Rare Diseases

Advances in Predictive, Preventive and Personalised Medicine

Volume 6

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Rare Diseases

Integrative PPPM Approach as the Medicine of the Future

Springer

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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, and 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, subpopulations, 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 Neurosciences (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 ophthalmic diseases, neurodegenerative pathologies, cancer, cardiovascular disease, Diabetes mellitus, hyperhomocysteinemia, etc. She is the *cofounder* of the theory of individual patient profiles, author of fundamental works in *systems medicine* (holistic approach considering molecular patterns at epi/genomic, transcriptional and post/translational levels). 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. Her awards include: 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* (BioMed Central, 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 of *Advances in Predictive, Preventive and Personalised Medicine*, Springer 2012; *European Representative* in the EDR-Network at the NIH/NCI, http://edrn.nci.nih.gov/; *Advisor and Evaluator* of projects dedicated to personalised medicine at the EU-Commission in Brussels, NIH/NCI, Washington, DC, USA, and Foundations and National Ministries of Health in several countries worldwide.

Preface

Rare diseases (RDs) or orphan diseases are a group of diseases with a low prevalance. In EU, a disease is classified as rare if it affects less than 5 persons per 10,000 individuals. Globally, there are more than 300 million individuals affected by rare diseases. From about 7,000 RDs, still more than half have no identified causative gene or a diagnosis.

Almost 80 % of RDs have a genetic origin with symptoms appearing in prenatal and early postnatal periods. Amongst RDs there are rare cancer types, congenital malformations, and consequently developed infectious diseases. These are usually severe, chronic and life threatening pathologies, which from case-to case vary dramatically in the corresponding grade of clinical severity and by the individual outcome. Due to the wide spectrum of RDs and a lack of sufficient knowledge about individual RDs, the correct diagnosis is difficult to make. Furthermore, currently there are no appropriate treatment approaches for most of the RDs. The only reasonable approach seems to be a development of methods for early diagnosis of RDs that might lead to the creation of the optimal care management saving lives and improving life quality within the patient cohort.

Due to unfavoured economical aspects, such as a limited number of responding patients, problematic conduction of corresponding clinical trials and consequently high costs of potential treatment, the drug development for RD is currently stagnating, and manufacturers are not really motivated to bring new products to the market. Consequently, there is a real need for R&D in finding new drugs well regulated by healthcare responsible institutions guided by new guidelines for effective treatments tailored to the person diagnosed with RD.

The improvement in RDs healthcare is initiated by legislations in EU and the USA to create an integrative medical approach for RDs.

How is the emerging paradigm of PPPM related to the healthcare of RDs? Due to the molecular background of most RD pathologies, it is expected that the multimodal approach (*omics, pharmacogenetics, medical imaging, etc.) with multidisciplinary professionals should be instrumental for the “personalisation” to diagnose individual RDs, to create effective preventive measures and to develop targeted therapies – the integrative medical approach by predictive, preventive and

personalised medicine (PPPM). Recent achievements in bio/medical sciences let us trust in a prompt translation of innovative technologies into daily clinical practice.

Besides its general add-value for the public health promotion, the advanced RD healthcare provides an excellent "proof-of-principles" for the personalisation of healthcare systems in a global scale. RDs is an important source for related scientific, methodological and technological progress: all medical branches may benefit from comprehensive efforts if made in the promotion of the scientific and technological field of RDs including ethical considerations, creation of the robust platform for the professional communication, synergies with patient organisations, "doctor-patient" collaboration and new philosophy of integrative medicine by PPPM to advance current healthcare.

The European Association for Predictive, Preventive and Personalised Medicine (EPMA) actively promotes the scientific and technological efforts, expert recommendations and creation of new guidelines in the field of RD healthcare. This initiative has been triggered through The EPMA Journal launched in 2010 as the professional forum in PPPM. The book series *Advances in PPPM* overview multidisciplinary aspects of advanced bio/medical approaches and innovative technologies aiming at remarkable improvements in healthcare performance. Integration of individual professional groups into the overall concept of PPPM is a particular advantage of this book series.

The current book is dedicated to all aspect related to the prediction, prevention and personalised treatments of RDs. This volume is intended to serve as a reference source for scientific and medical centres involved in the field with a special emphasis on healthcare promotion and innovations intended to combat RDs, save the affected lives and enhance the life quality of this patient cohort.

I wish to thank the book contributors, book series editor and Springer for the excellent performance and highest professional level in the book preparation. I express this cordial thank on behalf of all the patients with rare diseases to whom I would like to dedicate this book *"Rare Diseases: Integrative PPPM Approach as the Medicine of the Future*".

Ankara, Turkey

Meral Özgüç
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Dr. Özgüç is currently Professor of Medical Biology at the Faculty of Medicine, Hacettepe University, Ankara, Turkey, where she received her Ph.D. in Medical Biology in 1985. She completed her undergraduate studies at Fairleigh Dickinson University in chemistry and received masters degree in biochemistry from Columbia University in the USA. Immediately afterwards, she worked for 3 years as Research Associate in the Department of Research Hematology, Childrens Hospital of Philadelphia, before joining the Hacettepe faculty in 1980. She served as Assistant Dean of the Faculty of Medicine (2006–2009), and currently she is the Director of the Hacettepe DNA/Cell Bank for Rare Diseases-Center for Genomics.

Her work, which is supported by State Planning Agency, Scientific and Technical Research Council of Turkey (TÜBİTAK) and through international grants, is focused on a genomic medicine approach for the study of rare diseases. She is actively involved in the formulation of national policies to create an awareness of and to promote genomics in public health. Her scientific publications concentrate in

the area of identification of new disease genes and genomic variants and development of diagnostic tests. She is also involved in networking activities, governance and bioethical aspects of sample acquisition and data management of biobanks. She is member of European, Middle Eastern and African Society for Biopreservation and Biobanking.

She has worked as a member of various international committees involved in genomics and health such as OECD – Working Party on Biotechnology and Human Health Related Biotechnologies, ESF – Integrated Approaches to Functional Genomics, EC-FP6 Genomics and Biotechnology for Health (National Contact Point), and UNESCO-International Bioethics Committee. Currently she is the chair of the Bioethics Committee of the Turkish National Commission for UNESCO and serves as a member of National EPMA Board in the section for Neonatal Diagnostics and Population Screening.