Preventive and Predictive Genetics: Towards Personalised Medicine

Advances in Predictive, Preventive and Personalised Medicine

Volume 9

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What This Book Series is About . . .

Current Healthcare: What is Behind the Issue?

For many acute and chronic disorders, the current healthcare outcomes are considered as being inadequate: global figures cry for preventive measures and personalised treatments. In fact, severe chronic pathologies such as cardiovascular disorders, diabetes and cancer are treated after onset of the disease, frequently at near end-stages. Pessimistic prognosis considers pandemic scenario for type 2 diabetes mellitus, neurodegenerative disorders and some types of cancer over the next 10–20 years followed by the economic disaster of healthcare systems in a global scale.

Advanced Healthcare Tailored to the Person: What is Beyond the Issue?

Advanced healthcare promotes the paradigm change from delayed interventional to predictive medicine tailored to the person, from reactive to preventive medicine and from disease to wellness. The innovative Predictive, Preventive and Personalised Medicine (PPPM) is emerging as the focal point of efforts in healthcare aimed at curbing the prevalence of both communicable and non-communicable diseases such as diabetes, cardiovascular diseases, chronic respiratory diseases, cancer and dental pathologies. The cost-effective management of diseases and the critical role of PPPM in modernisation of healthcare have been acknowledged as priorities by global and regional organisations and health-related institutions such as the Organisation of United Nations, the European Union and the National Institutes of Health.

Why Integrative Medical Approach by PPPM as the Medicine of the Future?

PPPM is the new integrative concept in healthcare sector that enables to predict individual predisposition before onset of the disease, to provide targeted preventive measures and create personalised treatment algorithms tailored to the person.

The expected outcomes are conducive to more effective population screening, prevention early in childhood, identification of persons at-risk, stratification of patients for the optimal therapy planning, prediction and reduction of adverse drug-drug or drug-disease interactions relying on emerging technologies, such as pharmacogenetics, pathology-specific molecular patterns, sub/cellular imaging, disease modelling, individual patient profiles, etc. Integrative approach by PPPM is considered as the medicine of the future. Being at the forefront of the global efforts, the European Association for Predictive, Preventive and Personalised Medicine (EPMA, http://www.epmanet.eu/) promotes the integrative concept of PPPM among healthcare stakeholders, governmental institutions, educators, funding bodies, patient organisations and in the public domain.

Current Book Series, published by Springer in collaboration with EPMA, overview multidisciplinary aspects of advanced bio/medical approaches and innovative technologies. Integration of individual professional groups into the overall concept of PPPM is a particular advantage of this book series. Expert recommendations focus on the cost-effective management tailored to the person in health and disease. Innovative strategies are considered for standardisation of healthcare services. New guidelines are proposed for medical ethics, treatment of rare diseases, innovative approaches to early and predictive diagnostics, patient stratification and targeted prevention in healthy individuals, persons at-risk, individual patient groups, sub/populations, institutions, healthcare economy and marketing.

Prof. Dr. Olga Golubnitschaja

Book Series Editor

Dr. Golubnitschaja, Department of Radiology, Medical Faculty of the University in Bonn, Germany, has studied journalism, biotechnology and medicine and has been awarded fellowships for biomedical research in Paediatrics and Neuro-sciences (Medical Centres in Austria, Russia, UK, Germany, the Netherlands, and Switzerland). She is well-cited in the research fields of "gene hunting" and "subtractive hybridisation" applied to predictive prenatal and postnatal diagnostics published as

O. Labudova in years 1990–2000. Dr. Golubnitschaja is an expert in molecular diagnostics actively publishing in the fields of perinatal diagnostics, Down syndrome, diabetes mellitus, hyperhomocysteinemia, cardiovascular disease, neurodegenerative pathologies and cancer. She is the *cofounder* of the theory of multi-pathway organ-related blood fingerprintingwith specific molecular patterns at epi/genomic, transcriptional and post/translational levels and author of fundamental works in *integrative medicine.* Dr. Golubnitschaja holds appointments, at the rank of Professor, at several European Universities and in International Programmes for Personalised Medicine and is author of more than 300 international publications in the field. Awards: National and International Fellowship of the Alexander von Humboldt-Foundation; Highest Prize in Medicine and Eiselsberg-Prize in Austria; She is *Secretary-General* of the "European Association for Predictive, Preventive and Personalised Medicine" (EPMA in Brussels, www.epmanet.eu), Editor-in-Chief of *The EPMA-Journal* (BMC in London); Book Editor of *Predictive Diagnostics and Personalized Treatment: Dream or Reality,* Nova Science Publishers, New York 2009; Book Co-editor *Personalisierte Medizin,* Health Academy, Dresden 2010; Book Series Editor *Advances in Predictive, Preventive and Personalised Medicine,* Springer 2012; *European Representative* in the EDR-Network at the NIH/NCI, http://edrn.nci.nih.gov/; and *Advisor and Evaluator* of projects dedicated to personalisedmedicine at the EU-Commission in Brussels, NIH/NCI,Washington, DC, USA, and at Foundations and National Ministries of Health in several countries worldwide.

Preface

Traditionally, medical research comprised of the identification of the pathological causes of a disease, its epidemiology and empirical investigation of treatment response. Intensive genetic research, marked by the completion of the human genome project in 2003, heralded a new era in medical research. While epidemiology and gross pathology are still mainstay useful tools, genetics and genomics have gradually been shown to increase the resolution of drug response research, showing great potential in also informing and identifying the role of genes and their encoded products in the pathophysiology of diseases. This information is already being applied to effective early diagnosis, better risk assessment (prognosis), as well as targeted effective and safe treatment allocation (prediction and monitoring).

Genetic testing and genomics support personalised medicine by translating genome-based knowledge into clinical practice, offering enhanced benefit for patients and health-care systems at large. Current routine practice for diagnosing and treating patients is conducted by correlating parameters such as age, gender and weight with risks and expected treatment outcomes. In the new era of personalised medicine the healthcare provider is equipped with improved ability to prevent, diagnose, treat and predict outcomes on the basis of complex information sources, including genetic and genomic data. The support of regulatory bodies and policy makers internationally has been critical for the rapid translation of personalised medicines into the clinic. Notwithstanding, inequality in the utilisation of targeted therapies in different health care systems across the world exists, and ethical considerations, as well as economic cost-effectiveness analyses are in need to inform decision making. In addition to the benefits of pharmacogenomics in diagnosis and treatment, prevention of illness using genomic information is important to reduce the burden on the healthcare system, a methodology proven effective in many therapeutic areas, but, paradoxically still facing challenges in others. In current settings screening programmes (e.g. BRCA1/2 screening) address this by identifying susceptible families and preventive measures or ensuring appropriate treatment at the earliest stages of disease, hence increasing health management effectiveness.

The integration of pharmacogenomics into the various health care systems have been the responsibility of the respective national health authorities, which in turn follow recommendations by leading regulatory bodies such as the European

Medicines Agency and the US FDA. The dynamics and logistics of this integration therefore vary substantially across the globe. To this end, implementation of pharmacogenomics is an important component of PPPM (Predictive, Preventive and Personalised Medicine), which is the main focus of the European Association for Predictive, Preventive and Personalised Medicine (EPMA). Since 2009, EPMA (http://www.epmanet.eu/) embarked on various initiatives to promote PPPM including the launch of the EPMA Journal to ensure dissemination of current aspects of PPPM, and the organisation of the first World Congress in September 2011 bringing together participants from over 40 countries to discuss education, policy and implementation of PPPM. In addition, EPMA took the initiative to publish a series of books in advances in PPPM, including the present one entitled "**Preventive and Predictive Genetics: Towards Personalised Medicine**". The editors take this opportunity to thank all contributing authors and trust that the content meets the expectation of all readers.

The Editors

Godfrey Grech, PhD
and Iris Grossman, PhD

Acknowledgement of Reviewers

The Editors wish to acknowledge the reviewers for their generous contribution in assessing the Chapters providing constructive critique and recommendations. The reviewers provided the means to enhance the quality of the book and hence we sincerely are grateful.

Beena Koshy, Peter Shaw, Ann Daly, Anderson Wayne H, Dr Alex Gatt, Aruna Bansal, Michael Barnes, Godfrey Grech, Joseph Borg, George Patrinos, Christian Scerri.

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Godfrey Grech, PhD

Senior Lecturer,
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Dr. Godfrey Grech is Senior Lecturer at the University of Malta. Since 2006, Dr. Godfrey Grech is responsible for the coordination of an MSc in Biomedical Sciences and currently runs the Molecular Pathology laboratory at the University of Malta. Following his doctorate studies at Erasmus Medical Centre, Rotterdam, he published in high impact journals and presented in International conferences such as the American Society of Hematology, the EPMA Congress and the European Pathology Congress. In the last few years, Dr. Godfrey Grech was selected to lead the research arm of the National Transfusion Centre and was given the role of a Principle Investigator on the National Breast Cancer Research Project. In addition, he is highly recognised by the clinical sector and runs numerous projects with Mater Dei Hospital and was instrumental to set up infrastructures that allow the use of fresh surgical sections in molecular pathology research. Currently he runs various collaborative projects with International Institutions including Erasmus Medical Centre and the Molecular Medicine Institute in Leeds. The main research topic aims to identify biomarkers to classify breast cancer patients into a specific therapeutic group that shall benefit from activation of phosphatases as a main therapeutic option.

Dr. Godfrey Grech was nominated and is elected on international scientific committees including the International Scientific Council of the European Group for Molecular Pathology (EMP); Global Leader at the Genomic Medicine within the National Human Genome Research Institute (NHGRI) of the U.S. National Institutes of Health (NIH); member of the Pharmacogenomics Working Group of the Global Genomic Medicine Consortium (G2MC); Leader of the Cancer Position Paper at the European Association for Predictive, Preventive & Personalised Medicine (EPMA); and national contact point for the PharmacoGenetics for Every Nation Initiative (PGENI).

Iris Grossman, PhD

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Dr. Iris Grossman is CEO and president of the pharmacogenetics management consultancy IsraGene Ltd., as well as VP, global head of the Personalized Medicine and Pharmacogenomics (PMP) unit for Teva Global R&D. She has dedicated her research career, in both industry and academia, to the advancement of the field of personalised medicine. Dr. Grossman is currently charged with defining and implementing the global PMP strategy for Teva, a top-10 global pharmaceutical company, covering both discovery and development R&D programmes. Israel's leading financial magazine, Globes Magazine, selected Dr. Grossman as one of the country's top 40 professionals under 40 years of age in 2013.

This followed several years of spearheading pipeline pharmacogenetic programmes for industry and academia as director of pharmacogenetics at Cabernet Pharmaceuticals Inc. Dr. Grossman moved into consultancy having been responsible for running large-scale pharmacogenetic programmes at GlaxoSmithKline, with an emphasis on infectious and neurological diseases.

In academia, Dr. Grossman was a key member of Professor David Goldstein's team at the Center for Population Genomics and Pharmacogenetics, Institute for Genome Sciences and Policy, at Duke University. Dr. Grossman received her PhD from the Technion – Israel Institute of Technology, where her research project, conducted in collaboration with the Weizmann Institute for Science, investigated pharmacogenetic markers of multiple sclerosis treatment response.