EDITORIAL

Advances in precision medicine — time for a new journal

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On January 20, 2015, President Barack Obama announced a major research initiative, "Tonight, I am launching a new personalized medicine initiative to bring us closer to curing diseases like cancer and diabetes and to give all of us access to the personalized information we need to keep ourselves and our families healthier".[1] The announcement itself indicates commitment and high expectations. Indeed personalized or precision medicine (PM) is presently considered to represent one of the most important trends in medicine. It may be regarded as another milestone in the 'evolution' of medicine beginning from the theory of ancient humoralism. This dominated medicine and science over a period or several thousands of years until the mid-nineteenth century when it was replaced by the introduction of modern cellular pathology. Further essential milestones on the way to PM are the discovery of the DNA by Watson and Crick in 1953 and the Human Genome Project determining to sequence the DNA that was completed in 2003[2].

Precision medicine represents an approach for the prevention and treatment of diseases that take individual biological variability into account. There is no formal uniform standardized definition for 'personalized' or 'precision' medicine (Table 1). We prefer the definition by the European Union 'providing the right treatment to the right patient, at the right dose at the right time'[3]. The general idea of PM is not new; for example blood typing has been used to guide blood transfusions for more than a century. The prospect of applying this concept broadly, however, has been considerably enhanced by recent developments such as the establishment of large-scale biologic databases (e.g. the human genome sequence), powerful technologies and methods for patient characterization such as genomics, proteomics, metabolomics, and computational tools for analysing 'big data'[1].

Table 1. Attempts to define personalized medicine (adapted after Landeck *et al*. 2015[5])

European Union Providing the right treatment to the right patient, at the right dose at the right time.
Personalized Medicine Coalition The use of new methods of molecular analysis to better manage a patient's disease or predisposition to disease.
President's Council of Advisors on Science and Technology The tailoring of medical treatment to the individual characteristics of each patient.
American Medical Association Health care that is informed by each person's unique clinical, genetic, and environmental information.
National Institute of Health A form of medicine that uses information about a person's genes, proteins, and environment to prevent, diagnose, and treat disease.

Disease diagnosis and monitoring based on physiological and morphological characteristics are venerable established practices. More recently the term 'biomarker' evolved in connection with the increasing interaction between molecular biology research and medicine. A biomarker is 'a characteristic that is objectively measured and evaluated as an indicator of normal biological and pathogenic processes, or phar-

macologic responses to a therapeutic intervention'[4]. Markers can be sub-grouped into diagnostic- and drug-response markers. Many more types can be defined by their specific application. Table 2 gives a summary on the different purposes of modern biomarkers related to pharmacotherapy[5].

At present, there are approximately 50 drugs approved in the EU[5] with a recommended or mandatory required biomarker determination either for efficacy or side effect prediction, and considerably more than 137 in the USA as of November 2015[6]. It can be assumed that many more are coming. This means that the majority of therapeutic products of the future will come as a double pack: a diagnostic test and a drug.

In the past, clinical biomarker analyses were typically performed in local labs and sometimes under relatively uncontrolled conditions. With the increasing use of biomarkers in the daily routine, health authorities such as the European Medicines Agency and the FDA are establishing better standards to regulate how to qualify and validate a new biomarker and the respective pre-analytical and analytical technologies used to assay the marker. This is in particular challenging for companion diagnostic biomarkers. Companion diagnostics are co-developed with a particular drug and their application is often listed as mandatory in the drug label. Thus, the regulatory aspects of such diagnostic development are of high and increasing relevance in the next future.

Advances in Precision Medicine (APM) would like to provide a vital forum and fruitful platform for the exchange of important information in all areas of the growing field of precision medicine and biomarker research, development and application in the broadest senses. It will follow an indication agnostic approach.

The target audiences of APM are the scientific and healthcare communities of basic scientists and clinicians from **academia, regulatory institutions, and industry**. This includes **pharma, diagnostic** and **device companies.**

We appreciate articles on all **stages in biomarker discovery** (research and development) as well as biomarker utilization, i.e. identification, validation and application. Additional to biomarkers and their assays, **novel technologies, new strategies and general developments** which may have application in the field of PM are welcome. This may apply for new approaches for marker, assay and device development strategies, collaborative approaches (e.g. industry, academic and governmental) and regulatory matters with impact on personalized medicine.

Innovative therapies, even if not guided by biomarkers, may be considered if they specifically target a particular molecule or a special patient subpopulation.

Validation studies are highly encouraged. There is a considerable discrepancy between the number of biomarkers identified and reported in the literature (~150,000) and the very few (~100) actually used in the daily practice[7]. It seems that there may be a major issue with regard to the reproducibility of published

Table 2. Biomarker types based on intended use (adapted after Landeck *et al*. 2015[5])

Purpose	Type	Definition	Example
Stratification and patient selection	**Predictive efficacy**	BM that categorizes patients by likelihood of response to a particular treatment, enabling enrichment of patients most likely to respond to therapy	Human epidermal growth factor receptor 2 (HER2) status for treatment with trastuzumab (Herceptin®)
	Predictive safety	BM that predicts whether a patient develops an adverse reaction to a prescribed drug, enabling enrichment of patients that can be safely treated with a specific drug	UGT1A1 mutation leading to increased toxicity of Irinotecan therapy (oncology)
	Prognostic	BM that categorizes patients by degree of risk for disease occurrence or progression in the absence of a therapeutic intervention	Oncotype Dx® or Mammaprint Dx® for prognosis of breast cancer
Drug response and measurement	**Pharmaco-dynamic**	BM showing that a biological response has occurred in a patient who has received a therapeutic intervention and for which the magnitude of change is linked to the response, depiction of target engagement	phosphorylated substrates of Bcr-Abl, c-Met, MEK kinases (oncology)
	Safety and toxicologic monitoring	BM used to detect or monitor adverse effects in patients receiving a therapeutic intervention	urine levels of kidney injury molecule 1 for renal toxicity, serum levels of alanine aminotransferase for liver toxicity
	Surrogate, response	Subsets of BM that are intended to serve as a substitute for a clinically meaningful endpoint, lab measurements correlate with patients' health status or survival	mean tumor volume as surrogate marker for progression-free or overall survival, HbA1c and blood glucose as surrogates for diabetes care

reports across laboratories and in particular across populations[8]. Thus there is a need for more transparency and major cooperative efforts for adequate biomarker validation. APM will therefore support publishing of **negative data**. Finally, the successful biomarker development frequently requires the joint efforts of several, often quite diverse partners[9,10]. Therefore we appreciate manuscripts on describing and encouraging such collaborations.

Articles include original articles, reviews, perspectives, editorials, commentaries, position papers, conference reports and letters to the editor. The journal welcomes unsolicited article proposals in all categories except for "Editorials". Authors are encouraged to refer to APM's "Section Policies" at www.apm@whioce.com for more information.

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We would like to thank WHIOCE Publishing Pte Ltd, Singapore (www.whioce.com) enabling us to establish this journal. We very much appreciate their generous support. Together we are devoted to making APM a high-quality, frequently cited journal that publishes superior scholarly articles and disseminates the latest advances in the field. To ensure high quality, the articles will be peer-reviewed. To achieve a broad reach it will be an open access journal, with moderate publication fees. Initially we will start with biannual publications, however, if there is demand we will certainly consider quarterly publications subsequently.

Finally, we would like to invite you to read our journal and to submit your most interesting work to us. Although we will publish original scientific work from the outset, we will provide in particular space for high quality reviews and perspective articles. Please feel encouraged to contact us to propose the submission of good quality papers. We are looking forward to becoming a vivid journal dedicated to one of the most dynamic, interdisciplinary and potentially even revolutionary fields of medicine.

Conflict of interest

LL has no conflict of interest to declare. RH is an employee of Oxford Gene Technology, Non-executive Board Member of Newron Pharmaceuticals SpA, Director of Early Clinical Development Consulting Ltd., and a previous employee of and shareholder of Astra Zeneca PLC. KA is a former employee and shareholder of Bayer AG.

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