

Emerging New Technology to Advance Personalized Medicine

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Since initial sequencing and analysis of the human genome was accomplished [1,2], a huge effort has been put into medical research focused on associating genomic variations with individual phenotypes. Personalized medicine is often defined as “the right treatment for the right person at the right time.” While the market for diagnostic tests and therapies that leverage this new science is growing, the biggest opportunities exist outside of the traditional healthcare sector. The Personalized Medicine market is projected to grow by 11.56 percent annually and is expected to reach US \$148.4 billion by 2015. While personalized medicine is already being considered in drug development strategies, it is still at an early stage with respect to clinical applications that support patient-specific therapy.

Genetic polymorphisms and mutations in drug metabolizing enzymes, transporters, receptors, and other drug targets (*e.g.*, toxicity targets) are linked to inter-individual differences in the efficacy and toxicity of medications as well as risk of genetic diseases. The inter-individual variation in the rate of drug metabolism has been known for many years. Pharmacogenomics dealing with heredity and response to drugs is part of science that attempts to explain variability of drug responses and to search for the genetic basis of such variations or differences. Validation of clinically important genetic polymorphisms and development of new technologies to rapidly detect clinically important variants are critical issues for advancing personalized medicine.

The highest impact on personalized medicine is often seen for drugs with a narrow therapeutic index, with important examples emerging from treatment with antidepressants, oral anticoagulants, and chemotherapeutics, which are metabolized by *CYP2D6/CYP2C9*, *VKORC1*, and *TPMT*, respectively. To apply the ever increasing amounts of pharmacogenomics knowledge to clinical practice, specific dosage recommendations based on genotypes will have to be developed to guide the clinician; and these recommendations will have to be evaluated by the use of prospective clinical studies. Such efforts will lead to the development of personalized medicines, which would be expected to exhibit higher efficacy with fewer adverse drug reactions, thereby improving the therapeutic index for drugs whose pharmacokinetics, pharmacodynamics, and safety are influenced by pharmacogenetics. In fact, to improve drug safety, the FDA has started to update labels of previously approved drugs as new clinical and genetic evidence accrues [3]. Increases in efficacy and safety by the individualization of medical treatment may have benefits in financial terms, if information is presented to show that personalized medicine will be cost-effective in healthcare systems.

While the scientific community has largely accepted the utility of sequencing for research purposes [4,5], the use of the next-generation sequencing (NGS) technology in a clinical setting has yet to be fully addressed or accepted by the medical community. To effectively advance personalized medicine, it is necessary to be able to rapidly and conveniently test for patients' genetic polymorphisms and/or mutations. Recent years, new technologies are evolving to transform

diagnostic devices for rapid testing at the Point-of-Care (POC). Portable devices are being engineered for use in a range of settings to perform robust assays for the diagnosis of disease that will improve patient management, and result in greater convenience and speed to answer. Current isothermal nucleic acid amplification methods include nucleic acid sequence-based amplification (NASBA) [6], transcription-mediated amplification (TMA) [7], signal-mediated amplification of RNA technology (SMART) [8], helicase-dependent amplification (HDA) [9,10], recombinase polymerase amplification (RPA) [11,12], loop-mediated amplification (LAMP) [13,14], cross-priming amplification (CPA) [15], smart amplification (SmartAmp) [16,17], rolling circle amplification (RCA) [18], and ramification amplification (RAM) [19]. Among them, SmartAmp has the capability of clinical genotyping [17].

The next important step is to incorporate pharmacogenomics data into routine clinical practice. A key requirement for the advancing personalized medicine resides in the ability of rapidly and conveniently testing patients' genetic polymorphisms and/or mutations. The POC diagnostics is a growing field that is gradually becoming more user-friendly with the introduction of portable devices and quicker nucleic acid detection. Successful POC diagnostics require 4 major elements, such as rapid reaction, low cost, low energy consumption, and simple analysis (with minimal technical training and inclusion of controls but no off-instrument processing or reagent preparation). Development of personalized medicine including POC diagnostics may require integration of various segments of biotechnology, clinical medicine, and pharmacology.

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