica Taipei
Taiwan
and
Graduate Institute of Chinese Medical Science
China Medical University
Taichung
Taiwan

Li, Peng-Gao
Public Health Genetics Unit
Department of Public Health and Epidemiology
Capital Medical University
Beijing
Republic of China

Liu, Fen
China Capital Medical University
Beijing
China

Loggenberg, Kelly, MSc
Genetic Counsellor
Department of Human Genetics
The University of Cape Town
South Africa

Lok, Chun Yu, DPhil
Weatherall Institute of Molecular Medicine
University of Oxford
John Radcliffe Hospital
Headington
Oxford
UK

Lunt, Peter, MD FRCP
Department of Clinical Genetics
Bristol Children's Hospital
St. Michael's Hill
Bristol, England
UK

Luzzatto, Lucio, MD
Direttore Scientifico, Istituto Toscano Tumori (ITT)
Professor of Haematology
University of Firenze
Via Taddeo Alderotti 26N
50139 Firenze
Italy

Madon, Prochi F, PhD
Dept. of Assisted Reproduction and Genetics
Jaslok Hospital and Research Centre
Mumbai
India

Mahajan, Anubha, PhD
Genomics and Molecular Medicine Unit
Institute of Genomics and Integrative Biology (CSIR)
Mall Road
Delhi
India

Maher, Eamonn R, MD FRCP
Medical and Molecular Genetics
School of Clinical and Experimental Medicine
University of Birmingham
Birmingham B15 2TT
UK

Megarbane, Andre, MD, PhD
Medical Genetics Unit
Saint Joseph University
Beirut
Lebanon

Merryweather-Clarke, Alison T, DPhil
Blood Research Laboratory
Nuffield Department of Clinical Laboratory Sciences
John Radcliffe Hospital
Headington
Oxford OX3 9DU
UK

Manjunatha KR, PhD
Department of Human Genetics
National Institute of Mental Health and Neurological Sciences (NIMHANS)
Bangalore, Karnataka
India

Maksimova, Nadezda R
Yakut Research Center of Complex Medical Problems
Russian Academy of Medical Sciences
Yakutsk, 677019
Russia

Marques de Faria, Antonia Paula, MD, PhD
Department of Medical Genetics
School of Medical Sciences
University of Campinas (Unicamp)
Campinas-SP
Brazil

Matte, Ursula
Gene Therapy Center
Hospital de Clinicas de Porto Alegre
Rua Ramiro Barcelos
Porto Alegre, RS
Brazil

Mehra, Narinder, PhD
Department of Immunology and Transplantation
All India Institute of Medical Sciences
New Delhi
India

Melegh, Béla, MD, PhD, DSc
Department of Medical Genetics
University Pécs
Szigeti
Hungary

Mittal, Uma
Genomics and Molecular medicine
Functional Genomics Unit
Institute of Genomics and Integrative Biology, (IGIB-CSIR)
Mall Road
Delhi
India

Mohan, Viswanathan
Dr. Mohan's Diabetes Specialities Centre
WHO Collaborating Centre for Non Communicable Diseases Prevention & Control
Madras Diabetes Research Foundation
ICMR Advanced Centre for Genomics Of Diabetes
Gopalapuram
Chennai
India

Mokni, Mourad
Dermatology Department—La Rabta Hospital
Hereditary Keratinisation Disorders Research Unit-La Rabta Hospital
Tunis
Tunisia

Möller, Marlo
Department of Human Genetics
University of Wittwatersand
Johannesburg
South Africa

Moustafa, Julia El-Sayed
Department of Genomics of Common Disease
School of Public Health
Imperial College London
London
UK

Mukerji, Mitali, PhD
Senior Scientist-Genomics and Molecular medicine
Functional Genomics Unit
Institute of Genomics and Integrative Biology (IGIB-CSIR)
Mall Road
Delhi
India

Myburgh, Renier
Departments of Immunology
Faculty of Health Science
University of Pretoria
South Africa

Naik, Swati, MD
Kennedy-Galton Centre
Department of Clinical Genetics
Northwick Park Hospital
Harrow
Middlesex
UK

Nair, Pratibha, MSc
Centre for Arab Genomic Studies
Dubai
United Arab Emirates

Nazarenko, Ludmila P
Research Institute of Medical Genetics
Siberian Branch of Russian Academy
of Medical Sciences
Tomsk
Russia

Nogovitsina, Anna N
Yakut Research Center of Complex
Medical Problems
Russian Academy of Medical Sciences
Yakutsk
Russia

Obeid, Tasneem
Centre for Arab Genomic Studies
Dubai
United Arab Emirates

Old, John, PhD
The Oxford Thalassaemia and Haemoglobinopathy Unit
The Churchill Hospital
John Radcliffe NHS Trust
Headington
Oxford
UK

Olopade, Olufunmilayo I, MD
Center for Clinical Cancer Genetics &
Global Health
Section of Hematology/Oncology
Department of Medicine
The University of Chicago
Chicago, IL
USA

Padilla, Carmencita, MD
Department of Pediatrics
College of Medicine and Institute of Human Genetics
National Institutes of Health
University of the Philippines Manila
Manila
The Philippines

Pang, Tikki
Research Policy & Cooperation
World Health Organization
Avenue Appia
Geneva
Switzerland

Pattanapongthorn, Jintana
Department of Health, Ministry of Public
Health and
Thalassemia Research Center, Institute
of Molecular Biosciences
Mahidol University
Thailand

Patton, Michael A, MD, FRCP
Department of Medical Genetics
St Georges Hospital & Medical School
University of London
London
UK

Paz-y-Miño, César, MD, DB
Decano del Instituto de
Investigaciones Biomédicas
Facultad de Ciencias de la Salud
Quito
Ecuador

Pena, Sérgio DJ, MD, PhD, FRCP(C)
Universidade Federal de Minas Gerais
Av. Afonso Pena
Belo Horizonte
Brazil

Penchaszadeh, Victor B, MD
Mailman School of Public Health
Columbia University, New York
USA
and
Argentine Forum for Health Research,
Buenos Aires
República de la India
Buenos Aires
Argentina

Penn, Claire, PhD
Health Communication Project
School of Human and Community
Development
University of the Witwatersrand
South Africa

Pepper, Michael S, MD PhD
Professor, Department of Immunology
Faculty of Health Sciences
University of Pretoria
P.O. Box 2034
Pretoria 0001
South Africa

Phadke, Shubha R, MD, DM
Department of Medical Genetics
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Raebarelli Road
Lucknow
India

Pitchappan, Ramasamy M, PhD
Department of Immunology
Madurai Kamaraj University
Madurai-625021
Tamil Nadu
India

Pollitt, Rodney J, PhD
Department of Paediatric Pathology
The Children's Hospital
Sheffield Children's Hospital NHS Foundation
The University of Sheffield
Sheffield
UK

Puri, Ratna D, MD, DM
Center of Genetic Medicine
Sir Ganga Ram Hospital
Rajinnder Nagar
New Delhi
India

Puzyrev, VP
Research Institute of Medical Genetics
Siberian Branch of Russian Academy of Medical Sciences
Tomsk
Russia

Qubbaj, Wafa, PhD
Assisted Reproductive Technology Unit
Department of Pathology and Laboratory Medicine
King Faisal Specialist Hospital and Research Center
Riyadh, 11211
Saudi Arabia

Rajab, Anna, PhD, FRCP
Genetics Unit, Directorate General of Health Affairs
Ministry of Health, Sultanate of Oman
Muscat
Sultanate of Oman

Ramesar, Raj, PhD
MRC Human Genetics Research Unit
Division of Human Genetics
Institute for Infectious Diseases and Molecular Medicine
University of Cape Town
Cape Town
South Africa

Rappuoli, Rino
Chiron Vaccines
Via Fiorentina 1
53100 Siena
Italy

Ray, Jharna, MSc, PhD
S. N. Pradhan Centre for Neurosciences
University of Calcutta
Ballygunge Circular Road
Kolkata
India

Rebai, Ibtihel
National Institute of Neurology.
La Rabta
Tunis
Tunisia

Robson, Kathryn JH, DPhil
Blood Research Laboratory
Nuffield Department of Clinical Laboratory Sciences
John Radcliffe Hospital
Headington
Oxford OX3 9DU
UK

Rodríguez-Labrada, Roberto, BSc
Centre for the Research and Rehabilitation of Hereditary Ataxias
Holguín
Cuba

Rojas-Martínez, Augusto, MD, DSc
Centro de Investigación y Desarrollo en Ciencias de la Salud
Universidad Autónoma de Nuevo León. Calle Carlos Canseco
S.N. Colonia Mitras Centro
Monterrey, C.P. 64460
Mexico

Romdhane, Lilia
Molecular Investigation of Genetic Orphan Diseases Research Unit
Pasteur Institute of Tunis
Tunisia

Rotimi, Charles N, PhD
Center for Research on Genomics and Global Health
National Human Genome Research Institute
The National Institutes of Health
Bethesda, MD 20851–5635
USA

Rozario, Santi, PhD
Department of Religious Studies
and Theology
School of History, Archaelogy and Religion
School of Sociology and Social Work
University of Tasmania
Australia

Saggar, Anand MD, FRCP
Department of Medical Genetics
St Georges University of London
Cranmer Terrace
London SW17 0RE
UK

Schlebusch, Carina M.
Human Genomic Diversity and Disease|Research Unit
Division of Human Genetics
School of Pathology
National Health Laboratory Service & University of the
Witwatersrand
Johannesburg
South Africa

Schuller-Faccini, Lavinia
Brazilian Institute of Population Medical Genetics
INAGEMP, Medical Genetics Service
HCPA and Department of Genetics—UFRGS
Porto Alegre, RS
Brazil

Séguin, Béatrice PhD
The McLaughlin–Rotman Centre for
Global Health
Program on Life Sciences, Ethics and Policy
McLaughlin Centre for Molecular Medicine
University of Toronto
Ontario
Canada

Sekar, Kanthimathi
Madras Diabetes Research Foundation
ICMR Advanced Centre for Genomics of Diabetes
Gopalapuram
Chennai
India

Sellars, Sean, MA, FACS
Emeritus Professor
Division of Otolaryngology
Faculty of Health Sciences
University of Cape Town
South Africa

Coskun, Serdar, PhD
Section Head, Assisted Reproductive Technology
Department of pathology and Laboratory Medicine
King Faisal Specialist Hospital and Research Center
Riyadh, 11211
Saudi Arabia

Shaw, Alison
Ethox Centre, Department of Public Health
and Primary Care
University of Oxford
Badenoch Building, Old Road Campus, Headington
Oxford
UK

Silao, Catherine Lynn
Institute of Human Genetics
National Institutes of Health
Manilla
The Philippines

Singer, Peter A, PhD
The McLaughlin–Rotman Centre for Global Health
Program on Life Sciences, Ethics and Policy
University Health Network/McLaughlin Centre for
Molecular Medicine
The Faculty of Medicine, Medical Sciences Building
University of Toronto
Toronto, Ontario
Canada

Singh, Jai Rup, PhD
Vice Chancellor
Central University of Punjab
Bathinda, Punjab
India

Singh, Arvind Rup, PhD
45 Taft Ave
Providence, RI 02906
USA

Soberón, Guillermo, PhD
Socio y Representante en Sonora at Aita
Infraestructura
Representante regional at Aita S. C., Varios, Campus
Guaymas at Tecnológico de Monterrey, Director
Campus Guaymas at Tecnológico de Monterrey
Universidad Nacional Autónoma de México, Universidad
Nacional Autónoma de México, Instituto Tecnológico y
de Estudios Superiores de Monterrey
Mexico

Soodyall, Himla, PhD
Professor, Human Genomic Diversity and Disease Research Unit
Division of Human Genetics
School of Pathology
National Health Laboratory Service & University of the Witwatersrand
Johannesburg
South Africa

Song, Manshu
China Capital Medical University
Beijing
China

Srivastava, Achal K, MD
Neuroscience Centre
All India Institute of Medical Sciences
New Delhi, 10029
India

Swaroop, Anand, PhD
National Eye Institute
National Institutes of Health
Bethesda, MD
USA

Syama, Adhikarla, PhD
Dept of Immunology
Madurai Kamaraj University
Madurai-625021
Tamil Nadu
India

Tadmouri, Ghazi Omar
Centre for Arab Genomic Studies
Dubai
United Arab Emirates

Tandon, Nikhil, MD, DNB
Department of Endocrinology
All India Institute of Medical Sciences
New Delhi
India

Teebi, Ahmed, MD (Deceased)
The Hospital for Sick Children
Toronto
Canada

Therrell, Bradford L, BD
Department of Pediatrics
University of Texas Health Science Center at San Antonio
San Antonio, Texas
USA
and
National Newborn Screening and Genetics Resource Center
Austin, Texas
USA

Thong, Meow Keong, MD
Genetics & Metabolism Unit
Department of Paediatrics
Faculty of Medicine, University of Malaya
Kuala Lumpur
Malaysia

Tsigankova PG
Research Centre for Medical Genetics
Russian Academy of Medical Sciences
Moscow
Russia

Turnpenny, Peter D, FRCP
Consultant in Clinical Genetics
Royal Devon & Exeter Hospital
Exeter
England
UK

Urban, Michael, FCPaed, MMed(Paed)
Senior specialist in Medical Genetics
University of Cape Town and Groote Schuur Hospital
Capte Town
South Africa

Vasani, Meera, PhD
Professor of Psychiatry
Director—National Drug Dependence Treatment Centre
All India Institute of Medical Sciences
New Delhi
India

Velázquez-Pérez, Luis, MD, PhD
Centre for the Research and Rehabilitation of Hereditary Ataxias
Holguín
Cuba

Venkatesan, Radha
Madras Diabetes Research Foundation
ICMR Advanced Centre for Genomics Of Diabetes
Gopalapuram
Chennai
India

Venkatesh HN
Department of Human Genetics
National Institute of Mental Health and Neurological Sciences (NIMHANS)
Karnataka, Bangalore
India

Verma, Ishwar C, FRCP
Formerly Professor/Head, Genetics Unit
All India Institute of Medical Sciences, New Delhi
Senior Consultant—Center of Medical Genetics
Sir Ganga Ram Hospital
Rajinder Nagar, New Delhi
India

Villems, Richard
Department of Evolutionary Biology
University of Tartu and Estonian Biocentre
Riia 23, Tartu
Estonia

Wanapirak, Chanane
Department of Obstetrics and Gynecology
Faculty of Medicine
Chiangmai University
Thailand

Wang, Youxin
China Capital Medical University
Beijing
China

Wang, Yun
China Capital Medical University
Beijing
China

Wang, Wei, MD, PhD
School of Public Health and Family Medicine
Capital Medical University
College of life Sciences, Graduate University
Chinese Academy of Sciences
Beijing
China

Wasant, Pornswan, MD
Professor of Pediatrics
Division of Medical Genetics
Department of Pediatrics
Faculty of Medicine Siriraj Hospital, Mahidol University
Bangkok
Thailand

Watermeyer, Jennifer, PhD
Health Communication Project
School of Human and Community Development
University of the Witwatersrand
South Africa

Weatherall, Sir David J., DM FRS
Weatherall Institute of Molecular Medicine
University of Oxford
John Radcliffe Hospital
Headington
Oxford
UK

Wessels, Tina-Marié, MSc
Genetic Counsellor
University of the Witwatersrand
Johannesburg
South Africa

Winichagoon, Pranee
Thalassemia Research Center
Institute of Molecular Biosciences
Mahidol University
Thailand

Wonkam, Ambroise, MD
Senior Clinical Geneticist
Department of Human Genetics
The University of Capetown
South Africa

Wu, Lijuan
Capital Medical University
Beijing
China

Yoshimatsu, Toshio F.
Center for Clinical Cancer Genetics and Global Health
Department of Medicine
The University of Chicago, IL
USA

Yun, Hong-Min
Peking University Shenzhen Hospital
Shenzhen
Guangdong Province 518036
China

Yunusbayev, BB
Institute of Biochemistry and Genetics
Ufa Science Center of Russian Academy of Sciences
Prospekt Oktyabrya Ufa
Russia

Zainullina, A
Institute of Biochemistry and Genetics
Ufa Scientific Center, Russian Academy of Sciences
Ufa, 450054
Russia

Zhang, Ling
School of Public Health and Family Medicine
Capital Medical University, Beijing
College of life Sciences, Graduate University, Chinese Academy of Sciences
Beijing
China

Zheng, Yonglan
Center for Clinical Cancer Genetics and Global Health
Department of Medicine
The University of Chicago
USA

Zinchenko, RA
Research Center for Medical Genetics
The Russian Academy of Medical Sciences
Moscow
Russia

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