

Editorial

Individualized Medicine: An Alternative but not Opposing Path to Gene Therapy

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A decade ago, the human genome project was released making available an individual's or an organism's approximate 23,000 protein-coding genes with the underlying and seemingly well-founded hope at the time that gene therapy was closer than ever [1]. In a strict sense, gene therapy equates with replacing a faulty gene or adding a new one in order to cure a disease or improve the organism's ability to fight disease. However, this implies that challenges pertaining to uptake and regulated expression of foreign genes by host cells ought to be addressed. Specifically, gene delivery to the right cells, activation of gene expression, immune responses and ability to escape the body's natural surveillance systems are well documented and critical issues remaining problematic to date [2]. Despite an explosion in the understanding of the basic biological processes underlying many human diseases, the prospects for the widespread use of successful gene therapy are yet to meet the hype and excitement of the early days. Thus, the question arises: "Is gene therapy an unattainable dream? Have we made strides in spite or because of its severe hurdles?"

The industry has historically proven to be adaptable and resilient in its ability to capitalize on the enormous masses of data stemming from various technologies introduced over the years. Consequently, it has: 1) Exploited genomics results and the congruent choice of receptors on a support basis in hopes of revolutionizing major bottlenecks in gene therapy, and 2) Focused on a path deviating from the original, highly ambitious goal of gene-based disease treatment toward genetic testing and personalized medicine [3,4]. Admittedly, we are removed from the days when we dreamed that surgically replacing a defective gene to cure a genetically inherited disease would be a smashing success. Nevertheless we adopted a two-fold approach, in that we shifted toward addressing the immune-mediated response and the complications stemming from insertional mutagenesis in gene therapy protocols, while at the same time pursued genetic tests and molecular diagnostics to enable disease treatment on an individual level. Addressing the variability in patients and their responses to therapeutic interventions, as opposed to treating all individuals as a continuum, has expedited the momentum in clinical medicine.

Personalized medicine is an integrated approach to targeted therapy driven by and adjusted to the genetic variability of

patients' responses to drug treatments. In spite of obstacles and unlike gene therapy, which is still in clinical trials at best, [5] personalized medicine has made its way to clinical practice with FDA-approved companion diagnostics. The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) joined forces in envisioning an in-sync scientific and regulatory approach to steering patients to the right drug. The critical steps to marrying personalized medicine with the clinic are: 1) Identification of individuals with a predisposition for a certain disease; 2) Assessment of the precise nature of a disease; 3) Matching an individual's genetic profile with the likely effect of a particular drug; 4) Development of policy and education strategies. It would help to address the objectives of the two disciplines, pharmacogenomics and pharmacogenetics, inherently associated with three of the critical steps at the outset, even though they have consistently been used interchangeably. *Pharmacogenetics* is the study of genetic variation that is deemed responsible for varying responses to drugs, while *pharmacogenomics* is the broader application of genomics to drug discovery. Thus, matching an individual's genetic profile to the likely effect of certain drugs [6] can help avoid hypersensitivity reactions to certain medications, [7,8] correlate tumor mutations with drug efficacy, [9-11] and identify poor metabolizers, that will inadvertently reduce the drug's efficacy. Genomics technologies have brought the cost of sequencing from the original US\$1 billion price tag to approximately \$1,000, [4] and in turn enabled the identification of novel targets, including mutants in disease states. The latter has successfully been coupled with drug discovery specifically aimed at the mutant protein [12]. The aforementioned technologies resulted in 1,000 to 1,300 genetic tests for a total of 2,500 rare and common conditions; genetic testing uses diagnostic approaches to analyze various aspects of an individual's genetic material, as well as gene by-products (biomarkers), such as proteins, enzymes, metabolites. Diagnostic testing identifies patients who can benefit from targeted therapies. It would thus follow that the success of personalized medicine is highly dependent upon the accuracy of diagnostic tests that identify patients who can benefit from targeted therapies. This is also tied with the review and approval processes by the FDA in order to avoid erroneous usage of these tests. Consequently, the road to individualized medicine is mapped out and well on its way to making headways.

Have we then moved fast enough in the last 10 years? Given the complexity of the human body and the molecular processes involved, we have definitely made advances that are noticeable. Gene therapy may have not materialized yet, but the reality that almost all genetic tests are available in clinical settings provides us with the reassurance that the last decade has been prolific in moving forward by appreciating individualized responses to therapy and how to circumvent them. Besides, the potential of microRNAs to be used as vectors modulating gene expression offers a new avenue in gene therapy that parallels the progress made in personalized medicine.

REFERENCES

1. Personalized Medicine: Trends and prospects for the new science of genetic testing and molecular diagnostics. 2012; 1-52.
2. Friedmann T, Roblin R. Gene therapy for human genetic disease? *Science*. 1972; 175: 949-55.
3. Hamburg MA, Collins FS. The path to personalized medicine. *N Engl J Med*. 2010; 363: 301-4.
4. Kraus WE, Haga SB, LcLeod HL, Staples J, Ginsburg GS. The Duke Center for Personalized Medicine 2012 Symposium: 'At the interface of Clinical Research and Clinical Medicine'. 2012; 475-478.
5. Herzog RW, Cao O, Srivastava A. Two decades of clinical gene therapy-success is finally mounting. *Discov Med*. 2010; 9: 105-11.
6. Hudson KL. Genomics, health care, and society. *N Engl J Med*. 2011; 365: 1033-41.
7. Mallal S, Nolan D, Witt C, Masel G, Martin AM, Moore C, et al. Association between presence of HLA-B*5701, HLA-DR7, and HLA-DQ3 and hypersensitivity to HIV-1 reverse-transcriptase inhibitor abacavir. *Lancet*. 2002; 359: 727-32.
8. Hetherington S, Hughes AR, Mosteller M, Shortino D, Baker KL, Spreen W, et al. Genetic variations in HLA-B region and hypersensitivity reactions to abacavir. *Lancet*. 2002; 359: 1121-2.
9. Lièvre A, Bachet JB, Boige V, Cayre A, Le Corre D, Buc E, et al. KRAS mutations as an independent prognostic factor in patients with advanced colorectal cancer treated with cetuximab. *J Clin Oncol*. 2008; 26: 374-9.
10. Di Fiore F, Blanchard F, Charbonnier F, Le Pessot F, Lamy A, Galais MP, et al. Clinical relevance of KRAS mutation detection in metastatic colorectal cancer treated by Cetuximab plus chemotherapy. *Br J Cancer*. 2007; 96: 1166-9.
11. De Roock W, Piessevaux H, De Schutter J, Janssens M, De Hertogh G, Personeni N, et al. KRAS wild-type state predicts survival and is associated to early radiological response in metastatic colorectal cancer treated with cetuximab. *Ann Oncol*. 2008; 19: 508-15.
12. Flaherty KT, Puzanov I, Kim KB, Ribas A, McArthur GA, Sosman JA, et al. Inhibition of mutated, activated BRAF in metastatic melanoma. *N Engl J Med*. 2010; 363: 809-19.

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