

Bridges to the Future: Precision Medicine Workshops in the 2023 Smart Diaspora Conference

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Romania is one of the European countries with the highest number of medical specialists working abroad. It is estimated that in the last decade more than 20,000 physicians chose to leave Romania for Western Europe or North America. The series of collaborative scientific conferences of Romanian diaspora launched initially in 2011, gained traction under the presidency of Klaus Iohannis who, in the fall of 2015, in order to counteract the „brain drain” exodus of highly educated professionals, encouraged the implementation of „brain regain” projects.

The 2023 edition of the conference “Smart Romanian Diaspora and Its Friends – Higher Education, Science, Innovation, and Entrepreneurship” was held in Timisoara from the 10th to the 13th of April. The event brought together several renowned experts from various academic fields, both from Romanian diaspora and from Romania, in order to discuss top trending research subjects in plenary sessions and dedicated workshops.

Personalized Medicine represented the topic of two workshops hosted by the Victor Babeş University of Medicine and Pharmacy from Timișoara. The speakers were Romanian specialists from Romania, USA, and Western Europe and the intention of these workshops was to exchange ideas and information about brand new concepts in contemporary oncology with the goal of developing research projects of mutual interest in the immediate future.

Contemporary personalized medicine has been defined broadly as „the use of combined knowledge (genetics, or otherwise) about a person to predict disease susceptibility, disease prognosis or treatment response and thereby improve that person’s health” or, more restrictively, „the use of combined knowledge (genetics, or otherwise) about a person to predict disease prognosis or treatment response” or just to predict treatment response (1).

A related expression, “precision medicine” has been introduced (2) and has been used interchangeably with “personalized medicine”. In the National Cancer Institute dictionary their definition is identical (3) i.e.: „a form of medicine that uses information about a person’s genes, proteins, and environment to prevent, diagnose, and treat disease. In cancer, personalized medicine uses specific information about a person’s tumor to help diagnose, plan treatment, find out how well treatment is working, or make a prognosis. Examples of personalized medicine include using targeted therapies to treat specific types of cancer cells, such as HER2-positive breast cancer cells, or using tumor marker testing to help diagnose cancer.”

Precision medicine got a lot of attention since 2015 when Barack Obama, President of United States at that time delivered a historical speech in which he promised a significant financial to several United States research institutions in order to help implement in the near future the precision medicine paradigm in the American health care system (4).

The first workshop “Multidisciplinary Interactions at the Frontier of Personalized Medicine” was chaired by Professor Irinel Popescu, a leading expert in liver transplantation, the founder and director of the Fundeni Center for Excellence in Translational Medicine in Bucharest. The second workshop

"Personalized medicine: innovative approaches for prevention, diagnostic and treatment" was chaired by Professor Virgil Păunescu, an expert in immunology and founder and director of Oncogen Research Center in Timișoara.

We will present some highlights from the two workshops relevant to the oncology field.

The first workshop „**Multidisciplinary Interactions at the Frontier of Personalized Medicine**” was mainly focused on Gastrointestinal malignancies.

Professor Irinel Popescu opened the workshop with a presentation about the role of liquid biopsies and digital droplets polymerase chain reaction (ddPCR) for diagnostic and cancer treatment. DdPCR is a new method that improves the precision of traditional PCR by allowing more precise quantification of genetic material. Recent clinical studies have demonstrated the role of liquid biopsies for the diagnosis and management of several malignancies and the concept of minimal residual disease (MRD) has been successfully used in the treatment of colorectal cancer.

The presentation of Dr. Dan G. Duda from Massachusetts General Hospital and Associate Professor of Radiology at Harvard Medical School in Boston, US, focused on the role of the tumor microenvironment, highlighting the need for therapies that target the interaction between cancer cells and stromal components. Professor Dan G. Duda is a strong advocate of integrating basic science into clinical practice and applying to patients' care the 'bench-to-bedside' concept. He emphasized the significance of genomic profiling and functional studies in identifying potential drug targets and optimizing treatment strategies in gastrointestinal (GI) malignancies.

Dr. Ovidiu Andronesi, a radiologist from Massachusetts General Hospital and Associate Professor of Radiology at Harvard Medical School in Boston, US explained how radiological biomarkers are poised to change the landscape of contemporary oncology. His research has focused on using radiomics – a field that extracts many quantitative features from standard radiological imaging data – to identify unique signatures associated with various cancer types.

Dr. Liliana Bordeianou, a GI surgeon, Chief of the Colorectal Surgery Division at Massachusetts General Hospital and Professor of Surgery at Harvard Medical School in Boston, US, discussed the role of minimally invasive surgical techniques, such as laparoscopic and robotic surgery, and emphasized their role in reducing post-operative complications, shortening recovery times, and improving overall patient outcomes.

Dr. Michael Bogdan Margineanu, a post-doctoral researcher based in London, UK, presented interesting new findings regarding the relationship between intestinal microbiota and the brain of cancer patients.

Overall, this workshop acknowledged the paradigm shifts in cancer research that highlight the growing recognition of environmental influences on cancer phenotypes, as opposed to the traditional views that placed genetics at the forefront of cancer research. It is becoming more and more clear that environmental exposures such as diet, lifestyle, radiation, pollution and even climate changes can interact with an individual's genetic background to either initiate or promote cancer growth. This new focus has highlighted the complex interplay between genes and environment, moving beyond a purely deterministic genetic perspective. By understanding how environmental factors modulate genetic risk, researchers hope to develop more personalized prevention and treatment strategies, ultimately improving cancer care and patient outcomes. This shift represents a more holistic approach to cancer research, recognizing that cancer is a multifactorial disease influenced by a combination of genetic and environmental factors.

The main topic of the first workshop, human microbiota, is of high interest in modern medicine, particularly in oncology, due to the growing understanding of its complex role in human health and disease. The trillions of microorganisms that reside in the human body have been found to significantly influence immune function, metabolism, and even the efficacy of some treatments such as chemotherapy. This understanding has prompted a shift in perspective in oncology, recognizing that microbiota may contribute to cancer development, progression, and response to treatment. Conversely, other microorganisms might exert protective effects, metabolizing potential carcinogens or modulating the immune system in a manner that suppresses tumorigenesis. Thus, the

geographical differences in microbiota, influenced by various environmental and cultural factors, can partially explain the regional disparities in cancer incidence and offer valuable insights for targeted prevention and treatment strategies. The potential to harness these microbial interactions for personalized therapies and to overcome treatment resistance has ignited extensive research and clinical interest. As a result, the study of microbiota is now seen as a frontier with the potential to revolutionize oncological care, and it has become a focal point in both translational and clinical research.

The second workshop **"Personalized medicine: innovative approaches for prevention, diagnosis and treatment"** had a broader scope and focused on several hot topics in contemporary oncology research and practice.

Professor Virgil Păunescu presented personalized approaches in immunotherapy. First he discussed the experience of the Oncogen Institute in producing CAR-NK cells constructs and then he introduced the concept of synthetic long peptides (SLP) vaccines for the treatment of Human Papilloma Virus (HPV) related cancers. The HPV directed SLP vaccines are particularly important for Romania where cervical cancers are much more common than in countries of Western Europe.

Professor Ștefan Constantinescu from Ludwig Institute for Cancer Research Brussels from Belgium, and University of Oxford, Oxford in UK, presented his work on signalling, epigenetic regulators, chromatin dynamics and differentiation in blood cancers and leukaemia focusing on the role of calreticulin mutants in these disorders. The molecular basis of progression over time from clonal hematopoiesis to chronic myeloproliferative neoplasms and myelodysplasia and then to secondary acute myeloid leukaemia was discussed in his presentation.

Professor Monica Neagu, Chief of the Immunology Department of the „Victor Babeș” National Institute of Pathology from Bucharest presented the key events of the transformation of a normal melanocyte into melanoma highlighting the original work of her group on the role of circulating hormones like epinephrine, norepinephrine and leptin in melanogenesis.

Professor Cristiana Tănase, Chief of the Biochemistry-Proteomics Department of the „Victor Babeș” National Institute of Pathology from Bucharest presented her original work on a set of serum biomarkers that can be used for the diagnostic, prognostic and monitoring of patients with glioblastoma.

Professor Tudor Oprea from the University of New Mexico, and Chief Executive Officer of Expert Systems based in United States, presented the role of artificial intelligence and machine learning in genome “hunting” for new targets and drug design and repurposing. His presentation had a visionary conclusion: “the natural extension of current models in medicine could lead to the development of computational reasoning tools specific to medicine (artificial intelligence in medicine - AIM) with advanced cognitive computing capabilities and data sets as complete as possible. Such platforms could mine clinical data in real time, taking advantage of -omics, biomarkers, biomedical data and electronic medical records (EMRs), providing real-time patient services”.

The current interest for personalized medicine is due on one hand to its ability to improve patient care while also making the healthcare system more efficient and more cost-productive. “The ultimate end point is the selection of a subset of patients, with a common biological basis of disease, who are most likely to benefit from a drug or other treatment, such as a particular surgical procedure. (...) Fewer side effects and lower costs are likely to result using a precision medicine approach to focus on those patients who are most likely to benefit, early in the drug development process” (2).

The new paradigm of precision medicine involves not only a deep understanding of diseases at the molecular level potentially leading to innovative diagnostic and therapeutic methods but, also essentially, to key changes in policy and regulation that allow the rapid implementation of new diagnostic techniques and treatment protocols to patients.

To this end, the creation of research and innovation networks with a focus on personalized medicine represents a unique strategic opportunity to bring together stakeholders, create synergies and stimulate efforts to accelerate the evolution of healthcare towards personalized medicine.

One of the key takeaways from the workshops was the importance of multidisciplinary and transdisciplinary collaborations for achieving the goals of Personalized Medicine: **the right treatment, in the right dose, for the right patient, at the right time** (4). For this aspiration to be implemented into clinical practice, there is an urgent need for standardized, consensual methods in order to allow an efficient approach and a mutually beneficial collaboration between Romanian diaspora physicians and Romanian physicians in this rapidly evolving field. The two workshops provided a unique multidisciplinary perspective from clinicians, researchers, and experts from different fields who shared their knowledge, research data, experiences and visions for the immediate future. They presented strong evidence that integrating and harmoniously targeting various components of the cancer process may lead to better outcomes.

Such events bring us one step closer to our common purpose: a more dynamic, updated and standardized medical practice, creating bridges in the near future between US and Western Europe medicine practice and Romania. This common endeavor to find optimal strategies is part of the noble mission of adding opportunities for all patients, and improving the medical care by sharing experiences and learning from each others.

Overall, the two workshops were a unique opportunity for experts in various disciplines to exchange ideas and explore new avenues for collaboration that will hopefully shape the immediate future of Personalized Oncology in Romania and turn the „regain brain” dream of President Iohannis into reality.

Abbreviations

HER2 – human epidermal growth factor receptor 2

PCR – polymerase chain reaction

ddPCR – digital droplets polymerase chain reaction

MRD – minimal residual disease

CAR-NK – chimeric antigen receptor-transduced natural killer cells

SLP – synthetic long peptides

AIM – artificial intelligence in medicine

EMRs – electronic medical records

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