A LONG JOURNEY FOR A UNIQUE DREAM
RETHINKING ABOUT PRECISION MEDICINE BEFORE THE LAUNCH OF PRECISION MEDICINE IN CARDIOLOGY

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ABSTRACT

Precision medicine has long been thought to hold the promise that patients would benefit most by tailoring the medicine and dose to the individual. In clinical settings, cardio- and cerebro-vascular diseases are now facing significant challenges for their diagnosis and therapy that need to be improved further. Just because of such an expectation and need, many precision medicine initiatives and efforts are being made worldwide. Currently available information on this active research area is emerging rapidly, and a unique forum is needed to facilitate the exchange of the latest findings and in-depth thinking about personalized, predictive, and precision medicine across the medical disciplines. It is anticipated that precision medicine would likely be more precise to guide optimal drug selection and dose adjustment for some (if not all) diseases in the future.

KEY WORDS
Cardiology; pharmacogenomics; precision medicine; optimal therapy
EDITORIAL

Every patient is unique in his or her genetic makeup, lifelong exposure to environmental and occupational risk factors, behavioral characteristics, lifestyle, and socioeconomic backgrounds, which would lead to pronounced individual variability either in the susceptibility to disease, or in the disposition of adverse drug reactions and even life-threatening toxicity. It is generally accepted that precision medicine may hold that promise [1–5]. Since US President Barack Obama announced the Precision Medicine Initiative (PMI) in January 2015 [4,6,7], precision medicine has become one of the hottest words worldwide, and subsequently, similar PMI research projects were launched by other countries, in particular China [8] and India [9]. Although PMI's near-term goal is to focus just on cancer therapy, its longer-term effort is to advance precision medicine to all areas of health and ultimately to generate knowledge applicable to a wide range of diseases and their treatments [6]. As the number one killer worldwide, cardio- and cerebro-vascular diseases, including coronary artery disease and stroke, are facing significant challenges for further improved diagnosis and therapy, by which patient individuals would benefit most [10,11]. At such a special time, a peer-reviewed, open-access journal — Precision Medicine in Cardiology (PMC) — is now launched, which will provide scientists and clinicians in the cardiovascular community with a unique forum to facilitate the exchange of their latest findings and in-depth thinking about personalized, predictive, and precision medicine across the medical disciplines, with a major focus on cardiology and related issues.

Precision diagnosis is the foundation of precision medicine. This rule is also suitable for cardiovascular diseases. In general, the pathogenesis and progression of a disease are a complicated and dynamic process, but the same disease or clinical manifestation would be presented in clinics or hospitals at different time for different individuals over their entire lifetimes. In other words, we will all become patients at some time in our lifetimes. To minimize or avoid misdiagnosis or over-diagnosis of disease, precision diagnosis should be well established on the basis of the new expert consensus, that is, tremendous amounts of patients and otherwise healthy subjects at a given time point will be recruited to be well characterized and monitored in prospective longitudinal cohort studies across a country or worldwide as suggested for cancer research initiative by the PMI [6], and then they will be linked to their electronic health records (EHR) and other clinically useful data derived from their biospecimens, genetic testing, molecular profiling, wearable or implanted technologies, mobile monitoring devices, health Apps, cloud-based database, and more. After vertical integration and further clinical validation, multidimensional data would help clinicians stratify the all patients of the same disease or clinical phenotype into various subgroups who are of relative molecular homogeneity and who are predicted to share similar disease risk, clinical care, and treatment outcomes. For the cardiovascular community, the PMI is an unprecedented opportunity for scientists and cardiologists to work together to advance precision medicine to cardiology and related clinical care [1,10–21], and therefore, potential short-, medium-, and longer-term goals have been proposed for cardiovascular disease in the PMI [10].

On the other hand, precision medicine is the major purpose of performing precision diagnosis. To ensure that most (if not all) individuals could receive the right diagnosis and the right treatment at the right time, precision medicine should be evidence-based (currently genotype-guided) rather than empirical medication [1–4,17,22,23], different from the traditional drug therapy approaches (i.e., trial-and-error or one-size-fits-all strategy). First of all, precision diagnosis of cardiovascular diseases is essential to achieve their precision medicine. In terms of the fact that the etiology and molecular profiling of cardiovascular disease are of high heterogeneity, classical classification and traditional diagnosis of disease are inappropriate for the need of precision medicine in cardiology [24]. Thus, the whole population with the same disease diagnosed by the traditional approaches should be sub-classified into different subsets of high homogeneity according to its unique genetics and molecular biology before taking the medicine. For example, not all patients with dyslipidemia respond well to the statins, and a significant minority of statin-treated patients fail to statin therapy, or experience adverse drug reactions such as myopathy [25]. Recent evidence has documented that patients with familial or severe inherited forms of dyslipidemia, such as homozygous familial hypercholesterolemia, respond well to the proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors evolocumab and alirocumab, not to the statins [25]. Another well-established example is widespread use of clopidogrel in patients with acute coronary syndrome or those undergoing percutaneous coronary intervention for stenting [26,27], with increased dose of clopidogrel or switching to other antiplatelet drugs less dependent on CYP2C19-mediated bioactivation recommended for the CYP2C19-deficient patients. Not limited to the above examples, currently available information or knowledge related to this area is emerging rapidly, with the major focus either on characterizing diseases based on their underlying molecular biology and genetics or on identifying the patients who would respond well to the drug therapy or fail, or who would be at increased risk for developing adverse drug reactions. However, the approved precision diagnosis-treatment pairs for cardiovascular diseases are limited to date.
[10], and there will be a long road to achieve this vision.

The PMI is still in its infancy for its planning and implementing. Because the PMI is being oversold or overhyped sometimes, it is generating unrealistic over-expectations to the public, and even to scientists and clinicians [5,17,28–30], and several questions were posed for the advocates of precision medicine [28,29]. Despite marked heterogeneity across disease signatures and treatment outcomes, remarkable progress has been made to better understand some cancers [31], rare genetic variants [17, 25, 32], and even cardiovascular diseases [33], and to identify novel therapeutic targets for drug development [1,34]. Although the term "precision" does not imply "accuracy" [35], striving for increased precision means to ensure greater predictability and consistency in disease risk stratification and optimal treatment selection. As pointed out by Sir William Osler [36], medicine is a science of uncertainty and an art of probability. One day in the future, when the unknown pieces of the puzzle (diagnostics and therapeutics of disease) are narrowed to smaller over time, the so-called "precision medicine" would likely be more precise, and we would be closer to the vision than we expected [2–4, 37–39].

Welcome aboard, and we hope that you enjoy your journey with us to shape this new journal under editorial guidance, and that you will consider actively contributing to its success. And we believe that we will make a difference when we all are working together.

CONFLICT OF INTEREST
There is no any form of conflict of interest.

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REFERENCES