REVISTA ROMÂNĂ DE MEDICINĂ DE LABORATOR

Supliment 3 la Vol. 26, Nr. 4, Octombrie, 2018

ASOCIAȚIA DE MEDICINĂ DE LABORATOR DIN ROMÂNIA
CCAMF - UMF Tirgu Mures
Str. Gh.Marinescu 38, Et 3, Cam. 107,
Tirgu Mureş, 540139
Tel/fax 40 265 20 89 42/40 265 20 89 52
www.rrml.ro, www.almr.ro, www.raml-conference.ro

REVISTA ROMÂNĂ DE MEDICINĂ DE LABORATOR

Romanian Journal of Laboratory Medicine

Publicaţie Oficială a ASOCIAȚIEI DE MEDICINĂ DE LABORATOR DIN ROMÂNIA

Supliment 3 la Vol. 26, Nr. 4, Octombrie, 2018

Creditări RRML

Thomson Reuters Scientific - ISI Web of Knowledge - Începand cu anul 2008, RRML este indexată în ISI Web of Knowledge - Web of Science - Science Citation Index Expanded (Thomson Reuters Scientific). Factor impact 2016: 0.325
Elsevier Bibliographic Databases - RRML este indexată în bazele de date SCOPUS şi EMCARE, începând cu anul 2008.
Index Copernicus Master journal List - din anul 2009.
CNCSIS - Din anul 2008, RRML este inclusă în categoria A de publicaţii a CNCSIS, cu codul CNCSIS 739.
CM R - RRML a fost inclusă în Nomenclatorul Publicaţiilor Medicale al CMR începând cu anul 2007. Medicii abonaţi la această publicaţie sunt creditaţi cu 10 credite EMC.
OBBCSS R - Începând cu anul 2007 , OBBCSSR a creditat RRML cu 7 credite EMC.
Directory of Open Access Journals (DOA J) - Începand cu 2016 RRML este indexată în DOAJ.

Table of contents

* The responsibility for the content of the abstracts belongs entirely to the authors.

UNIVERSITATEA DE MEDICINĂ, FARMACIE, ȘTIINȚE ȘI TEHNOLOGIE DIN TÂRGU MUREȘ

I P H P M
Innovations in Population Health & Personalized Medicine

FIRST INTERNATIONAL CONFERENCE ON INNOVATIONS IN POPULATION HEALTH AND PERSONALIZED MEDICINE

12-13 December 2018
Târgu Mureş

University of Medicine, Pharmacy, Science and Technology
Târgu Mureş, Romania

Web: https://iphpm.org

Organizing committee

Leonard Azamfirei, Rector and Professor, Honorary Chair
William W. Au, Professor and Chairman
Rodica Bălașa, Vice Rector, Professor and Co-Chair
Minodora Dobreanu, Director of CCAMF, Professor and Co-Chair
Catalin Dogar, Information and Public Relations Department Officer

Honorary guests

Patriciu-Andrei Achimas-Cadariu, Director, Oncology Institute and "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napaca, Romania; Former Minister of Health of Romania
Alexandru-Sorin Costescu, Scientific Officer, European Commission on Innovative and Personalized Medicine, Health Directorate, Directorate-General Research and Innovation, Brussels, Belgium

Conference Secretariat

Aura Rusu, Associate professor, Faculty of Pharmacy. Email: aura.rusu@umftgm.ro

Advisory committee

Angela Borda, Vice Rector and Professor
Oana Marginean, Vice Rector and Professor
Camil-Eugen Vari, Vice Rector and Professor
Ovidiu Cotoi, Dean, Faculty of Medicine and Professor
Cristina Bica, Dean, Faculty of Dentistry and Professor
Daniela Lucia-Muntean, Dean, Faculty of Pharmacy and Professor
Lucian Puscasiu, Director of C.S.D. and Professor
Claudia Banescu, Member of C.S.D. and Professor
Simona Gurzu, Member of C.S.D. and Professor
Adrian Man, Deputy editor, Romanian Journal of Laboratory Medicine and Associate professor
Valentin Nadasan, Desktop publisher, Romanian Journal of Laboratory Medicine and Associate professor

University Press Team

Silviu Morariu, Coordinator University Press and Professor
Denes Lorand, Deputy Director University Press and Associate Professor
Kinga Bota, Desktop publisher University Press
Teodora Mindru, Information and Public Relations Department
Lucian Morariu, Desktop publisher University Press
Catalin Dogar, Information and Public Relations Department
Boangăr Gabriela, Information and Public Relations Department

Support Team

Daniela Dumangiu, Secretary
Claudia Pop, Secretary
Email: conference@iphpm.org

PhD students

Sebastian Andone
Monica Budau
Laura Barcutean
Valentin Ion
Cristina Radu

Students (volunteers)

Ioana Cupse
Cristina-Andreea Moldovan
Roxana Nicoleta Muntean
Anca Trif
Andrada Pintea

BASIC SCIENCE AND TRANSLATION OF SCIENTIFIC KNOWLEDGE INTO CLINICAL APPLICATIONS

INVOLVEMENT OF INHERENT DNA REPAIR VARIATIONS IN THE DEVELOPMENT, PREVENTION, INTERVENTION AND PROGNOSIS OF CANCER.

William Au[1]

UMFST Târgu Mureş, Romania and Shantou University Medical College, Shantou, China[1]

Introduction: Genetic predisposition and inherent drug response have been well-documented to be key factors for the development of cancer and for poor response to therapy. However, mechanisms for these outcomes and their interactions with environmental factors have not been well-characterized. Therefore, cancer risk, prevention, intervention and prognosis determinations have still mainly been based on population, rather than on individualized, evaluations.

Material and method: From the evaluation of publications, this review indicates that inherent and/or toxicant-provoked reduction in DNA repair capacity is a determining mechanism for health effects.

Results: The mechanism can be evaluated by developing a novel assay for quantitative and functional determination of DNA repair capacity. In addition, the assay will integrate the understanding of DNA repair defects, toxicant-perturbed DNA repair capacity, DNA methylation, and miRNA expression, and a bioinformatics approach to analyze a large amount of genomic data.

Conclusion: Functional and quantitative determination of DNA repair capacity on an individual basis would dramatically change the evaluation and management of health problems from a population to a personalized basis. Consequently, innovative genomic- and mechanism-based evidence can be increasingly used to develop a more precise cancer risk assessment, and target-specific and personalized medicine.

Keywords: DNA repair, post-transcriptional modification, personalized medicine, precision medicine

MUTATIONAL SIGNATURES AS CLUES TO CANCER AETIOLOGY AND CARCINOGENIC MECHANISM

David Phillips[1]

School of Public Health & Environmental Sciences, King's College London, London, UK[1]

Introduction: Whole genome sequencing of human tumours reveals distinct mutation patterns that hint at the causative origins of cancer.

Material and method: We examined mutational-signatures in human induced pluripotent stem cells (iPSCs) exposed to environmental agents that are known or suspected carcinogens. 79 agents were tested at concentrations that produced measurable cytotoxicity. Signatures in tumours from smokers and non-smokers were also compared.

Results: 41 gave characteristic substitution mutational-signatures that, in some cases, exhibit similarity with signatures found in human tumours. Some treatments also yielded double-substitution and indel signatures. Investigating mutation distribution asymmetries across genome topography reveals fully functional mismatch and transcription-coupled repair pathways in iPSCs. Detailed analyses demonstrate that primary adducts can be resolved by disparate repair/replicative pathways, resulting in an assortment of signature

outcomes even for a single mutagen. Smoking is associated with increased mutation burdens of multiple distinct mutational signatures, which contribute to different extents in different cancers. One of these signatures, mainly found in cancers in tissues directly exposed to tobacco smoke, is attributable to misreplication of DNA damage caused by tobacco carcinogens.

Conclusion: Smoking a pack a day for a year causes 150 mutations in lung cells. This compendium of experimentally-induced mutational-signatures permits further exploration of roles of environmental agents in cancer aetiology.

Keywords: Mutations, Cancer, Environmental mutagens, Tobacco

ROMANIAN VERSUS EUROPEAN PRACTICES TOWARDS DIETARY FIBERS

Monica Tarcea[1], Levente Nemes[1], Victoria Szucs[2], Nicoletta Pellegrini[3], Evita Straumite[4], Yalcin Erkan[5], Marcela Leal[6], Raquel Guine[7]

UMFST Târgu Mureș[1] National Agricultural Research and Innovation Center, Budapest, Hungary[2] Department of Food Science, University of Parma, Italy[3] University of Agriculture, Jelgava, Latvia[4] Department of Food Engineering, Abant Izzet Baysal University, Turkey[5] Faculty of Health Sciences, Maimonides University, Argentina[6] Department of Food Industry, Agrarian School, Polytechnic Institute of Viseu, Portugal[7]

Introduction: The goal of our study was to evaluate the Romanian practices regarding dietary fibers from food products versus other European countries.

Material and method: We made a qualitative survey based on a questionnaire applied in 2015, over 670 Romanian consumers from different counties, focused on the practices and knowledge towards ingestion of foods rich in fibers. The same questionnaire was applied in other 7 European countries, part of an international project design.

Results: Our results showed that ingestion of food rich in fibers (fruits, vegetables, and whole grains) was lower than European recommendations. The female participants ate more whole grains and fruits than males (p

Conclusion: We emphasize the need for more efficient community interventions for young people about the importance of dietary fibers for non-communicable diseases prevention and a healthy lifestyle.

Keywords: dietary fibers, labelling, food safety, nutritional status

MICRORNA ON POST-TRANSCRIPTIONAL GENE EXPRESSION AND ON CAUSATION OF HEALTH CONSEQUENCES

Alberto Izzotti[1]

School of Medicine University of Genoa and Cancer Prevention at the National Research Institute for Cancer Research San Martino Hospital, Genoa, Italy[1]

Introduction: MicroRNAs are master regulators of messenger-RNA fate, therefore, they can have a profound impact on the development of diseases.

Material and method:

A review on microRNA on cancer and cancer therapy.

Results: Among the transcribed messenger RNAs, only 3% go through the quality check by microRNA before they are translated into protein. Such a high control rate is aimed at preventing the development of mutation-related diseases. Therefore, only the parallel occurrence of gene mutation and irreversible microRNA alteration is able to trigger the pathogenic progression of a mutation-related diseases such as cancer. This situation also reflects on cancer therapy. Indeed small molecules and monoclonal antibodies targeting single mutations are effective only on a small number of patients bearing the targeted mutation. Conversely, microRNA are always altered in cancer with high specificity characterizing each cancer and the same cancer at different stages. The decoding of microRNA alterations in cancer is the prerequisite for their correction by microRNA delivery, a new strategy that is demonstrating to be effective in cancer therapy.

Conclusion: Epigenetic events, e.g. microRNA on gene expression, is a more potent driving force for cancer than mutational events and for cancer therapy.

Keywords: MicroRNA, cancer therapy, gene expression

SINGLE MOLECULE REAL-TIME LONG READS SEQUENCING: APPLICATION TO GENE-FUSION DETECTION IN ESOPHAGEAL CANCER

Xu Jianzhen[1]

Computational Systems Biology Lab, Department of Bioinformatics, Shantou University Medical College, Shantou, China[1]

Introduction: Esophageal squamous cell carcinomas (ESCC) are a leading cause of cancer death worldwide and approximately 70% of them occur in China, especially in the Chaoshan (Southeastern) region. Whether oncogenic gene fusions play a role in ESCC remains unknown.

Material and method: Deep sequencing has transformed the transcriptional analysis of cancers through RNA-seq technology. The advent of third generation sequencing, such as single molecule real-time (SMRT) sequencing, provides significantly longer reads and offers new possibilities to uncover cancer transcriptome. An integrative bioinformatics pipeline was developed to analyze Pacbio long reads.

Results: We used the Pacbio platform to sequence full long reads from 4 ESCC cell lines and 1 normal cell line. Bioinformatics analysis discovered ~1,500 novel fusion gene pairs totally.

Conclusion: Few of the newly discovered fusion gene pairs were found in ChimerDB gene fusion database. The new information generated by bioinformatics will be useful to generate new investigations.

Keywords: long reads sequencing, Esophageal cancer, transcriptome, gene fusion

APPLICATION OF LABORATORY MEDICINE TECHNOLOGY FOR SIGNIFICANT IMPROVEMENT IN PRECISION MEDICINE - IS LABORATORY MEDICINE READY FOR THE ERA OF PRECISION MEDICINE?

Minodora Dobreanu[1]

UMFST Târgu Mureș[1]

Introduction: Laboratory Medicine (LM) is fundamental to the practice of clinical medicine by providing extensive information on multiple biomarkers in biological fluids and tissues. These are essential in most pathologies for diagnosis, screening or management of patient condition, but also for public health, research and teaching.

Material and method: Nowadays LM is an accurate and precise field, less than 15% of total errors being analytic, but most diseases are diagnosed yet based on phenotypic tests, which are not 100% specific or/and sensitive and the obtained results are compared with a reference range values from an assumed healthy population.

Results: Nowadays, Precision Medicine (PM) analyzes the cause of an individual patient's disease at the molecular level. Molecular genetics is a rapidly developing field, offering health care providers new tools to quickly and accurately diagnose and utilize precise medications which are most likely to be effective, but also for disease prediction and prevention. In daily practice LM contribution in individual PM is mainly for therapeutic drug monitoring.

Conclusion: More and more efforts are done to introduce DNA sequencing to solve unexplained disorders and to apply pharmacogenomics testing to improve patient care, to determine which medication is most compatible with patient's genetics.

Keywords: Laboratory Medicine, Precision Medicine, Laboratory Medicine technology, omics

APPLYING CRISPR TO IDENTIFY DETERMINANTS OF ARSENIC TRIOXIDE CELLULAR TOXICITY

Luoping Zhang[1], Amin Sobh[1], Chris D. Vulpe[1]

University of California, Berkeley, USA[1]

Introduction: Millions of people worldwide are exposed to high levels of arsenic from contaminated drinking water. Its exposure is associated with increased risk of skin, lung and bladder cancers. However, arsenic trioxide (ATO) is also a chemotherapeutic drug particularly effective for acute promyelocytic leukemia. To better understand the "*dual role*" of arsenic, we aimed to determine its cellular toxicities and responses applying a novel CRISPR technology.

Material and method: We employed a *primary* genome-wide CRISPR-based loss of function screening to identify modulators of ATO cellular toxicity, further validated our preliminary results with a *secondary* screen of candidate genes and *finally* confirmed individual targets with gene-specific CRISPR knockouts.

Results: Multiple genes were directly affected from ATO exposure. Disruption of *KEAP1* (an inhibitory

partner of the key antioxidant transcriptional factor Nrf2) or any of the genes involved in selenocysteine metabolism (such as: *EEFSEC, SECISBP2, SEPHS2, SEPSECS, PSTK*) dramatically increased ATO tolerance. However, loss of the multidrug resistance gene *ABCC1* increased sensitivity to ATO.

Conclusion: Our data suggests intracellular interactions between arsenic and selenium could impact arsenic bioavailability and toxicity. Together our work revealed that cellular responses to ATO modulated its toxicity, which may influence arsenic *carcinogenic* and *anti-cancer* activities.

Keywords: Arsenic toxicity, CRISPR screening, Functional toxicogenomics, Selenium

THE USE OF MLPA ANALYSIS IN PREDICTING THE TYROSINE KINASE INHIBITORS RESPONSE IN CHRONIC MYELOID LEUKEMIA PATIENTS

Alina Bogliș[1], Florin Tripon [1], Andrei-George Crauciuc[1], Beata-Magdolna Balla[1], Adriana-Stela Cosma[1], Claudia Bănescu[1]

UMFST Târgu Mureș[1]

Introduction: Chronic myeloid leukemia (CML), produced by BCR/ABL fusion gene, a pathogenic translocation t(9;22), can be treated by tyrosine kinase inhibitors (TKIs) with strong antiproliferative effects. However, interindividual genetic variability, through the acquisition of compound mutations, plays a role in TKIs response for CML patients. It is already known that polymorphisms in cytochrome P450 (GYP) and glutathione S-transferases (GST) genes are involved in the TKIs response. Progress in the molecular analysis improved diagnosis and treatment of CML patients.

Material and method: Several studies on CML were reviewed using PubMed, and we discuss and focus on clinical diagnostics, molecular testing approaches, as well as the efficiency of TKIs response in CML patients that target copy number variations (CNVs). Multiplex ligation-dependent probe amplification (MLPA) remain a rapid and accurate clinical method for detection of the CNVS.

Results: Using specific, commercial kits to perform MLPA analysis and detect CNVs genotypes in GST and CYP genes can demonstrate the predictive response to TKIs therapy. These CNVs can associate a worse response or an optimal response in CML patients to TKI therapy.

Conclusion: Therefore, detection of the CNVs in CML patients by MLPA would be a rapid and effective analysis to assess a guided treatment.

Keywords: chronic myeloid leukemia, copy number variations, tyrosine kinase inhibitor, GST and CYP gene

APOLIPOPROTEIN E LEVELS: A POTENTIAL BIOMARKER IN STATIN TREATMENT RESPONSE

Valeriu Moldovan[1], Laszlo Hadadi[1], Liliana Demian[1], Adina Hutanu[1], Razvan Serban[1], Bogdan Manescu[1], Claudia Bănescu[1], Minodora Dobreanu[1]

UMFST Târgu Mureș[1]

Introduction: ApolipoproteinE is a multifunctional protein with major roles in lipoprotein metabolism. It

has three isoforms: ApoE3-normal, ApoE2 associated with type-III-hyperlipoproteinemia and ApoE4 with Alzheimer's.

Material and method: 142 patients diagnosed by cardiac catheterization with atherosclerotic cardiovascular disease (AD) before the age of 55 treated with statins (Atorvastatin, Rosuvastatin, Simvastatin), and 24 unrelated, untreated, similarly-aged healthy controls (CT) were enrolled. They were all genotyped with the ApoE Mutation-Detection on a LightCycler2.0 Real-time-PCR, serum lipid levels were assessed by Cobas400Plus (Roche Diagnostics) and ApoE by ProSpecBN (Siemens).

Results: Genotyping allowed for allele stratification: 16 cases AD-ApoE2, 126 AD-ApoE3+ApoE4, 4 CT-ApoE2, 20 CT-ApoE3+ApoE4. No differences were found ($p>0.05$) for TotalCholesterol, Triglycerides, HDL-C and LDL-C levels in all genetic subgroups. TotalCholesterol and Triglycerides levels were significantly higher ($p<0.005$) and HDL-C was lower ($p<0.05$) in the AD-ApoE>0.063g/l subgroup compared to the AD-ApoE=0.023-0.063g/l and CT, while LDL-C showed no difference. ApoE2 alleles were also more frequent (21%) in the AD-ApoE>0.063g/l subgroup.

Conclusion: In our study, ApoE serum levels above the reference range were an indicator for inadequate TotalCholesterol, Triglycerides and HDL-C response to treatment, possibly related to the presence of the ApoE2 allele.

Keywords: atherosclerotic cardiovascular disease, Apolipoprotein E, type III hyperlipoproteinemia

METAGENOMIC ANALYSIS OF INTESTINAL MICROBIOTA IN COLORECTAL CANCER

Delia-Mihaela Herghea[1], Patriciu Achimaș-Cadariu[2]

UMF Iuliu Haţieganu Cluj Napoca[1] Oncological Surgery and Oncology Gynaecology Department, UMF Iuliu Haţieganu Cluj Napoca[2]

Introduction: Numerous studies have highlighted the role of dysbiosis both in the carcinogenesis process in the large intestine and in the progression of the disease. The structure of intestinal microbiota in patients with colorectal cancer is not yet fully clarified, but recent research has revealed differences in its structure compared to healthy subjects.

Material and method: Analysis of scientific data.

Results: Laboratory methods used for intestinal microbiota analysis have evolved from classical techniques of clinical microbiology, to molecular techniques and metagenomic analysis. 16S rRNA gene amplicon sequencing and metagenomic analysis allow the taxonomic characterization of intestinal microbiota. Fecal or rectal mucosa samples, tumor biopsy samples taken during colonoscopy, or tumor tissue samples taken during surgery can be analyzed. Data from literature highlights the predominance of bacteria in Bacteroides, Fusobacterium, Porphyromonas and Prevotella in colorectal cancer. However, there is a variability in the results obtained in various studies due to the differences in the samples under analysis and the working technique.

Conclusion: Sequencing techniques and metagenomic analysis are research methods that can be used to characterize intestinal microbiota in patients with colorectal cancer. Standardization of sampling methods and

operational procedures will lead to increased quality and comparability of metagenomic analysis results.

Keywords: metagenomic analysis, intestinal microbiota, colorectal cancer

CLINICAL APPLICATIONS OF PRECISION AND PERSONALIZED MEDICINE

ENHANCEMENT OF CRITICAL CARE MEDICINE USING PRECISION AND PERSONALIZED APPROACHES

Leonard Azamfirei[1]

UMFST Târgu Mureș[1]

Introduction: Critical care medicine (CCM) is generally the most complex and challenging area of medical care while CC therapy is imprecise. Therefore, application of precision and personalized medicine (PPM) can significantly enhance efficacy in CCM.

Material and method: Using sepsis as an example, the usefulness of PPM in CCM will be presented.

Results: Sepsis ICU patients can be initially diagnosed as sub-types based on gene expression, and pathophysiological and clinical conditions while they can be undergoing rapidly changing pathophysiological conditions and having an adverse response to therapy. Therefore, rapid collection and precise interpretation of patient's data are needed for making precision decisions. To reach the goal, specific emphasis is recommended: 1) To provide a precise and personalized diagnosis of patients using enhanced laboratory analyses; 2) To develop disease-specific biomarkers for selection and for monitoring of therapeutic interventions; 3) To develop real-time management and informatics interpretation of data for making informed and bed-side decisions.

Conclusion: Introduction of PPM into critical care medicine is needed and will involve inputs from multi-disciplinary expertise. These inputs may include the development of novel clinical trials, novel biomarkers, genomic analysis, real-time informatics, experimental models and integrative computational models, etc.

Keywords: sepsis, PPM, CCM, biomarkers

ECTOPIC PREGNANCY. DIFFICULTIES IN DIAGNOSIS AND TREATMENT

Ioan-Ovidiu Gheorghe[1], Cristina Paun[1], Nicolae Raca[1]

UMF Craiova[1]

Introduction: The authors present the results of a study carried out over a period of 5 years related to the diagnosis and treatment in the clinic II load angular jointing Obstetrics - Gynecology, in Craiova

Material and method: Our study included monitoring of the incidence of uterine ectopic pregnancy according to age, parity, abortions. A study of the difficulty of diagnosis with a full range symptoms and signs was carried out, with a focus on: hormonal tests, ultrasound, celioscopy, etc. and, also, on how complicated it is to decide upon a conservatory medical or surgical treatment.

Results: In ectopic pregnancy, the doubling occurs after a week, the HCG values being inconclusive for ectopic pregnancy. Out of 700 cases of ectopic pregnancy, 108 had values under 100U.I/ml. The HCG values are not conclusive for the prognosis of ectopic pregnancy either. The values are important for the treatment with methotrexate.

Conclusion: Local examination and ultrasound, although quite important, cannot give an express

diagnosis of angular pregnancy, but they may show an empty uterus.

Keywords: ectopic pregnancy, angular pregnancy, immunological tests, extrauterine pregnancy

EFFECTIVENESS OF BISPHOSPHONATED THERAPY AND PERSONALIZED DIET UPON A GROUP OF FEMALE PATIENTS WITH OSTEOPOROSIS FROM TÂRGU MUREŞ, ROMANIA

Oana-Cristina Cinpeanu[1], Ionela-Maria Pascanu[1], Monica Tarcea[1]

UMFST Târgu Mureș[1]

Introduction: Osteoporosis is a real public health problem and is a major cause of fragility, disability, morbidity, and mortality, especially in the elderly. The present paper aims to analyze retrospectively for a period of two years, the effectiveness of bisphosphonate therapy in a group of patients from Targu-Mures County.

Material and method: We monitored data collected from the archive of Endocrinology Ambulatory in Targu-Mures, for a group of 100 female patients with newly diagnosed osteoporosis.

Results: The present study confirms the increase of bone density both at 1 year and 2 years of antiresorptive therapy, their efficacy, and place in osteoporosis management. There is a close correlation between the age of the patients and the decrease in bone mass density, the older they are, the lower the T score is, also, the younger they are, the faster they recover, with negative correlations, however. We can have good results with a personalized diet and a proper treatment.

Conclusion: Bisphosphonates have proven effective in both bone mineral density recovery and fracture risk prevention. The severity of the T-score is predominantly encountered in older age categories over 70 years. Patient empathy by the therapist as well as good adherence to treatment are major determinants in the management of osteoporosis.

Keywords: bone density, T score, osteoporosis, bisphosphonate

THE IMPORTANCE OF GENETIC TESTINGS IN CHILDREN ADMITTED TO THE NEUROLOGY DEPARTMENT

Sabina Radu[1], Anamaria Todoran Butila[1]

UMFST Târgu Mureș[1]

Introduction: For initiating the best treatment management, physicians have been considering genetic testings from which more precise diagnosis and targeted therapy can be initiated.

Material and method: In our Neurology Department, we have been emphasizing the role of advanced testings. The first case presented, at the age of 3 months, with severe muscle hypotonia and plurimalformative syndromes (congenital heart malformation, cryptorchidism, skeletal anomaly) which developed, over 10 years, with mental and motor retardation. At 4 years of age, we requested a cytogenetic evaluation. The second patient, 4 years old, presented with increased levels of muscle enzymes (transaminase, creatine phosphokinase,

lactate dehydrogenase) and with clinical features specific to Duchenne dystrophy.

Results: Cytogenetic test of the first case confirmed the presence of chromosomal anomaly, a 49, XXXXY karyotype. For the second case, laboratory test revealed a deletion of exons 49-50 from the dystrophine gene in X chromosome.

Conclusion: Genetic testings, especially for patients with plurimalformative syndromes, are necessary for providing causal explanations of clinical abnormalities and therefore, for more precise diagnosis. With better understanding of the genomic abnormalities in our two cases, we will be able to design targeted therapy.

Keywords: Phenotype, genetic testing, Duchenne dystrophy, chromosomal abnormality

CLINICAL UTILITY OF A MULTIPLEX PANEL IN A PREDICTION OF FUNCTIONAL DEPENDENCE IN DAILY LIFE ACTIVITY AFTER ISCHEMIC STROKE

Adina Hutanu[1], Mihaela Iancu[1], Rodica Balasa[1], Smaranda Maier[1], Minodora Dobreanu[1]

UMFST Târgu Mureș[1]

Introduction: Experimental studies have revealed the importance of BDNF and PDGF-AB/BB in neural and vascular plasticity modulation; however, data regarding the clinical implication of PDGF-AA and AB/BB are scarce.

Material and method: To determine the clinical utility of a multiplex panel in a prediction of functional dependence in daily life activity after ischemic stroke, a panel of ten biomarkers was analyzed by xMAP technology in 114 ischemic stroke patients admitted during 24 hrs after onset.

Results: Significant associations between plasma BDNF, RANTES, PDGF-AA, PDGF-AB/BB, and Barthel Index were found. Lower peripheral levels were found in group with BI≤80 and a functional dependence in daily life activity. A similar pattern was observed for mRS, lower plasma values being measured in patients with unfavorable outcome (mRS=3-6). In multivariate logistic regression analysis BDNF, PDGF-AA and PDGF-AB/BB were independent predictors for functional dependence in daily-life activity. Inclusion of each significant biomarker in the clinical model, increased area under the ROC curve without significance. Higher plasma levels of sVCAM and NCAM were univariate predictors of risk for unfavorable mRS at 3months. After adjusting for clinical known risk factors, BDNF, PDGF-AB/BB, and PAI-1 were negatively associated with unfavorable outcome risk.

Conclusion: BDNF, PDGF-AA, and PDGF-AB/BB were independent post-stroke predictors of functional dependence in daily-life activity.

Keywords: stroke, Barthel index, PDGF, functional dependence

CONTEMPORARY MELANOMA TRATMENT- KEY PARADIGM IN ONCOLOGY

Paul Doru[1], Alina Musetescu[2]

Division of Hematology and Medical Oncology, Weill Cornell, New York, USA[1] Dermatalogy Department, "Dr. Victor Babes" Clinical Hospital, Bucharest, Romania[2]

Introduction: Melanoma is the least common but at the same time the deadliest form of skin cancers, being one of the cancers with the greatest metastatic potential. Over the last decade, we have experienced an important advancement in the understanding of the biology and the molecular background of the disease.

Material and method: The purpose of the present paper is to review the present landscape of melanoma treatments: show how the molecular biology discoveries led to new molecular classifications and to the development of more effective therapies adapted to distinct melanoma subtypes; illustrate how personalized treatments and immunotherapies have changed the overall survival rate and the outcomes of this aggressive disease.

Results: Contemporary immunotherapy compounds (checkpoint inhibitors, oncolytic viruses) and targeted agents based on the distinct genetic melanoma subtypes are not only less toxic than chemotherapy and older immunotherapy approaches (interferon, interleukin 2) but they are associated with significant improvement in survival both in adjuvant and metastatic settings. The molecular classification using next-generation sequencing (NGS) techniques, combination therapies, and emerging new immunotherapy approaches allow more precise treatments tailored to the specific patient.

Conclusion: There has been a revolution in the management of melanoma in the last decade with significant improvements in overall survival and outcomes. The promising results using precision medicine in the therapy of melanoma is a key paradigm for orienting the treatment of other malignant diseases in the modern era.

Keywords: melanoma, skin cancer, immunotherapy

HOMEOPATHY - A PERSONALIZED MEDICAL SYSTEM

Adrian Alecu[1], Mariana Alecu[1]

UMFST Târgu Mureș[1]

Introduction: Traditionally homeopathy is known as a holistic and personalized medical system but it is not enough publicly assessed according to the modern principles of personalized health care.

Material and method: Homeopathic principles and methods were evaluated according to the Horizon 2020 Work Programme of the European Commission

Results: The homeopathic semiology is highly personalized, taking into consideration the patient as a whole, analyzing the disease as the result of the interactions between the personal terrain and the etiological factors from the environment. Thus the 3 major guides for the homeopathic pharmacological prescription: terrain (genetic influence, type of personality and way of reaction), etiology (internal and external factors causing the disease), and the disease itself, which in fact is just the individual reaction of the person with

certain terrains. The symptomatic core for the disease can be different for different people, even if the etiology is the same, leading to different prescriptions.The homeopathic pharmacology is based mainly in the sequential dilution and kinetic activation of the drugs.

Conclusion: Well-known for the homeopathic physicians, the concept of personalized medicine gains new relevance and can lead to better success in healthcare. With emphasis on homeopathic semiology, this discipline contributes towards the adoption of personalized medicine.

Keywords: homeopathy, personalized, holistic, integrative

STRATIFIED MEDICINE FOR NEUROLOGICAL DISEASE

Mark Slevin[1]

Manchester Met's Healthcare Science Research Centre, Manchester Metropolitan University, Manchester, UK[1]

Introduction: InIn neurological disease, medical advancement has so far lagged behind other fields of science and treatment capability. There have been no major advancements in treatment within the last two decades. The focus of this presentation will be on the potential impact of patient stratification for diagnosis, prognosis and treatment

Material and method: Possible new interventions for determining pre-symptomatic development of dementia will be discussed along with indicators of stroke development and early discrimination of sub-type along with traumatic brain injury as a result of accident or sports injury.

Results: Current and future state-of-the-art and likely new therapeutics and diagnostics will be discussed and how this will affect patient quality of life and health care processing

Conclusion: A final conclusion will be made describing the likely impact of these developments on society

Keywords: dementia, neurological, stroke

PERSONALIZED MEDICINE IN EUROPE - PROGRESS, CHALLENGES AND CURRENT DEVELOPMENTS

Alexandru-Sorin Costescu[1]

EC, Innovative and Personalised Medicine Unit, Health Directorate, Directorate-General Research and Innovationand Innovation, Brussels, Belgium[1]

Introduction: Personalised medicine has evolved as an approach that helps to address the main challenges of existing healthcare systems by developing tailored strategies for prediction, prevention, diagnosis and treatment for individuals or groups of individuals. The final goal is to offer patients the most effective healthcare interventions, in a timely manner and ensuring an optimal use of resources available.

Material and method: The following main challenges have been identified in relation to adoption of personalized medicine, therefore both ongoing and future efforts aim at these directions: a) developing awareness and empowerment, b) integrating big data and ICT solutions; c) translating basic to clinical research and beyond; d) bringing innovation to the market; e) shaping sustainable healthcare.

Results:

As personalized medicine approaches use extensive patient and population data, efforts are being made to integrate large amounts of information into clinical practice while ensuring data protection and patient privacy. Consequently, healthcare systems will have to evolve and become better at generating, storing and processing health-related information, in order to facilitate the appropriate actions.

Conclusion: In order to become fully functional, personalized medicine requires major changes in the way medicines are tested and evaluated, in the way healthcare is delivered and healthcare systems are structured.

Keywords: personalised medicine, personalised health, precision medicine, health data

DNA REPAIR IN PERSONALIZED BRAIN CANCER CHEMOTHERAPY

Bernd Kaina[1]

Institute of Toxicology, University Medical Center, Mainz, Germany[1]

Introduction: Malignant brain tumors have a very poor prognosis, which is thought to be due to drug resistance. First-line chemotherapeutics is temozolomide. The mechanism of cell death triggered by temozolomide is well described. It rests on conversion of O6-methylguanine through mismatch repair into DNA double-strand breaks (DSB). Consequently, repair pathways have a great impact on temozolomide resistance.

Material and method: Cell and molecular biological methods, including Westerns and FACS, have been used.

Results: It is shown that the expression of MGMT is related to patient's survival. We have established methods of determining the MGMT promoter methylation status, which corresponds to MGMT silencing, showing MS-HRM to be superior to MS-PCR. Temozolomide induces both apoptosis and cellular senescence, which is triggered by the same damage, O6-methylguanine. The pathways involved have been elucidated and it will be shown that p53 plays a critical role. We also analyzed mutated IDH1, which is linked to favorite prognosis, as to its involvement in DNA repair and obtained evidence for a link to the ALKBH2-directed repair pathway.

Conclusion: MGMT, MMR and HR strongly determine the response of glioblastoma cells to temozolomide. The data will be discussed as to therapeutic applications and the attenuation of side effects such as hematotoxicity.

Keywords: gliomas, MGMT, DNA repair, drug resistance

IMPROVING MANAGEMENT IN RESPIRATORY SLEEP DISORDERS BY AN AVAILABLE COMPREHENSIVE DATABASE

Gabriela Jimborean[1], Mioara Szatmary[1], Alpar Csipor[1], Edith-Simona Ianosi[1]

UMFST Târgu Mureş[1]

Introduction: Respiratory sleep disorders (RSD) especially sleep apnea and hypoventilation syndromes have an important burden on health population, severe complications and a high cost for the health system

Material and method:

Proposal for an electronic database for RSD patients

Results: in our database each patient with RSD will have a file recorded in a structured web-based report form that includes all case issues: demographic data, risk factors (body mass index, smoking, exposure, comorbidities), medical history, symptoms, investigations (sleep questionnaires, Epworth scale, polygraphy/polysomnography, sleep diaries, EKG, cardiac consult, metabolic parameters, spirometry, effort tests), "Positive Airways Pressure" titration, medication, means of treatment, evolution under treatment. The database will be accessible to all specialists from the interdisciplinary team that is caring the RSD and their complications (pulmonologists, cardiologists, internal medicine specialists, nutritionists) and will permit data transfer (telemedicine). Our database could be implemented in a regional or national frame.

Conclusion: Sleep disorders database is expected to enable an analysis of the risk factors, complication and treatment methods in RSD. It is an interdisciplinary project (physicians and computer-specialists) meant to improve disease prophylaxis, the early diagnosis, the targeted treatment of RSD and the general knowledge in the field.

Keywords: sleep apnea, electronic regional/national database, telemedicine

PERSONALIZED APPROACH OF THE DIAGNOSIS AND TREATMENT IN OBSTRUCTIVE SLEEP APNEA PATIENTS (EXPERIENCE OF THE PULMONOLOGY DEPARTMENT OF THE UMPHST TG. MURES, ROMANIA)

Gabriela Jimborean[1], Alpar Csipor[1], Bianca Ciurba[1], Oana Fagaras[1], Mioara Szatmary[1], Edith-Simona Ianosi[1]

UMFST Târgu Mureş[1]

Introduction: Sleep apnea (SA) is responsible for a significant health impact: hypertension, ischemic cardiopathy, atherosclerosis, risk of stroke, diabetes, dyslipidemia, sexual dysfunction, cognitive decline, and work/traffic accidents). SA exhibits multiple mechanisms of appearance and phenotypes, so a personalized approach is required

Material and method: Analysis of the methods to achieve the best diagnosis and treatment approach in SA patients in the Pulmonology Clinic sleep laboratory

Results: In 200 SA patients (84% severe, 15% with concomitant hypoventilation) we analyzed the risk factors, severity, complications and methods of improving treatment compliance. Polygraphy was preferred and a short hospitalization with interdisciplinary consults (to assess complications) was performed. 78(39%) were smokers, 71(35.5%) alcohol abusers, 190(95%) had overweight or obesity (58-29% gr-II obesity, 52-26% morbid obesity), 152(76%) cardiovascular complication, 52(26%) diabetes. We have chosen treatment with Continuous Positive Airways Pressure and targeted methods to decrease modifiable risk factors, weight loss and physical activity (together with nutritionists and kinetotherapists), education (monthly counseling, smoking, and alcohol cessation), positional therapy and comorbidities monitoring. Other methods (bariatric surgery, upper-airway surgery, dental appliances) are still expensive

Conclusion: Personalized medicine in SA is possible: diagnosis and treatment tailored to each patient's

stage and need by interdisciplinary approach and education for decrease in modifiable risk factors

Keywords: Sleep apnea, Personalised diagnosis and treatment, Modifiable risk factors

VACCINE-RELATED HUMORAL IMMUNITY IN CHILDREN WITH CANCER

Adrienne Horvath[1], Zsuzsanna-Erzsebet Papp[1]

UMFST Târgu Mureș[1]

Introduction: The malignant disease itself, chemotherapy and radiotherapy lead to secondary immunodeficiency. The aim of the paper is to evaluate serum anti Tetanus Toxoid IgG antibody levels in patients with leukemias and solid tumors treated at the Department of Pediatrics of the Mures County Clinical Hospital.

Material and method: Thirty-two patients aged 3 months-18 years suffering from leukemias and solid tumors and a control group of 16 children admitted with non-malignant diseases were assessed for serum IgG anti Tetanus Toxoid levels. Results under 0.1 U/mL, were considered unprotective. Vaccination history was taken from parents and vaccination booklets.

Results: Ineffective serum levels of IgG anti Tetanus Toxoid was found in 40% of cancer patients compared with 12.5% in controls. Nine patients out of 23 with leukemias, 3 children out of 9 with solid tumors and 2 children out in 16 in the control group had antibody levels under 0.1 U/mL. The medians of IgG anti Tetanus Toxoid serum levels reached lowest levels in leukemic patients (0.17 U/mL) and were highest in the control group (0.39 U/mL).

Conclusion: We found the most severe secondary vaccine-related immunodeficiency in leukemic patients followed by solid tumors, compared to the control group. The intensity of chemotherapy influences the postvaccinal humoral immunity.

Keywords: humoral immunity, postvaccinal, child, cancer

PERSONALISED MEDICINE AND THE EYE: PROMISES, CHALLENGES AND OPPORTUNITIES

Mark Radford[1]

Queensland Eye Institute Foundation, Brisbane, Australia[1]

Introduction: Over 253 million people in the world are visually impaired, with 35 million people who are blind and 217 million people who have severe or moderate visual impairment (Vision Loss Expert Group, 2017).

Material and method: Over 1 billion people have near-vision impairment simply because they do not have a pair of spectacles.

Results: From artificial intelligence, bionic eyes, stem cell therapy, genetics and gene therapy, new surgical techniques (including minimally invasive glaucoma surgery), to simply spending more time in the

school play yard.

Conclusion: This paper will provide a brief look at the promises, challenges and opportunities for one of the most significant health care burdens in the world: eye disease, impaired vision and blindness.

Keywords: Ophthalmology, eye disease, artificial intelligence, gene therapy

ASSESSING THE IMPACT OF PRECISION MEDICINE ON TRENDS IN CLINICAL RESEARCH BASED ON THE AGGREGATE ANALYSIS OF CLINICALTRIALS.GOV (AACT) DATABASE

Mihaly Imre[1], Eniko-Reka Imre[1]

UMFST Târgu Mureș[1]

Introduction: Precision medicine (PM) is seen as an opportunity for a paradigm shift in healthcare. Several forecasts were released during the last years, predicting its impact on clinical research and on the pharmaceutical industry. Our aim was to confirm whether these predictions are fulfilled and to assess how PM is impacting the research industry.

Material and method: The "Aggregate Analysis of ClinicalTrials.gov Database" was queried using pgAdmin4 for a predefined set of keywords. The resulted dataset was analyzed descriptively, as well as for trends, slope and signals.

Results: A number of 7408 trials were selected. PM trials were almost nonexistent before 1995. After this year, the number of potential PM related studies increased constantly (R^2=0.95). One fourth were funded by the pharmaceutical industry, while the rest were funded by academic institutes. A constant increase was seen in both these groups, however the industry proved to be more restrained (slope of 8.16 vs 29.44 trials/year). No impact on clinical research industry was revealed.

Conclusion: An interest from both the academics as well as the pharmaceutical industry was observed, however involvement of the industry is still low and characterized by moderation, while the overall impact of PM studies on clinical research is not yet significant.

Keywords: precision medicine, clinical research industry, Aggregate Analysis of ClinicalTrials.gov (AACT) Da, trends in clinical research

PERSONALIZED PROPHYLACTIC THERAPY IN CHILDREN WITH HAEMOPHILIA

Mihaela-Ioana Chincesan[1], Alina Grama[1], Andreea Dinca[1]

UMFST Târgu Mureș[1]

Introduction: Haemophilia, a rare chronic disease, is a hereditary clotting disorder, characterized by Factor VIII or IX deficiency, secondary to a chromosome X gene mutation. Musculoskeletal bleeding is the most common manifestation in patients with Haemophilia, affecting daily activities, as well as the quality of life.

Material and method:

Prophylaxis is the optimal therapy for severe Haemophilia, with the role of preventing bleeding and disabling arthropathy, and also improving the quality of life. Personalized treatment according to the needs of each patient, should govern the medical practice in the field of Haemophilia.

Results: The body weight-based regimen has its limitations and should be replaced with personalized, patient-centered treatment regimens. Thus, the individualization of therapy should take into account the age of the patient, pharmacokinetics data, bleeding phenotype, articular status, adherence to treatment, intensity of physical activity, venous approach and other factors.

Conclusion: Personalized medicine is already an applicable concept in Haemophilia management, even though still at the beginning. It is necessary for the patient to be educated regarding the disease and the treatment. The costs and the availability of resources can also be barriers to adopting personalized medicine in the patient with Haemophilia.

Keywords: haemophilia, prophylactic therapy, children

BILATERAL NEUROBLASTOMA WITH MULTIPLE METASTASES IN INFANT. CASE PRESENTATION AND THERAPEUTIC OPTIONS.

Roxana-Cristina Mares[1], Emoke Horvath[1], Radu Prisca[1], Oana-Cristina Marginean[1], Carmen Duicu[1], Alina Grama[1], Andreea Dinca[1], Mihaela Chincesan[1]

UMFST Târgu Mureș[1]

Introduction: Neuroblastoma is a malignancy of the sympathetic nervous system arising from neuroblasts. It is the most common solid tumor in children.

Material and method: An 11-month-old female infant was hospitalized for the appearance of a large tumor in the left hypochondrium and a subcutaneous nodule in the right flank. On clinical examination, the child also presented bilateral exophthalmia and periorbital ecchymoses, as well as firm parietal tumors.

Results: Abdominal ultrasound revealed a voluminous tumor of the left adrenal gland, confirmed by the abdominal CT scan, which also showed a small tumor in the right adrenal gland. The Cranial CT examination revealed multiple skull metastases. The levels of urine vanil-mandelic acid and serum neuron-specific enolase were elevated (54 mg and 128 ng / ml respectively). A biopsy was performed from the cutaneous nodule and the histopathological examination confirmed the suspicion of neuroblastoma, classified according to the European Infant Neuroblastoma Study 1998 as Stage IV. Carboplatin and Etoposide chemotherapy was initiated, subsequently the treatment will be adapted according to the outcome of the genetic testing of the n-, protooncogene from the cutaneous metastasis.

Conclusion: Bilateral neuroblastoma is, finding.The presence of exophthalmia-myc proto-oncogene is decisive for treatment and prognosis.

Keywords: Neuroblastoma, infant, n-myc, chemotherapy

THERAPEUTIC PHOTOCROSSLINKING OF COLLAGENOUS TISSUES: DEVELOPING UV-ASSISTED MEDICAL TREATMENTS

Traian Chirila[1]

Queensland Eye Institute, Brisbane, Australia[1]

Introduction: Ultraviolet (UV) radiation has been a tool to assist medicine for almost 200 years, first as part of solar radiation exposure to improve certain diseases, symptoms and then as a method to kill pathogens. Besides disinfection and sterilization, a current major application of UV radiation is in dermatology. Seldom used, the term "UV medicine" refers generally to dermatologic applications. More recently, procedures have been developed that use the UV-A region and target the tissular collagen.

Material and method: A new brand of UV medicine is emerging within ophthalmology, where therapies have been developed by using the exposure to UV-A radiation (320 to 400 nm wavelength) in order to crosslink photochemically collagen and such imparting additional strength and rigidity to the targeted tissues.

Results: The treatment of keratoconus and other keratoectatic disorders by UV-A crosslinking is already an established medical procedure associated with significant clinical success. Tentative treatment of progressive myopia is also discussed. In our laboratories we have discovered that the irradiation with UV-A of tarsal collagen in eyelids may become an effective treatment for the eyelid laxity and related disorders. We have also carried out research for using the same strategy to arrest the progression of aortic abdominal aneurysms.

Conclusion: This presentation discussed the status of the "new" UV medicine in ophthalmology and its prospect for vascular disorders.

Keywords: UV radiation, collagen crosslinking, keratoconus, eyelid laxity

NEU ONCOGENE DRIVEN HEAD AND NECK CANCER – CASE REPORT

Enikő-Réka Fejér[1], Florin Bacanu[1], Paul Doru[2]

Sanador Hospital, Bucharest, Romania[1] Division of Hematology and Medical Oncology, Weill Cornell, New York, USA[2]

Introduction: Head and neck cancers are aggressive tumors. 2-3 % out of them are HER2 positive.

Material and method: We present a case of submandibular gland adenocarcinoma treated with targeted therapy. The 64-year-old, male patient was admitted to hospital with left laterocervical mass cT2 N2b M0 stage in October 2012. He underwent tumor excision and regional lymph node dissection. The histopathological report revealed ductal carcinoma of the submandibular gland. Positron emission tomography confirmed postsurgery residual disease in bilateral submandibular lymph nodes, followed by tongue base excision and neck dissection. The patient underwent concomitant radiochemotherapy 66 Gy + Cisplatinum ended in February 2013. In the follow-up period in October 2014, we found left upper pulmonary lobe increased metabolic activity, and oligometastatic status was confirmed after resection. The molecular profiling of the surgical sample identified HER2 driver gene in the tumor. He started Trastuzumab therapy 600 mg subcutaneously q3w, underwent periodically to circulating tumor cell monitoring and continued treatment until

August 2015 when treatment was withheld due to unacceptable cardiac toxicity.

Results: In October 2018 patient is clinically, imagistically disease free.

Conclusion: Close monitoring and personalized treatment can improve prognosis and patient survival in head and neck cancers.

Keywords: head and neck cancer, targeted therapy, oncogen, Her2

SOLID PSEUDOPAPILLARY NEOPLASM OF THE PANCREAS - CASE PRESENTATION

Andreea-Ligia Dincă[1], Mihaela-Ioana Chincesan[1], Anne-Mary Turcu[1], Radu Prisca[1], Emoke Horvath[1], Cristina Mares[1], Cristina-Oana Marginean[1]

UMFST Târgu Mureş[1]

Introduction: Solid pseudopapillary neoplasm of the pancreas (SPN) is an extremely rare tumor, that typically affects young women in the second and third decades of life. It accounts for 1-2% of all pancreatic exocrine tumors, and It is a relatively benign tumor, with favorable prognosis.

Material and method: We present the clinical-pathological and imagistic features of SPN, as well as the outcome of surgery in the case of a 9-year-old patient diagnosed in the Pediatric Hematology-Oncology Department of Tîrgu Mureş in December 2017.

Results: The patient presented to the Emergency Service complaining of severe abdominal pain, vomiting, loss of appetite. Abdominal ultrasound revealed an inhomogeneous mass, located left latero-aortic, raising the suspicion of a neuroblastoma, later aborted by abdominal-pelvic CT scan and laboratory tests. Block excision of the tumor with caudal pancreatectomy was performed, and the histopathological examination placed the diagnosis of SPN. The patient was not given any adjuvant therapy, and she remained asymptomatic without tumor recurrence phenomena at subsequent re-evaluations.

Conclusion: Given the small number of reported cases, the diagnosis, evaluation and establishment of a therapeutic protocol is so far a therapeutic challenge. Genetic tests can be a diagnostic alternative for personalized therapy in rare tumors, providing the clinician with helpful information in establishing subsequent therapy.

Keywords: SPN, CHILDREN, PANCREATECTOMY

PERSONALIZED MEDICINE FOR PATIENTS WITH PHENILKETONURIA

Ana Pitea[1]

UMFST Târgu Mureş[1]

Introduction: Phenylketonuria, PKU is a rare inherited autosomal-recessive metabolic condition, as a result of an enzyme deficiency (phenylalanine hydroxylase, PAH). It can be discovered due to newborn screening. Untreated, the disease causes neurological damage, as profound mental retardation, seizures and autistic behavior (the inability to metabolize phenylalanine, Phe, into tyrosine leads to elevated blood Phe concentrations which can cross the blood–brain barrier).

Material and method:

The paper presents the particularities that make this disease to be one that requires a personalized approach.

Results: PKU may appear in various clinical phenotypes and biochemical phenotypes, depending on enzyme regulation and enzyme function. The treatment of PKU consists of a diet low in phenylalanine, enzyme substitution and a number of innovative methods of therapeutic approach are in progress. The diet should be initiated as early as possible, to be properly followed and very strict, by calculating the daily intake of Phe in food(weighing each food), in order not to exceed individual tolerance. Pharmacotherapeutic treatment is only indicated in well-selected patients who are responsive to tetrahydrobiopterin after a proper pre-test.

Conclusion: EachPKU patient is unique and requires a therapeutic approach based on diet(adjusted to personal Phe tolerance) or make and medication, a personalized option depending on the response to treatment.

Keywords: diet, phenilketonuria, personalized medicine, tetrahydrobiopterin

THE UTILITY OF GENETIC TESTING IN PROGNOSIS AND PERSONALIZED TREATMENT OF MYELOPROLIFERATIVE DISORDERS AND MYELOID LEUKEMIA

Claudia Bănescu[1]

Center for Advanced Medical and Pharmaceutical Research University of Medicine, Pharmacy, Sciences and Technology of Târgu Mureş, Romania[1]

Introduction: Major advancements in sequencing technologies for genome analysis were observed in the last years and they have increased our comprehension of the genetic basis of hematological malignancies. Myeloproliferative neoplasms (MPN), acute and chronic myeloid leukemia (AML, CML) are clonal stem cell disorders characterized by acquisition of specific somatic mutations, considered driver mutations.

Material and method: Currently, clinical research in MPN and myeloid leukemia (AML, CML) is focused on the identification of driver mutation and the development of new drugs that can modify the disease natural history.

Results: Extensive diagnostic investigations such as cytogenetic analysis and molecular testing, are necessary for identifying driver events and to establish the eligibility of the patient for the new drugs that have the potential to improve survival and treatment response. Also, the latest technologies will allow us to identify subgroup of patients who might response better to a specific therapy. Investigation of the dynamics of molecular response by monitoring the dynamics of FLT3-ITD, BCR-ABL, JAK2 V617F, CALR mutant alleles is recommended in patients with AML, CML or MPN during target treatment like various tyrosine kinase inhibitors (TKIs) or JAK inhibitor therapy.

Conclusion: Molecular analysis has an important role in deciding when the patients may need a change of therapeutic strategy.

Keywords: genome, myeloproliferative neoplasms, myeloid leukemia

CUTTING EDGE ISSUES IN POPULATION HEALTH AND PERSONALIZED MEDICINE

DIETARY FACTORS IN CANCER PREVENTION: FROM OBSERVATIONAL TO INTERVENTION RESEARCH

Young-Joon Surh[1]

Tumor Microenvironment Global Core Research Center, Seoul National University, Seoul, Korea[1]

Introduction: Many studies have shown that high consumption of vegetables and fruits is associated with reduced risk for cancer. However, exact mechanisms for the association have not been well characterized.

Material and method: Data from publications and from my own laboratory were reviewed and summarised for this presentation

Results: Dietary botanicals contain compounds which have cancer chemopreventive activities: in cruciferous vegetables (e.g., cabbage and broccoli), allium vegetables (e.g., garlic and onion), green tea, citrus fruits, soybeans, tomatoes, berries, and ginger, as well as in medicinal plants. Several lead compounds, such as genistein (from soybeans), lycopene (from tomatoes), brassinin (from cruciferous vegetables), sulforaphane (from asparagus), indole-3-carbinol (from broccoli), and resveratrol (from grapes and peanuts) are in preclinical or clinical trials for their cancer chemopreventive potential. Some marine products also contain distinct bioactive substances that exert chemopreventive effects. As oxidative stress and inflammatory tissue injuries are implicated in the pathogenesis of human malignancies, antioxidant and anti-inflammatory substances in the diet are of particular interest in terms of their chemopreventive potential.

Conclusion: Natural products have great potential in cancer prevention because of their safety, low cost, and oral bioavailability. This presentation will highlight selective dietary cancer preventive compounds and their mechanisms of action.

Keywords: Dietary factors, cancer prevention, intervention research

AIR POLLUTION AND BODY WEIGHT OF PERSISTENT ORGANIC POLLUTANTS AT AN ELECTRONIC WASTE RECYCLING AREA OF CHINA

Qilin Qin[1], Xijin Xu[1], Qingyuan Dai[1], Kai Ye[1], Chenyang Wang[1], Xia Huo[1]

Jinan University[1]

Introduction: The main content of our oral report is the concentrations of POPs in the atmosphere of an electronic waste (e-waste) recycling town, Guiyu, in Southeast China. The process of e-waste dismantling released large amounts of POPs into the surrounding environment, thus entering the human body [1, 2]. Previous studies have shown that these pollutants cause various diseases to local residents [3-6]. In general, dietary intake is generally accepted to be the primary exposure route for some organic compounds. However, we assess the evidence for the association between air pollution and human body weight, to provide an indication of the severity of respiratory exposure.

Material and method: We use various databases to collect relevant data, and several formulae to calculate health risks of POPs.

Results: In the e-waste recycling area, especially in Guiyu, residents' respiratory exposure to POPs is

higher than that in other areas. Furthermore, except for PBDEs, the HQ of the other pollutants were rated higher than 1 by respiratory exposure only, and all of them are at risk of carcinogenesis.

Conclusion: Respiratory exposure route may be more important than dietary exposure route in the e-waste recycling area, especially in Guiyu. This calls for attention to respiratory exposure in highly polluted areas.

Keywords: POPs, E-waste, Atmospheric pollution, Respiratory exposure

CONTRIBUTIONS OF TRADITIONAL CHINESE MEDICINE ONTO POPULATION HEALTH AND PERSONALIZED MEDICINE

Flaviu Moldovan[1], C. Wang[1], Y. Xiao[1]

UMFST Târgu Mureș[1]

Introduction: Traditional Chinese Medicine (TCM) shows efficacy in preventing heart disease compared to Western medicine (WM). The success is based on maintaining body homeostasis, reducing daily stress, and emphasizing healthy diets and physical exercises.

Material and method: Review on TCM's contributions to health, and to collaboration with WM for enhancement of population health and personalized medicine. Strengths, shortcoming and recommendations will be presented.

Results: WM is sometimes perceived as being over-medical and over-specialized in which the patient is not treated as a whole person but by a stream of medical specialists; In China, TCM and WM offer integrated services through the use of shared biomedical knowledge; Herbal treatments and acupuncture are the two forms of TCM which are gaining acceptance around the world; Through more rigorous testing, especially with clinical trials, critical issues of TCM on quality, safety and efficacy can be better accepted internationally; • In collaboration with WM and with integration of genomic studies, personalized medicine can be achieved.

Conclusion: The 11th edition of International Classification of Diseases - WHO and other documents contain guidelines on how to use TCM in medical practices. Integration of TCM with WM holds the promise to further improvement of population health and personalized medicine internationally.

Keywords: Traditional Chinese Medicine, herbal treatments, acupuncture

STRENGTHS AND WEAKNESSES OF SHORT-TERM SNOWBALL TRAINING FOR TRAINERS OF GENERAL PRACTITIONERS IN GUANGDONG PROVINCE, CHINA

Yinghua Xia[1], Zihui Hong[1], Xi Chen[1], Qun He[1]

Guangdong Institute of Public Health[1]

Introduction: China is in shortage of workforce for general practitioner (GP) services and is exploring for effective training models to improve its capacities. A model of short-term snowball training was to be piloted and evaluated in Guangdong Province .

Material and method: This is a case study combining qualitative and quantitative methods at the

Shayuan Community Health Service Center (CHSC), a government-designated training bases, upon its quality of GP service in the previous decade. The first-generation was fostered during self-development, and they trained the second generation by offering 6 weeks of well-designed training courses. We conducted in-depth interviews among 7 first-generation trainers and questionnaire survey among 58 second-generation trainers, whose recognition to GP service content, value identification and confidence to future development were measured. We also collected feedback from the second-generation about courses which consisted of four modules, GP theory, clinical diagnosis and treatment, diseases management, and special practice of family doctors.

Results: After the training course, the second-generation changed their incorrect recognition, improved value identification and enhanced confidence.However, practice skills courses did not meet the demands of the second-generation.

Conclusion: The snowball training model has strengths in disseminating recognition, but courses need to be modified for more practical skills.

Keywords: General practitioner, Snowball training, Capacity building

INNOVATIVE APPROACH TO APHASIA THERAPY

Annamaria Gyorfi[1], Olivian Vlad[1]

UMFST Târgu Mureș[1]

Introduction: Aphasia is a dysfunction of the higher integrating brain activity regarding language and speech. Treatment is generally based on speech language therapy. Finding ways to start speech therapy based on the communication skills that remain intact presents the main research interest for clinical linguistics.

Material and method: We analysed the emotional language of 48 aphasic patients registered in the AphasiaBank data base. We used an Excel spreadsheet for each participant to assess the frequency of emotive utterances in the transcripts. Subsequently, we applied a professional facial expression recognition software on the video recordings for objectivity in observations.

Results: Aphasic patients mostly express negative feelings due to the nature of their condition, but when thinking of important events in their lives they display happiness more often. Transcripts backed up with FaceReader show that in almost all cases patients are capable of using emotional language and of displaying emotions. This can be used to make therapy more successful.

Conclusion: Emotions and emotive utterances are stored in the right side of the brain while in most aphasic people the left side is affected. When communication is impaired any additional "tool" that facilitates communication can improve and accelerate the outcome of aphasia therapy.

Keywords: aphasia, emotional language, right hemisphere of the brain, FaceReader

PERSONALIZED TREATMENT TO ENHANCE CLINICAL OUTCOMES VIA CORRECT USE OF NATURAL PRODUCTS AND THERAPEUTICS

Manuela Neuman[1]

University of Toronto, CEO & CSO, In Vitro Drug Safety and Biotechnology, Banting Institute, Toronto, Canada[1]

Introduction: In order to provide better treatment for patients and more effective targeted drugs and complementary and alternative medicine, it is vital to understand disease mechanisms and to identify informative markers for patient susceptibility, disease progression, treatment response, and individual drug tolerance. The stratified medicine is a key paradigm for global health care, but also a challenge for clinicians, laboratory medicine specialists.

Material and method: The aims are to: analyze clinical relevant and biochemical individual dataset; illustrate how individual-therapeutic monitoring can translate data into effectiveness and discuss how biomarkers can identify unique biological mechanisms and personalize patient treatment. The integration of the data we obtain is essential to clinicians in interpreting, as well as for the outcome of such studies.

Results: Biochemical and toxicological knowledge should be applied to clinical trials and individual cases in order to facilitate development of novel therapeutics and to drive personalized medicine, throughout the biomarker discovery, validation, clinical implementation.

Conclusion: Technological developments are enabling larger studies that can rapidly deliver data. The translation of the data into meaningful, biological understanding is essential.

Keywords: personalized medicine, pharmacovigillance, biomarkers

HIGH-THROUGHPUT SCREENING FOR FOOD CARCINOGEN RESISTANCE GENES IN BUDDING YEAST IDENTIFIES MECHANISMS IN DNA DAMAGE TOLERANCE OF CARCINOGEN-ASSOCIATED DNA ADDUCTS

Michael Fasullo[1], Nick St. John[1], Julian Freedland[1], Frank Doyle[1], Cinzia Cera[1], Henri Baldino[1], Thomas Begley[1]

State University of New York at Albany and State University of New York Polytechnic Institute[1]

Introduction: The human response to carcinogens is highly variable. Genetic factors include DNA repair genes; however, only a few resistance genes have been described. We used budding yeast to determine genetic susceptibility to food-associated carcinogens, including aflatoxins (AFB1) and heterocyclic aromatic amines (HAAs), such as 2-amino-3-methylimidazo[4,5-f]quinoline (IQ).

Material and method: We introduced expression vectors that contain human P450 and NAT2 genes into the yeast deletion library. To determine resistance genes, we used a high-throughput approach for screening the yeast deletion library expressing specific P450 genes or expressing no P450 genes; the illumina platform was used to sequence DNA barcodes and statistical significance was determined for exactly matched barcodes.

Results: Screens for aflatoxin resistance in the collection expressing CYP1A2 identified 96 genes. In

particular, we observed that the CSM2/SHU functions to promote error-free template switching of AFB1-associated DNA adducts, while suppressing AFB1-associated mutations. Screens to identify genes involved in resistance to IQ included RAD18 and NTG1; polymorphic alleles of RAD18 and NTG1 are risk factors for colon cancer.

Conclusion: These screens provide a novel methodology for identifying genes that confer resistance to P450-activated carcinogens. Future experiments are planned to knock-down human orthologues of the yeast genes and conduct similar screens in human cell lines.

Keywords: Genomic screens, cancer, budding yeast, susceptibility genes

HEALTH QUALITY METRICS: SETTINGS OF INDIVIDUAL CANCER MANAGEMENT

Bahadir M. Gulluoglu[1]

Breast Surgery Unit, Marmara University School of Medicine, Istanbul, Turkey[1]

Introduction: Today as more improved survival rates are observed by better cancer management, oncology care has started to include new fields such as risk or genetic counselling, onco-geriatry and survivorship.

Material and method: However, despite advancements in medical treatment, there still remain care management challenges such as fragmentation, limited data access, poor data quality, lack of standardization and limited transparency for assessments. Therefore, patient-centered care became the optimum approach including psycho-social issues, quality-of-life, patient rights etc. So, all these require multi-level professional approach within integrated health care. Quality indicators in health care settings, structure, procedures and outcomes constitute the core assessment items.

Results: "Outcomes" are the real world gains experienced by patients. Clinical outcomes by means of efficacy of the medical and surgical treatments as well as their safety are considered to be the main audit issues. Beyond these, however, patient satisfaction is included as long-term outcome reflecting the quality-of-life. Today, value-based quality term is gradually replacing volume-based quality. Multidisciplinary environment results in better survival, quality-of-life, more satisfaction and sustainable financial grounds.

Conclusion: Visionary leadership for health care programmes is among the requirements for better care. Also, standards should include compliance with guidelines, disciplined team work, creating frequent common decision-making opportunities and data registration/auditing.

Keywords: health care quality, value-based, breast cancer, quality-of-life

INDIVIDUALIZED CARE: PATIENT CENTERED CARE VERSUS PERSONALIZED MEDICINE

Andrea-Ildiko Gasparik[1]

UMFST Târgu Mureș[1]

Introduction: The main similarity between patient centered care (PCC) and personalized medicine (PM) is their aim to move from standardized guidelines towards individual tailoring strategies. Although, both of them aspire to focus on the person, they approach the individual differently: one focusing on objective aspects (optimizing biological outcome parameters), and the other on: highlighting the subjective and aspiring to a holistic view of the patient. This paper focuses on PCC, aiming to evaluate particularities of doctors' communication with their patients in Romania from the perspective of patient centeredness.

Material and method: We observed and analyzed more than 600 ambulatory doctor-patient meetings: temporal structure, also noticing gestures and speech acts.

Results: Meetings were focused on tasks at the expense of discussions, which were brief, compared to other two cultures, USA and Japan (significance level (p=0.0001 and 0.0007, and 0.04 and 0.05 respectively). Patients" dissatisfaction correlated with the penury of speech acts and gestures, that would offer them comfort or emotional support.

Conclusion: Person-centered care approaches patients from a caring perspective, insisting on aspects usually ignored in the biomedical framework (PM). The observed shortages and dereliction of verbal and non-verbal communication and their impact on patients' comfort prove the importance of a conscious, patient centered communication.

Keywords: patient centered care, personalized medicine, doctor patient interaction, communication

PERSONALISED TREATMENT OF PATIENT WITH ACUTE ISCHEMIC STROKE DUE TO LARGE VESSEL OCCLUSION

Rares-Cristian Filep[1]

UMFST Târgu Mureș[1]

Introduction: Acute ischemic stroke due to large vessel occlusion is one of the leading causes of death and disability worldwide, with tremendous social and economic costs. Neuroimaging plays a central role in the selection of patients for treatment, follow-up and outcome evaluation.

Material and method: Up to the year 2015 the only clinically proven treatment was intravenous tissue plasminogen activator, for patients presenting up to 4.5 hours from symptom onset. Clinical trials used only structural/anatomic imaging parameters to identify suitable patients for plasminogen activator. More recent randomized controlled trials have proven the efficacy of intraarterial thrombectomy in eligible patients with acute ischemic stroke up to 6 hours, mainly selected based on neuroimaging findings like intracranial large vessel occlusion and infarct volume. In addition to anatomic imaging, employment of physiological imaging like cerebral perfusion and collateral status, enabled time-window prolongation to 24 hours, thus increasing the number of patients treated.

Results:

The shift from structural/anatomic to pathophysiological-based imaging selection lead to a large quantitative and qualitative improvement of patient-selection.

Conclusion: These neuroimaging biomarkers provide a framework for personalized medicine to precisely identify patients that can benefit the most from treatment.

Keywords: personalised, stroke, neuroimaging, thrombectomy

THE MICROBIOME – A POSSIBILITY FOR INDIVIDUALIZED PREVENTION AND THERAPY IN CELIAC DISEASE

Cristina-Oana Marginean[1], Lorena-Elena Melit[1], Maria-Oana Mărginean[1]

UMFST Târgu Mureș[1]

Introduction: Celiac disease (CD) is an immune-mediated disorder related to gluten sensitivity in genetically predisposed individuals. Despite the fact that the genetic predisposition is mandatory, not all individuals that carry a genotype are at risk of developing the disease

Material and method: Host-environmental interactions are essential for CD development in genetically susceptible individuals resulting in different pathways in disease development from patient to patient.

Results: The fact that the trigger for CD is known results in the perfect model to study autoimmune diseases. The composition of the gut microbiome has been postulated to be involved in the modifications of metabolomic pathways that are involved in the switch from tolerance to immune response to gluten. These changes are related to the function of the T regulatory cells, of the gut barrier, but also to specific modifications in gene expression of intestinal stem cells. It has been hypothesized that different bacterial metabolites regulate the gut barrier functionality with subsequent enterocyte TNF-alpha downregulation and upregulation of junctional proteins. Therefore, the so-called Precision Medicine represents the recognition of the unique path that every individual takes to arise at the final destination, CD.

Conclusion: The microbiome seems to own a major role as a potential target to prevent CD.

Keywords: microbiota, celiac disease, precision medicine

THE CLINICAL UTILITY OF GENETIC ANALYSIS IN CHRONIC LYMPHOCYTIC LEUKEMIA

Adriana-Stela Cosma[1], Claudia Bănescu[1]

UMFST Târgu Mureș[1]

Introduction: Chronic lymphocytic leukemia (CLL), the most common type of leukemia in adults, is characterized by uncontrolled lymphocytes growth. The presence of TP53 defects in CLL is associated with an adverse prognosis due to the resistance of chemoimmunotherapy. The clinical utility of TP53 mutations analysis is well known.

Material and method: Before initiating the first line of treatment in CLL it is recommended to perform TP53 gene assessment. Copy number aberrations (CNAs) of certain chromosomal regions (loss of TP53 on

17p13, RB1 13q14, ATM gene on 11q22) are frequently reported in CLL and may be investigated by multiplex ligation-dependent probe amplification (MLPA) method.

Results: Point mutations within the TP53 gene are evaluated by Sanger sequencing. Recently, high-throughput next-generation sequencing (NGS) has been introduced, which aids in identifying the TP53 defects with a low variant allelic frequency. NSG or bidirectional Sanger sequencing can be performed for analyzing the entire coding sequence (exons 2-11).

Conclusion: Molecular testing of CLL patients are important not only for prognostic and risk stratification but also for selection of the best therapy, therefore it will help clinicians to personalize treatment based on individual CLL patient-specific characteristics.

Keywords: TP53 gene, chronic lymphocytic leukemia, Receptor tyrosine kinase-like Orphan Receptor 1

UNIVERSITY INNOVATION LAB AS A MAGNET FOR THE DEVELOPMENT ENERGIES

Liviu Ciucan-Rusu[1], Dieter Hertweck[2]

UMFST Târgu Mureș[1] University of Reutlingen, HHZ[2]

Introduction: Innovation Hubs immerge from regional ecosystem and can be accelerators of organizational and social transformation. We propose a model of university innovation lab as a magnet for different flows of energies, designed to provide value-added services to support sustainable development.

Material and method: Two main streams guide our research: we collected facts and challenges from living practices and we modeled a framework using different innovative techniques. We worked on three approaches based on complementary techniques and software tools: innovation and design thinking (Scene2Model); model simulation (Vensim) and business model design.

Results: Based on the main findings and outputs of the case-studies, we transformed the basic idea of an innovation lab into a structured organizational model, we managed to model the influences of external factors to the lab, while the business model canvas is an integrative tool that provides us with the mapping of the organizational plan.

Conclusion: Based on the main findings and outputs of the case-studies, we transformed the basic idea of an innovation lab into a structured organizational model, we managed to model the influences of external factors to the lab, while the business model canvas is an integrative tool that provides us with the mapping of the organizational plan.

Keywords: Innovation Lab, Entrepreneurship, Transdisciplinary magnet, Innovation Models

BREAST CANCER SCREENING IN GEORGIA: ACCORDING TO THE POPULATION-BASED CANCER REGISTRY DATA

Irakli Kokhreidze[1]

Tbilisi State Medical University, Tbilisi, Georgia[1]

Introduction: Since January 1, 2015, Georgia has initiated the Population Cancer Registry to improve the epidemiological surveillance of cancer.

Material and method: To review the Registry record from 2015 2017 and to recommend future directions.

Results: The cancer incidence rate of 234.3 per 100,000 population is lower than that in EU countries. 56-57% of all cancer cases were in females and 44-43% in males. About 70% of new cases were among the 30 to 70 years age group and 25% were in the older age group. As an example, breast cancer is most common among females. The incidence rates ranged from 79.6-97.5 per 100 000 females from 2015 - 2017. Only 50% of the new breast cancer cases were detected at early (I and II) stages.

Conclusion: Increasing awareness of population of the importance of cancer screening is necessary. For example, the breast cancer screening schedule should be enhanced: identification of the target population by age (40-70 years), physical examination, US (Ultrasound), mammography and other investigative tools (FNA) in the case of suspicious of any malignancy, or routine follow-up. One percent of cases occur in the population aged under-15 and 15 - 20 years. The share of new cancer cases in women of reproductive age (15- 49 years) is 24-27%. The top five sites of cancer in women are the following: breast, thyroid gland, colorectum, corpus uterus, cervix uteri. About 40% of all sites cancers are registered at the first and second stages; 50% - at the III and IV stages; for 10% of cases a stage was not identified. By sex and site: in females, only 50% of new cases of breast and cervix uteri cancers, and more than 70% of the corpus uteri and thyroid gland cancers are revealed at the first and second stages; more than 60% of new cases of colorectal cancer have been detected in the III and IV stage of the disease. Recommendation: high oncological vigilance (knowledge of early symptoms) of sites, which are not screened but have got high morbidity. It is necessary at the expert level to review and change the format of the state screening program, including the primary health care in screening programs.

Keywords: Breast, cancer, screening, Georgia

INDEX OF AUTHORS

INDEX OF AUTHORS

Information and guidelines for authors

Manuscript submission

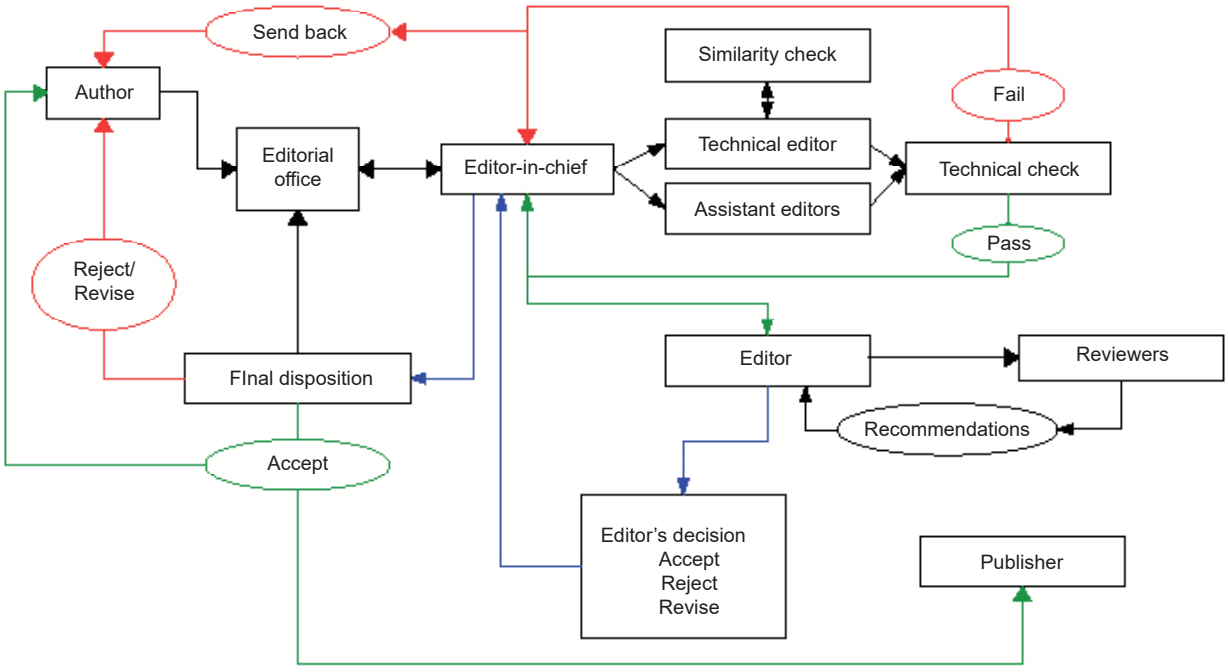
Manuscripts and all attached files (tables and illustrations) should be submitted in electronic form, using the on-line manuscript submission system Editorial Manager available for Romanian Journal of Laboratory Medicine at http://www.editorialmanager.com/rrlm.

Please note that general reviews and course notes are invited by the editor. Questions may be directed to Editor of this Journal at minodora.dobreanu@rrml.ro.

Submission documents

At the time of submission, the *Romanian Journal of Laboratory Medicine* requires an explicit statement (**License to publish**) by the corresponding author warranting that the manuscript, as submitted, has been reviewed by and approved by all named authors; that the corresponding author is empowered by all of the authors to act on their behalf with respect to the submission of the manuscript; that the article does not infringe upon any copyright or other proprietary right of any third party; that neither the text nor the data have been published previously (abstracts excepted); and that the article or a substantially similar article is not under consideration by another journal at that time. Upon submission of the manuscript, the corresponding author must provide the Editorial Board with documents proving that all those quoted for personal communications or listed in the *Acknowledgement* section have agreed to their inclusion. Authors are responsible for obtaining permission to reproduce copyrighted material from other sources and send an authenticated copy of the permission to the Editorial Board.

Each author must provide a clear **statement on potential conflicts of interest** in which he or she may be involved. The statement should include sources of funding, including internal support or grants from non - commercial institutions. The absence of funding should also be declared. The statement on conflicts of interest will be published



Workflow of the editorial process

at the end of the paper. Scanned copies sent electronically and fax submissions are not acceptable.

Authorship

All named authors should meet the criteria for authorship as stated in the „Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication" issued by the International Committee of Medical Journal Editors (www.icmje.org):

> *„Authorship credit should be based on 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3. [...]*
> *All persons designated as authors should qualify for authorship, and all those who qualify should be listed."*

The *Romanian Journal of Laboratory Medicine* considers all authors to be responsible for the content of the entire paper.

Authors are requested to describe their individual contributions to a study paper in a "**Cover letter**" (page 288) that will be signed, attached to and sent by e-mail (office@rrml.ro) together with the "**License to publish**" form, as soon as possible.

Individuals who supplied reagents, strains or facilities should not be listed as authors, but may be recognized in the *Acknowledgements* section. Individuals who gave advice on the manuscript should be acknowledged, but are not considered authors.

Research involving human subjects or experimental animals

If the scientific project involves human subjects or experimental animals, authors must state in the manuscript that the protocol has been approved by the Ethics Committee of the institution within which the research work was undertaken. Experiments on live vertebrates or higher invertebrates must be demonstrated to be ethically acceptable and in accordance with institutional and national guidelines or regulations for laboratory animals. If the manuscript reports medical research involving human subjects, authors must include a statement confirming that informed consent was obtained from all subjects, according to the World Medical Association Declaration of Helsinki, revised in 2000, Edinburgh.

Manuscript preparation

Before submitting a paper, please assure that the manuscript fit in one of the journal category described by the Journal's Editorial Policy.

The following article types are accepted: Review, Original research article, Original professional paper, Short Communication, Case study / Series case studies, Course Notes, and Letter to the Editor. Advertisements, news, and special issues are also acceptable as non-indexed publications.

The following article types are accepted, with their formatting limitations:

Manuscripts must be written in English and prepared in conformity to the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication" issued by the International Committee of Medical Journal Editors (www.icmje.org). Romanian authors will also provide a copy of the title, affiliation, abstract and keywords translated into Romanian.

Authors should consult someone proficient in the English language, if they feel it is necessary. If the manuscript is not conform to accepted standards of English usage, the manuscript will be rejected.

Articles must be written in Microsoft Word, Style: Normal + Justified, Font: Times New Roman, font size 12. All manuscripts must be typed double-spaced. Original source files, not PDF files, are required. In text editing, authors should not use spacing with spacebar, tab or paragraph mark, but use the indentation and spacing options in Format → Paragraph. Automatic paging is preferred.

Please do not import tables or figures into the text document, but only specify their insertion in

Article type	Manuscript word limit	Maximum number of references	Maximum number of figures and tables	Abstract (max 250 words)	Supplemental data (online only)
Review	5000	70	6	Yes	Yes
Original research article	3500	40	6	Yes	Yes
Original professional paper	3000	30	5	Yes	Yes
Short Communication	2500	25	4	Yes	No
Case study / case series	2000	25	3	Yes	No
Course Notes	2000	15	3	No	No
Letter to the Editor	1500	10	1	No	No
Editorial	2000	10	1	No	No

text (e.g. *Table No 3 insertion*). They have to be sent in separate files. Files should be labeled with appropriate and descriptive file names, **without diacritics** (e.g. Imunofluorescenta.doc, Imunofluorescenta Fig1.tiff, Imunofluorescenta Table2.doc). **The file names must not contain any self-revealing information** (e.g. authors' name).

Charts and tables should be designed in black and white or in greyscale, unless color reproduction is essential for the understanding of the message.

The preferred format for all digital image files is TIFF (Tagged Image File Format). PNG format is also acceptable. Resolution of images must be at least 300 dpi at the size they will appear in the print. Any special instructions regarding sizing should be clearly noted. Scanned images should be free of technical faults (e.g. shadows, wrong orientation). Authors should state the coloration technique and the magnification factor of all images of microscopic samples. Test your figures by sizing them to their intended dimensions and then printing them on your personal printer. The result should not look fuzzy, jagged, pixelated, or grainy.

Manuscript organization

The text of original papers will be organized in one document, in a so-called "IMRAD" structure: introduction (no more than 25% of the text), material and methods, results, comments or discussions and acknowledgements. **The manuscript should not include any self-revealing information.** All information about the author(s), affiliation, contact, as well as the abstract and keywords, will be provided only within the online submission process.

Material and methods have to be described in enough detail to permit reproduction by other teams. The same product names should be used throughout the text (with the brand name in parentheses at the first use). **Results** should be presented concisely. Tables and figures should not duplicate text. The **discussion** should set the results in context and set forth the major conclusions of the authors. Information from the Introduction or Results should not be repeated unless necessary for clarity. The discussion should also include a comparison among the obtained results and other studies from the literature, with explanations or hypothesis on the observed differences, comments on the importance of the study and the actual status of the investigated subject, unsolved problems, and questions to be answered in the future. In addition to the customary recognition of non-authors who have been helpful to the work described, the **acknowledgements** section must disclose any substantive conflicts of interest.

Abbreviations shall be preceded by the full term at their first apparition in text. A list of all abbreviations used shall be made at the end of the article.

Separate documents: tables, graphics, pictures and schemes will appear on separate documents. Tables will have a reasonable number of rows and columns. The tables, charts, schemes etc. should be sent in their original file format (for example, XLS files if they were created in Microsoft

Excel), together with the main manuscript, via on line system (http://www.editorialmanager.com/rrlm).

References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in parentheses. References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. The titles of journals should be abbreviated according to the style used in *Index Medicus*. Consult the list of Journals Indexed for MEDLINE, published annually as a separate publication by the National Library of Medicine. Authors are responsible for the accuracy and completeness of all references and are also responsible for ensuring that references are not used out of context.

For journal articles use the following form: authors' surnames and first names initials, article's title, the journal abbreviation according to the *Index Medicus*, year, volume, starting and ending pages of the article. If there are more than six authors, list the first six and add et al. We recommend to automatically insert the references using dedicated reference management solutions (e.g. Zotero, Microsoft word bibliography, Endnote web), according to **Vancouver citation style**.

e.g. "Zimmermann MB, de Benoist B, Corigliano S, Jooste PL, Molinari L, Moosa K, et al. Assessment of iodine status using dried blood spot thyroglobulin: development of reference material and establishment of an international reference range in iodine-sufficient children. J Clin Endocrinol Metab. 2006 Dec;91(12):4881-7"

For books or monographs: the names of the cited chapter's authors, chapter's title, the editors, the title of the book or monograph, the name and location of the publisher, the year of the appearance and pages.

Editorial process and peer review

The whole peer-review workflow is performed in the Editorial Manager online system. Manuscript submitted should contain original work, focused on the aims of this journal, should be clearly and correctly written in English, and should contain all essential features of a scientific publication. Submitted manuscripts are screened for completeness and quality of files and will not enter the review process until all files are satisfactory. In order to evaluate similarities with scientific literature, specialized text-matching software is used to screen all manuscripts accepted for scientific evaluation. The Secretariat will announce the corresponding author about the receipt and the status of the manuscript.

Authors may suggest reviewers for their manuscript, whether invited to do so by the Editor or not. The Editor may choose to use one or more of these reviewers, but is under no obligation to do so. Authors may ask that certain people not be asked to review their manuscript, but Editors are not held to accept these requests either. The articles are sent to reviewers with expertise in the laboratory medicine area, without revealing the authors' names and positions. Also, the reviewers' identities are not known by the authors. Following the reviewers' recommendations, the Editors decide if a paper is published or not. Submissions may be declined without external review as deemed appropriate by the Editor-in-Chief and the members of the Editorial Board. The authors of the manuscripts that have been rejected or need revision will be announced. Revised manuscripts should be resubmitted as soon as possible, but not later than 6 weeks. Although unusual, a resubmission may be rejected after revision if the response to suggestions and requests is considered inadequate.

Authors will receive a PDF file with the edited version of their manuscript for final proofreading. This is the last opportunity to view an article before its publication. The purpose of the proof is to check for typesetting or conversion errors and the completeness and accuracy of the text, tables and figures. Substantial changes in content are not allowed without the approval of the Editor. The authors are requested to return the corrected proofs within 7 days after their delivery or notify the Editors that no corrections are required. After online publication, further changes can only be made in the form of an Erratum, which will be hyperlinked

to the article. The corresponding author will receive a printed issue of the Journal free of charge.

Scientific misconduct / Corrections / Retraction Policy

Scientific fraud are rare events; however, they have a very serious impact on the integrity of the scientific community. Scientific misconduct is defined by the Office of Research Integrity as "fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the academic community for proposing, conducting, or reporting research". In cases where there is a suspicion or allegation of scientific misconduct or fraudulent research in manuscripts submitted or published, the Editors reserve the right to impose sanctions on the authors, such as: immediate rejection of the manuscript, banning author(s) from submitting manuscripts to the journal for a certain period of time, retracting the manuscript, bringing the concerns to the authors' sponsoring or funding institution or other appropriate authority for investigation

If the Editorial Board uncovers possible evidence of such problems it will first contact the corresponding author in complete confidence, to allow adequate clarification of the situation. If the results of such interactions are not satisfactory, the Board will contact the appropriate official(s) in the institution(s) from which the manuscript originated. It is then left to the institution(s) in question to pursue the matter appropriately. Depending on the circumstances, the *Romanian Journal of Laboratory Medicine* may also opt to publish errata, corrigenda, or retractions.

Serious errors in a published manuscript and infringements of professional ethical codes will result in an article being retracted. This will occur where the article is clearly defamatory, or infringes others' legal rights, or where the article is, or there is good reason to expect it will be, the subject of a court order, or where the article, if acted upon, might pose a serious health risk. In any of these cases all coauthors will be informed about a retraction. A Retraction Note detailing the reason for retraction will be linked to the original article.

Publication fee

A processing fee of 50 EUR (equivalent in RON) will have to be paid for articles accepted for evaluation by the editorial board of Romanian Journal of Laboratory Medicine (invited contributions excepted). Please note that the payment will only be required if your article and application passes the Technical check and is accepted for scientific evaluation (the article is "under Review"). The journal does not have article submission charges.

The publication fee for accepted article is 150 EUR (equivalent in RON), which have to be paid when article proof is sent to the correspondence author.

The author will bear the cost of publication for color illustrations, if their number exceeds two color figures (invited contributions excepted). The charge is 25 EUR (equivalent in RON) for each color figure, starting with the third color illustration). The authors will also bear the cost of English supervision (if the manuscript needs assistance). If reasonable corrections are necessary the charge is 10 EUR (equivalent in RON)/ supervised page.

The total charge for color figures and English supervision will be communicated by the Editorial Secretariat upon acceptance of the manuscript for publication.

All payments will be operated in RO-56BRDE270SV16682302700 bank account open for Romanian Association of Laboratory Medicine – CF 17383407 – at BRD-Groupe Société Générale SA, Agenţia Petru Maior, Str. Mihai Viteazu 31, Tîrgu Mureș, Romania. Please e-mail (office@rrml.ro) or fax a copy of the bank draft at the Editorial Secretariat (+40 265 217 425).

Cover letter and authors' contribution

According to the ICMJE, the *Romanian Journal of Laboratory Medicine* recommends that authorship be based on the following criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;
2. Drafting the work or revising it critically for important intellectual content;
3. Final approval of the version to be published;
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Those who meet all four criteria can be identified as authors; otherwise they should only be acknowledged.

Title

The authors attest that

- This paper has not been published previously;
- The manuscript is an original work without fabrication, fraud, or plagiarism;
- Have read the complete manuscript and takes responsibility for the content of the manuscript;
- There is no potential conflict of interest (employment, consultancies, stock ownership, equity interests, and patent-licensing arrangements);

Authors' contribution

Authors	Contributions	Signatures

Acknowledgements
