Personalized Medicine

A Healthcare Revolution

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Executive Summary

The Human Genome Project (HGP), which started in 1990 and was completed in 2003, spurred a revolution in biotechnology innovation around the world. The project's goal was the complete mapping and understanding of all human genes. Its successful completion has provided detailed information about the structure, organization and function of the human genome – the complete set of human genes. It also paved the way for a completely new approach to our healthcare – personalized medicine.

What is it?

Personalized medicine is the practice of using diagnostic tools to identify specific biological markers to help determine which medical treatments and procedures offer the best course of action for specific patients. This assessment is accomplished primarily by using the individual's genetic profile, which helps guide decisions regarding the prevention, diagnosis and treatment of disease. The goal is to provide the right treatment in the right dose to the right patient at the right time. In other words, medical treatment is being tailored to the individual characteristics of each patient.

To develop this genetic profile, an individual's genome has to be determined or sequenced. In the ten years since the completion of the HGP, there have been tremendous advances in genome technology that helped reduce the cost of sequencing. This reduced cost enabled the pursuit of research that led to medical advances and biomedical insights benefitting patients, including the development of over 100 drugs whose labels now include pharmacogenomic information.[1]

Personalized medicine is believed to have the potential to change the way we think about, identify and manage health problems. According to the Personal Medicine Coalition, it is already making an impact on both clinical research and patient care. They believe that as our understanding and technologies improve, this impact will become even more significant.

But with any new developments, no matter how impactful, some very important questions and concerns must be raised. With personalized medicine and its associated genetic sequencing, there are ethical, social and legal implications. But first let us consider the technology and how personalized medicine is approached by professionals and patients.

Technology

DNA sequencing, which is the process for determining the precise order of the building blocks or nucleotides in an individual's genome, has advanced the study of genetics and is also a method to test for genetic disorders. DNA sequencing can help find DNA variations that can affect gene activity and protein production which can lead to genetic disorders. It also identifies possible disease-causing mutations.

For example, BRCA1 and BRCA2 are human genes that produce tumor suppressor proteins. They help repair damaged DNA, but when either of these genes are mutated or altered, they may be unable to repair the damaged DNA and those cells are therefore more likely to develop additional genetic mutations that can lead to cancer. Mutations in BRCA1 and BRCA2 have been linked to an increased risk of female breast and ovarian cancer.

Today, there are more than 2,000 genetic tests for human conditions that allow patients to learn about their genetic risks for a disease. With the completion of the HGP, there are at least 350 biotechnology-based products that are currently in clinical trials.[2] These biotech-based products were developed from a deeper understanding of the disease at the genomic level. Therefore we should see a completely new generation of targeted interventions, such as substantially more effective drugs with fewer side effects compared to those available today.

The original sequencing method, called Sanger sequencing (named after its developer, Frederick Sanger), was a breakthrough that helped scientists determine the human genetic code, but it was expensive and time-consuming. The HGP took 13 years to sequence the first draft of the human genome and cost U.S. taxpayers approximately $2.7 billion.[3] More recently, technological breakthroughs have accelerated the process and dramatically lowered the cost of sequencing. In 2011, a company called Illumina developed a machine that could sequence DNA at a cost of $5,000. In January 2014, they announced a machine that could sequence a whole human genome for $1,000. The machine, called HiSeq X, Ten is able to partially sequence five human genomes in a single day or 16 full and complete human genomes over the course of three days.[4]

Because of these technological advances researchers today can find a gene suspected of causing an inherited disease in a matter of days rather than years. These genetic studies have also inspired a new initiative known as "The Cancer Genome Atlas," which aims to identify all the genetic abnormalities in 50 major types of cancer.[5]

Personalized Medicine Approach

The implementation of personalized medicine consists of the following steps:

- Risk Assessment –There are three methods of genetic testing used to identify or reveal a predisposition to disease – molecular, chromosomal and biochemical. By identifying changes in chromosomes, genes or proteins, the results can confirm or rule out a suspected genetic condition, or assist in determining an individual's chance of developing or passing on a genetic disorder.
- Prevention – Knowing one's disease predisposition will enable proactively managing one's health, including applying the necessary precautions to prevent the disease. This may mean a behavior and lifestyle change or treatment intervention. However, it offers the opportunity to focus on prevention and early intervention rather than on reaction at advanced stages of disease.
- Detection – Early detection of disease at the molecular level offers patients better chances of treatment and managing their disease, thus improving their quality of life.
- Diagnosis – An accurate disease diagnosis enables healthcare professionals to provide individualized treatment strategy for their patients.
- Treatment – Personalized medicine is based on the premise that one size does not fit all. Patients can have different responses to the same drug due to their unique genetic identity. The same drug and dose may trigger a serious adverse reaction in one patient,

while for others, the drug works as designed. Individualized treatment and therapy helps improve patient outcomes. As stated by John C. Lechleiter, Ph.D. President and Chief Executive Officer Eli Lilly and Company, "The power in tailored therapeutics is for us to say more clearly to payers, providers, and patients—'this drug is not for everyone, but it is for you.' That is exceedingly powerful."

- Management – Treatment response and progression of disease is actively monitored.

Charis Eng, M.D., Ph.D. Founding Chair of Cleveland Clinic's Genomic Medicine Institute and Director of its clinical arm, the Center for Personalized Genetic Healthcare, and a proponent of personalized medicine perhaps said it best. "I always tell my patients that genetic knowledge is power. It is not about good news or bad news; it is about understanding the underlying cause of disease and using it to tailor a roadmap of prevention."

Ethical, Legal and Social Implications

Genetic testing is the foundation for personalized medicine. Information generated from a genetic test is unlike other health information. DNA is a powerful personal identifier that can provide information about the individual, as well as that person's relatives and related groups. It also provides a window into the individual's potential future health conditions. However, along with these powerful insights come implications for individuals, their families and society at large, on social, moral and ethical levels. Below are examples of the ethical issues arising from the ability to detect faulty genes.

- Family matters – How will the results of genetic conditions affect other family members? The individual tested must weigh family responsibilities, including whether to share the genetic results with at-risk relatives. For example, consider Sarah who is undergoing genetic testing because her mother died of breast cancer. Her test result shows that she is carrying the gene that predisposes her to breast cancer and she has a 40-80% chance of developing the disease. However, she decides not to share her test results with other family members. Here's the conundrum.
    - Does Sarah's doctor or genetic counseling team have any obligation to inform her relatives, in spite of no previous contacts, regardless of Sarah's wishes? Doctors have an ethical responsibility to balance confidentiality/privacy of the individual as well as prevention of harm to others (duty of care).
    - Does this consideration change if her siblings are also her doctor's patients? Should the doctor have tried harder to encourage her to share her test results to minimize potential illness?
    - What if Sarah's other sister Penny, who is also her doctor's patient, applies for insurance and is required to provide relevant medical information, such as family history of cancer. Remember, she is unaware of Sarah's genetic testing. Should Sarah's doctor be obligated to share this information with the insurance company? And if he shares his insights, is it reasonable for the insurance company to use this information as they underwrite her potential coverage?
- Limitations of genetic testing – In some cases, genetic tests provide reliable and accurate information on which an individual can make decisions. In other cases the results may not be as definitive. A person may have a genetic variation but that does not mean they will necessarily develop the disease, nor can it predict the severity of the condition or the age at which symptoms will first appear. The lack of accuracy can be very distressing when trying to make a decision.
- Unintended implications of personalized medicine – Since the foundation of personalized medicine is the individual's genetic profile, other ethical implications could arise that are not specifically associated with personalized medicine.

  - Inappropriate applications of genetic testing - Beyond medical or health reasons, genetic testing can also be used to determine the sex of a baby in utero by checking the chromosomes. There are sometimes requests for such testing to ensure that a couple has a baby of a certain sex, or certain hair and eye color.
  - Selective termination of pregnancies[6] – Pre-natal testing can also detect fetal abnormalities, which can be a difficult for some parents to comprehend or address. Some will decide to continue the pregnancy and establish the professional, medical and social support that will be required. Others may choose to terminate the pregnancy. Do some health conditions – if any – present sufficient grounds to justify abortion, a decision that may conflict with moral, religious, ethical and cultural beliefs?

- Potential for discrimination – Employers and insurance companies could use an individual's genetic make-up to determine if the potential employee or insurance applicant will develop a condition for which they carry a predisposition, such as cancer or heart disease. In the U.S., the Genetic Information Act of 2008 prohibits the use of genetic information for health insurance coverage decisions, however it does not do so for life insurance, disability insurance or long term-care insurance.[7]
- Genetics technology application boundaries – As with any new technology, continued research on genetics will most likely yield more uses and applications. But where do we stop? Or could this new scientific tool be abused and used for the wrong purpose. Boundaries need to be considered.

  We now have the ability to clone genes in the laboratory, which is an essential step in the treatment of genetic conditions, called gene therapy. Gene therapy is costly, so does this mean it would only be available for the wealthy? Also, should gene therapy be allowed for enhancements of basic human traits such as height, intelligence or athletic ability? If permitted, generations from now the world could be populated with perfect human beings, one more perfect than the other. For some people this could be utopia, for others it could be the exact opposite.

  Genetic-cloning technology has been extended to cloning of whole animals. You likely remember that a few years ago scientists cloned a sheep called "Dolly." Mice have also been successfully cloned. At present, it is not yet possible to clone a human, but scientists are saying that it is now technically possible to do so in the future.[8] Reasons for supporting cloning humans include the egocentric wishes for immortality or providing an organ or bone-marrow donor for another family member suffering from an incurable disease. The moral, social and ethical issues associated with such genetic technologies are profound.

  For now, genetic technology is limited to providing health benefits through personalized medicine, but the potential exists for inappropriate future use targeting human enhancements.

To Test or Not To Test

That is the question. Genetic testing has benefits, as well as limitations and risks. Whether to test is a personal and complex decision. If you decide to have your DNA mapped, there are some things to keep in mind.

- Remember that other than looking for disease risk, genetic testing is used to make better treatment decisions regarding the use and dose of certain drugs and chemotherapies. For example, the drug Herceptin in combination with chemotherapy is more effective for those breast cancer patients with the HER2 gene.
- Having certain genetic variations does not necessarily mean that you will develop the disease.

- Go in with your eyes wide open and understand what the test is going to tell you. Is it to gain information you really want to know? What will you do with that information once obtained? You may remember in 2013 that Angelina Jolie underwent a preventive double mastectomy when she was informed that she had an 87% chance of developing breast cancer due to specific gene mutation BRCA1. Her choice was easier to understand since her mother and aunt both died from breast cancer. She also made a point that more women should have access to gene testing and lifesaving preventive treatment, whatever their means and background. By undergoing the double mastectomy procedure, she reduced her chances of getting breast cancer form 87% to 5%.[9] Recently in March 2015, she had her ovaries and fallopian tubes removed as well to reduce her chances of developing other cancers.
- Remember there are genetic counselors that will help you put things into perspective and help you with decisions regarding whether to share your information with your family. They can provide information about testing options and help you decide what is best for you and your family. Lastly, they can help you find referrals to medical specialists, as well as advocacy and support groups.
- If you find you are predisposed to a disease, you can take proactive steps. It may be frightening but it also empowers you to take action. You don't have to be a victim of your circumstances. If we knew in advance that we were to walk a road of suffering, how many of us would willingly choose that path?

Health Conditions & DNA Testing

DNA-based genetic testing is able to detect the predisposition to the following health conditions in an individual. Predispositions mean that the individual is more likely to be afflicted by the genetic condition, but does not necessarily mean that they will definitely be afflicted with that condition.

- Alzheimer's disease
- Asthma
- Atrial fibrillation
- Breast Cancer
- Celiac disease
- Colorectal cancer
- Coronary artery disease
- Gallstones
- Glaucoma
- Heart attack
- Hypertension
- Lung cancer
- Multiple sclerosis
- Prostate cancer
- Psoriasis
- Rheumatoid arthritis
- Type 1 and Type 2 diabetes
- Restless leg syndrome
- Skin cancer
- Venous thromboembolism

Healthcare Provider Challenges

As a fairly new healthcare practice, personalized medicine comes with unique challenges especially for healthcare providers. Simply keeping up with all the advancements is a significant task. Growth of research in this field is so rapid that it is making it difficult for even the most dedicated clinicians to keep up. This momentum requires hiring physicians and genetic counselors at the top of their field to interpret sophisticated genetic test results and translate them into effective prevention and treatment strategies.

Healthcare providers will also play a fundamental and important role in teaching patients to be co-managers of their own health. The dynamics of the doctor-patient role will change. Educated patients will increasingly participate in medical decision-making and choice as physicians will no longer be the single sources of knowledge.

Medicine customized to your needs

This new approach to healthcare will also change the way healthcare providers conduct business, from the services they provide to the way healthcare decisions are made and funded. Reimbursement decisions, for example, could become more complex as standard treatment protocols become less normative. Subjectivity on a case-by-case basis may be necessary requiring more collaboration among payers, providers and drug manufacturers; diagnostics, medical devices and therapeutics.

Personalized medicine could also affect technology capabilities and infrastructure. With the adoption of electronic health records (EHR), which is still in its infancy, a vast amount of patient information is already being collected such as patient histories, diagnostic reports, etc. This could multiply exponentially in the next several years along with all the genomic data that will ultimately evolve into billions of data points on every individual as analytical tools are being developed. With this emerging dependence on EHRs comes critical dependency on secure, fail-safe technology networks and a need for patient-oriented resources, such as personalized EHR apps and other innovations.

Conclusion

Personalized medicine is a scientific breakthrough that could revolutionize our healthcare. It's here and is gaining momentum as a powerful form of preventive medicine that could help millions improve their quality of life. Individualized analysis of a person's genome will enable physicians and genetic counselors to focus on what is needed to keep an individual in the best possible health. That could mean diet or lifestyle changes, targeted drugs and therapeutics, or medical surveillance. Medical science will be able to develop highly effective diagnostic tools to better understand the health needs of people. This in turn will lead to treatments that are custom tailored to the individual and their disease.

As further studies are conducted and improve our understanding at a molecular level of how diseases like cancer, diabetes, heart disease and even schizophrenia come about, we can expect a whole new generation of interventions, many of which will be drugs that are much more effective and precise than those available today.

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Additional resources

- http://www.geneplanet.com/genetic-analysis/list-of-analyses.html
- http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc_age_of_pmc_factsheet.pdf
- http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FactSheet23
- http://ghr.nlm.nih.gov/handbook/testing/genetictesting