Personalized Medicine

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With the completion of the Human Genome Project in 2003, the world's attention has focused on converting this vast storehouse of information into innovative health care solutions. The ultimate promise, assuming we know everyone's genotype, is to ensure that every person has optimum health throughout his/her life. This promise has many parts, including optimum nutrition, clean air and water supplies, up-to-date immunizations and regular health screenings. The part of the promise to be fulfilled by knowledge and information stemming from genomics, proteomics and other "omics" is yet unfolding, but the first cautious steps are being taken and are called "Personalized Medicine". Personalized Medicine implies that optimum health goes beyond the basics of clean air and water and takes advantage of the "omics" knowledge to allow the person and his/her clinicians to make therapeutic and lifestyle choices which take the "omics" into account.

Personalized Medicine does not have a crisp definition, but rather reflects a broad coalition of ideas brought to bear on the age-old notion of personalized care. The proud tradition of health care is to focus on every patient and to provide care that is cognizant of the person's individual situation and values, but the situation rarely includes specific genetic/genomic information. The Personalized Medicine movement incorporates the use of molecular analyses and methods evolving from knowledge of genomics to better manage a patient's disease or predisposition toward a disease. In the Genomics and Personalized Medicine Act of 2006[1], personalized medicine is defined as "... the application of genomic and molecular data to better target the delivery of health care, facilitate the discovery and clinical testing of new products, and help determine a patient's predisposition to a particular disease or condition". The belief of the scientific and health-care community is that knowledge of genomics will contribute to better health outcomes. The specific approaches are not yet fully developed but will include genetic/genomic screening programs, genetic/genomic risk analyses, and the use of diagnostic and therapeutic modalities that are still evolving but will certainly involve micro-arrays and other high-throughput analyses in addition to standard genetic tests.

While Personalized Medicine ultimately aims to adapt therapies to individual patients, the initial solution will divide patients into groups by genetic and other markers that predict disease progression and treatment outcomes. In this scenario, pharmacogenetics is at the center of the research and practice. Pharmacogenetics gives a partial explanation to the different responses of individuals to the same drugs. For example, the genetic variants for two genes (CYP2C9 and VKORC1) along with other patient data can explain a substantial portion of the variability seen in a person's response to Warfarin, a powerful and frequently prescribed anticoagulant[2]. The hope in the case of Warfarin is that the adverse drug reactions of excessive bleeding or clotting can be minimized by genetic testing to help predict in advance what is the optimal dose for a specific patient.

Genomic, proteomic or functional genomic biomarkers (features that are associated with the course of a disease) can help to define subtypes of diseases such as cancers that have previously been treated as single entities. This reclassification leads to new diagnostic and therapeutic procedures that hopefully can be shown to be cost effective and efficacious. One success story is the targeted use of genetic testing for mutations in the EGFR gene to determine which group of patients will be responsive to gefitinib as a treatment for non-small cell lung cancer[3]. Obviously this trend in health care has the potential to shift costs because of the increased use of expensive tests, but also has the potential to significantly improve outcomes and to avoid expensive treatment for those individuals who can be shown to have a non-responsive genotype.

Every component of the scientific community will play a part in making the promise of Personalized Medicine a reality, but the field of Biomedical Informatics is especially critical to making the vision come alive. The enormous quantity of complex data poses a daunting challenge to the use of this data in our traditional healthcare system. Biomedical Informatics is a field that

specializes in analyses of such data and the development of techniques to bring focused information out of the data sets. Almost 1000 public biological databases are available to researchers and health professionals with data on genomes, proteomes, metabolomes, etc, and can be used for basic data and as reference sets. Almost 1400 genetic tests associated with diseases [http://www.genetests.org] can be ordered by any healthcare practitioner (some tests can even be ordered by individuals over the internet without going through their physicians); there are over 20,000 genes and so the number of new genetic tests will continue to grow. This enormous quantity of information could be brought into play for a single individual if the cost of a full genome sequence were affordable and the scientific and healthcare community understood the implications of the results of such a large battery of genetic tests. But we are a long way from this. The cost for a full genome analysis is prohibitive at this time and will be for the next decade or so, although the NIH is giving grants to individuals who can work toward a full-genome sequence test for $1000.

It will take quite some time to create a synthesis of all of the genes and proteins and regulatory elements for any specific human, and it will take a very long time to make this synthesis understandable to all concerned. It is likely that the result will be a set of probabilities and risks for specific healthcare problems, a set of lifestyle recommendations (for example, avoid smoking if you have the Z allele of the SERPINA1 gene), and an expanding list of diagnostic tests and therapies. The recommendations will almost certainly include a set of medications that the person should avoid and another set of medications that would be more appropriate for his/her use; all of this would be based on both personal genomics and family history as well as the data from other tests and healthcare experiences, likely pulled from an analysis of data in the Electronic Medical Record (EMR).

The brave new world of Personalized Medicine is slowly emerging, but the complexities of the situation mean that the full blossoming will take years to arrive. To use this data effectively, the worldwide community must define semantic and logical standards that represent genotype-phenotype data so they can exchange information reliably about genetics, patients and health conditions. The understanding of the implications of specific tests is moving so rapidly that there needs to be a set of guidelines that are updated regularly and are readily available from a trusted source. Health care providers cannot be expected to memorize recommendations for the permutations of this large data set, and so it makes sense that computer systems will be called into play. Ultimately the genomic (and other omics) information on a patient would be linked to or stored as a component of the Electronic Medical Record. Decision support systems acting upon standard defined data items and guideline or protocol algorithms would process the data and dynamically send alerts or recommendations to the health care providers. The patients would have access to their lifetime medical data and the same recommendations and reminders via a Personalized Health Record. The public would have access to systems on the Internet to explain the implications of various diseases, risks and tests in a language that was understandable. The Genetics Home Reference [http://www.ghr.nlm.nih.gov] was created by the National Library of Medicine specifically to help consumers navigate through the complex issues of genetic disorders from patient questions to the specifics of research data[4].

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The University of Utah has expertise and resources that promise many contributions for the journey towards Personalized Medicine. There are many sources of data that will assist in defining genes associated with specific health problems. In fact, more single disease genes have already been discovered at the University of Utah than at any other university in the world, based, in part, on the use of its rich databases like the Utah Population Data Base (UPDB) to assist in finding gene-disease associations. There is a long and rich history of working with EMR's in the Department of Biomedical Informatics. There is a great potential for new pharmaceuticals and therapies based on the specific knowledge and definitions of biomarkers being developed. Most importantly, the scientists and healthcare professionals have a spirit of collaboration and find joy in working in multidisciplinary teams, an essential component for climbing this new scientific mountain. The knowledge of genetics, genomics, proteomics, and other "omics" alone cannot transform healthcare. Research on biomarkers has signaled molecular profiling as promising, but biomarkers with adequate specificity and sensitivity are still scarce for most diseases. To achieve the dream of Personalized Medicine, heterogeneous clinical and genomic data sources must be integrated into a scientifically meaningful and productive system. The results must be focused specifically on individuals throughout their lives, in sickness and in health. Then the vision of Personalized Medicine will become a reality.

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