

Personalized Bringing the Promise of Personalized and Precision Medicine (PPM) to Rare and Orphan Disorder Care: The Future of PPM through the View of Biodesign-inspired Hi-Tech Philosophy, Upgraded Mentality and Global Needs of the Consumers

Sergey Suchkov¹⁻⁶, Hiroyuki Abe^{5,9}, Shawn Murphy^{7,8}, David Smith¹⁰, William Thilly¹¹, Paul Barach¹²

¹The Russian Academy of Natural Sciences, Moscow, Russia

²Department for Clinical Allergology & Immunology, the Russian University of Medicine, Moscow, Russia

³EPMA, Brussels, EU

⁴PMC, Washington, DC, USA

⁵ISPM, Tokyo, Japan

⁶New York Academy of Sciences, USA

⁷MGH, Boston, MA, USA

⁸Harvard Medical School, Boston, MA, USA

⁹Abe Cancer Clinic, Tokyo, Japan

¹⁰Mayo Clinic, Rochester, MN, USA

¹¹MIT, Cambridge, MA, USA

¹²Wayne State University, School of Medicine, Detroit, MI, United State



A new systems approach to diseased states and wellness result in a new branch in the healthcare services, namely, personalized and precision medicine (PPM). The concept of PPM is becoming increasingly relevant for cancer treatment, moving from the 'one-size-fits-all' standard therapy to a more personalized scheme guided by molecular diagnostics.

A comprehensive molecular tumor analysis integrating a combination of NGS methods including whole-exome (WES), whole-genome (WGS) and transcriptome sequencing (RNAseq) offers the best chance for personalizing cancer care, enlarging the scope of therapy choices and offering potential new options for challenging cases, for instance metastatic tumors, rare cancer types, and cancers of unknown primary. Cutting-edge bioinformatics pipelines integrate the multiple data levels to construct Big Data and Data Sets and to generate a personalized tumor report. One key asset of this solution is the use of whole transcriptome data as a booster enhancing the sensitivity and information content of the diagnostic, predictive and prognostic tests. Up to now personalized and precision oncology has been largely relying on identifying key mutations in the tumor DNA by means of panel sequencing, a method scanning only designated cancer gene targets. Though the panel approach helps to orientate therapy choices for particular cancer types, many "hard to treat" tumors remain in need of more effective diagnostic solutions.

The improvement of methodology for OMICS-based (i.e., genomic) testing has made it one of the cornerstones of PPM-driven cancer clinical practice, which would incorporate various genomic, proteomic and other assays of human cancers into diagnostic, predictive, prognostic, and decision-making algorithms. A consolidated team of molecular pathologists, IT experts and cancer practitioners of the next step generation are becoming to play a crucial role in developing and implementing OMICS-based profiling tests in practice and communicate the results and their relevance with clinicians. Such approach is considered to be of utmost importance for successfully translating the latest advancements into a benefit to patients, illustrating a generation of the "next-generation cancer pathologists, cancer-related practitioners and oncologists globally".

Another essential aspect in which the cancer-related pathologists and practitioners play a crucial role is developing and implementing OMICS-based tests being integrated with the frame of IT algorithms, in clinical oncology and communicating the obtained results with other diagnostic and therapeutic disciplines (e.g., microbiology, clinical enzymology, genetics, immunology, etc) and clinicians.

Along with the above-mentioned, theranostics is an innovative concept of personalized therapy that focuses on both the accurate selection of patients and providing them with targeted radioligand cancer therapy to improve their

prognosis. As you see, the integrated value chain of PPM-related on-cology tools equips theranostics programs with state-of-the-art solutions at every step of the theranostics care pathway.

PPM has the potential to tailor therapy towards the oncogenic drivers of the tumor and modulate the tumor immune environment, whilst aiming to optimize tumor response and thereby taking into account the therapy-induced toxicities for each specific patient. Globally, PPM in oncology is not limited to optimizing anticancer therapies but can be utilized in tailoring the supportive care of patients diagnosed with malignancies, using the pharmacogenomics data to fine-tune targeted drug set pre-scription and then optimize the treatment strategies.

PPM-related cancer practice (Personalized and Precision Oncology/PPO) is guided by the specific biology of each patient's cancer – the type and subtype of the cancer, its set of genetic abnormalities, its vulnerability to certain therapies, including immunotherapy, and the patient's overall health. To-day, cancer-fighting drugs of the next step generation enable doctors to strike at cancer's fundamental roots in the human genome, whilst using targeted therapies engineered to attack tumor cells with specific abnormalities, while leaving normal cells largely unharmed. Some agents are designed to strike directly at cells with specific genetic changes that drive tumors' development and survival, or to inhibit overactive signaling pathways that allow cancer cells to grow and divide uncontrollably.

The latter means that we are entering an era of rapidly evolving transformation in cancer research as it relates to medical practice, and a shifting paradigm of standardized health care in which detailed molecular information regarding a patient's cancer is being used for PPM-related treatments. Moreover, there is an ever expanding repertoire of OMICS technologies and methods enabling liquid biopsies, and single cell profiling with the significant potential to revolutionize the world of oncology! We are seeing now a grand shift towards PPM-driven cancer practice to enable prevention, prediction and personalization in clinical oncology and healthcare as a whole.

Nowadays, taking into account the presence of different genetic changes in cancer patients or pre-cancer persons-at-risk, we would aim at making the need for PPO much greater to get the cancer patients cured! In this context, functioning approach named Cancer Care Team or Trans-Disciplinary Care Team, clinical practice and process, evidence-based decision-making, and smart targeted therapies are becoming crucial! The latter integrates multidisciplinary experts and develops real-time therapeutic strategy based on clinical phenomes and translational genomics and related OMICS technologies. That approach provides comprehensive, whole-process, and personalized diagnosis and treatment services for patients with complex cancer or complex drug resistance progression; provides guidance for further adjustment of drug use; and establishes a multidisciplinary cooperative team, improves the quality of clinical diagnosis and treatment, and optimizes the process of medical services.

Biography:

Dr Sergey V. Suchkov, MD, PhD

Sergey Suchkov was born in the City of Astrakhan, Russia, in a family of dynasty medical doctors. In 1980, graduated from Astrakhan State Medical University and was awarded with MD. In 1985, Suchkov maintained his PhD as a PhD student of the I.M. Sechenov Moscow Medical Academy and Institute of Medical Enzymology. In 2001, Suchkov maintained his Doctor Degree at the National Institute of Immunology, Russia.

From 1989 through 1995, Dr Suchkov was being a Head of the Lab of Clinical Immunology, Helmholtz Eye Research Institute in Moscow. From 1995 through 2004 – a Chair of the Dept for Clinical Immunology, Moscow Clinical Research Institute (MONIKI). In 1993-1996, Dr Suchkov was a Secretary-in-Chief of the Editorial Board, Biomedical Science, an international journal published jointly by the USSR Academy of Sciences and the Royal Society of Chemistry, UK.

At present, Dr Sergey Suchkov, MD, PhD, is:

- The Russian Academy of Natural Sciences, Moscow, Russia
- New York Academy of Sciences, USA
- Department for Clinical Allergology & Immunology, The Russian University of Medicine, Moscow, Russia
- Secretary General, United Cultural Convention (UCC), Cambridge, UK.

Dr Suchkov is a member of the:

- American Chemical Society (ACS), USA;
- American Heart Association (AHA), USA;
- European Association for Medical Education (AMEE), Dundee, UK;
- EPMA (European Association for Predictive, Preventive and Personalized Medicine), Brussels, EU;
- ARVO (American Association for Research in Vision and Ophthalmology);
- ISER (International Society for Eye Research);
- Personalized Medicine Coalition (PMC), Washington, DC, USA