

Introduction to Genomic Medicine

What is genomic medicine?

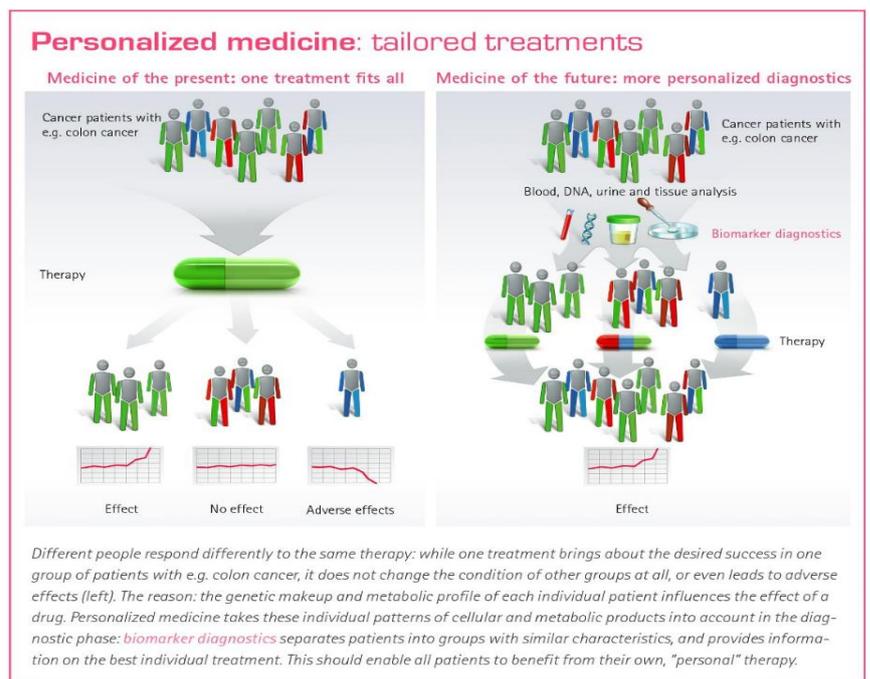
There are more than 7 billion people on our planet, each a massive collection of about 100 trillion cells. How do these cells know what to do? What tells them to work together to keep your brain thinking, heart pumping, and hair growing? The answer lies in a long, winding molecule called deoxyribonucleic acid, or DNA.

DNA could be referred to as an instruction manual on how cells work as it contains genes that carry instructions needed to build and maintain the many different types of cells that make us unique. Researchers call this complete set of DNA instructions a “genome.”

Our health is determined by our inherited or acquired genetic differences combined with our lifestyles and other environmental factors. Although greater than 99.9% of a DNA sequence is identical from person to person, the last 0.1% helps to explain these differences. Different people may have small variations in specific genes, and some people may have genes that others do not. These may increase susceptibility to a specific disease or provide protection from that illness. By combining and analysing information about our genome, with clinical and diagnostic information and then comparing that with data from others, patterns can be identified. Together this information can help to determine our individual risk of developing disease, detect illness earlier, provide accurate diagnosis, support disease monitoring and determine the most effective interventions to help improve our health, either by the use of medication or lifestyle choices. Genomic medicine describes these efforts.

Genomic medicine sometimes also known as personalized medicine is a move away from a ‘one size fits all’ approach to the treatment and care of patients with a particular condition, to one which uses new approaches to better manage patients’ health and target therapies to achieve the best outcomes in the management of a patient’s disease or predisposition to disease.

The developments of biobanks combined with novel approaches, such as gene editing, whole genome sequencing and the development of polygenic risk scores have been instrumental in identifying genomic causes of rare disease, understanding variation in complex disease, and characterizing mutations that cause many diseases.



Source: Bayer pharmaceuticals, personalized medicine <http://pharma.bayer.com/en/innovation-partnering/research-and-development-areas/oncology/personalized-medicine/>

Genome sequencing

Genomics relies on DNA sequencing. Sequencing a gene is like reading a book one letter at a time to look for any spelling mistakes. Whole genome sequencing is the equivalent of running spellcheck on every volume of a book in a library. Whole Genome Sequencing involves looking at an individual's entire DNA, rather than looking at specific genes or groups of genes. When analysed with other information about our health and the way we live our lives, it provides detailed information about the complex interactions within a person, and between them and their environment. It offers a greater understanding of the underlying causes, triggers and drivers of disease as well as the likely success or failure of drugs and interventions. Having the complete sequence of the human genome is similar to having all the pages of a manual needed to make the human body. With the drastic decline in the cost of sequencing whole genomes, ground-breaking comparative genomic studies are now identifying the causes of rare and common diseases.

Biobanks

Also known as, bio-repositories, bio-resources or tissue banks are repositories that store biological samples for research purposes and are vital for genomic research. A sample can be a piece of human tissue or bodily fluid such as blood, urine or saliva. One of the largest Biobanks in the world is the UK Biobank, which was set up more than 10 years ago and has to date collected health related information on 500,000 people across the UK, following them through time, to see what happens to them as they live their lives. In addition to information collected during the baseline assessment for all 500,000 participants, 100,000 UK Biobank participants have worn a 24-hour activity monitor for a week, and 20,000 have undertaken repeat measures. A program of online questionnaires is being rolled out (diet, cognitive function, work history and digestive health) and the UK Biobank has also embarked on a major study to scan (image) 100,000 participants (brain, heart, abdomen, bones &

carotid artery) as well as getting them sequenced. The UK Biobank is now being linked to a wide range of electronic health records (cancer, death, hospital episodes, general practice), and is developing algorithms to accurately identify different diseases. This creates an unparalleled resource for biomedical research that allows for in-depth understanding of the underlying genetics of disease, disease predisposition, and the interactions between genetic, lifestyle factors, and the environment. It also provides an opportunity to learn more about the biology of the diseases themselves, providing insights which can lead to the development of new treatments and preventative interventions.

Polygenic Risk Score (PRS)

Typically, researchers have focused on finding single-gene mutations that predispose individuals to have a significantly increased risk for disease. For example, *BRCA1* or *BRCA2*, two genes that confer increased risk for breast and ovarian cancer. Such simple one to one relationships between a gene and susceptibility to disease is very rare and affects only a small proportion of people. Rather, the risk for many diseases has a polygenic, or multi-gene, component involving many common genetic variants that each have a small effect, cumulatively affecting disease risk.

A polygenic score, also called a polygenic risk score, genetic risk score, or genome-wide score is an estimated score that measures an individual's genetic predisposition to specific diseases or complex traits. It sums up the effects of all the common genetic variants implicated for a disease observed within an individual. Each individual has their own score which tells them how genetically predisposed they are toward getting a disease.

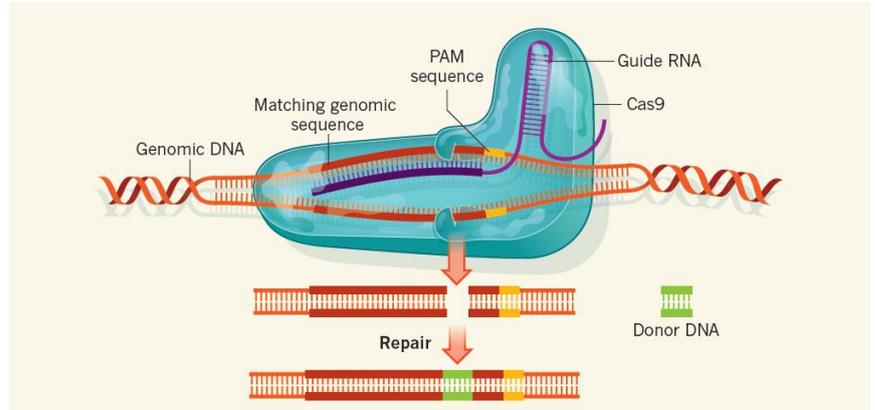
Whilst it is true that the overall predictive power for any given disease is modest with PRS, for many people with 'average risk,' quantifying the exact degree of genetic risk is not likely to be particularly useful. PRS is revolutionary in that it will pick out individuals who have particularly high or low genetic risk allowing preventive interventions and treatment to be targeted accordingly.

Read about a new genetic test that uses PRS to detect heart attack risk here <http://www.onlinejacc.org/content/72/16/1883>

Genome Editing

Genome editing also known as gene editing is a group of technologies that give scientists the ability to make highly specific changes in the DNA sequence of a living organism, essentially customizing its genetic makeup. These technologies allow genetic material to be added, removed, or altered at particular locations in the genome. Several approaches to genome editing have been developed. The most recent being CRISPR (clustered regularly interspaced short palindromic repeats) and CRISPR-associated protein 9 (CRISPR-Cas9). The CRISPR-Cas9 system has generated a lot of excitement in the scientific community because it is faster, cheaper, more accurate, and more efficient than other existing genome editing methods.

CRISPR – Hacking the biological hard drive



Source: Swiss Re Risk Dialogue Series – Genomic Medicine

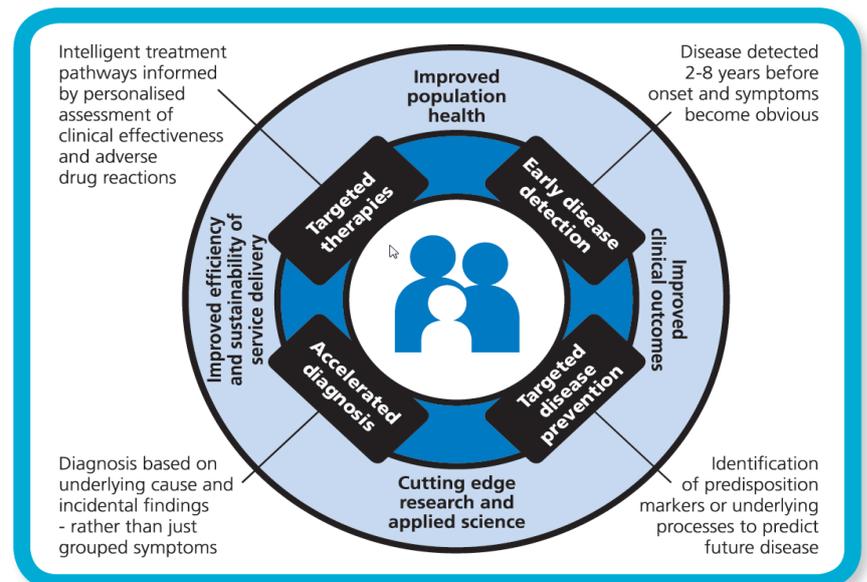
<http://institute.swissre.com/research/library/454681943.html>

Through the application of genome editing technologies, physicians might eventually be able to prescribe targeted gene therapy to make corrections to patient genomes and prevent, stop, or reverse disease. It is currently being explored in research on a wide variety of diseases, given that many diseases have a genetic basis, including single-gene disorders such as cystic fibrosis and hemophilia. It also holds promise for the treatment and prevention of more complex diseases, such as cancer, heart disease, mental illness, and human immunodeficiency virus (HIV) infection.

Read more here:

<https://www.genome.gov/27569224/how-is-genome-editing-used/>

How Genomic medicine can change the future of medicine



Source: NHS England

What does this mean for the insurance industry?

Anti-selection risk

The cost of whole genome sequencing for an individual has fallen over the years to less than \$1000 today with the cost predicted to decrease further in the future. As a result, there has been a proportionate increase in the number of genetic tests available, including predictive genetic tests, and an increase in access to direct-to-consumer tests. The number of companies providing direct-to-consumer genetic testing is growing, along with the range of health conditions and traits covered by these tests, as a result the cost of obtaining these tests have dramatically reduced over the years and continue to decrease making them readily accessible. Polygenic risk scores are accelerating this by providing risk relevant information on common complex diseases. This provides individuals with a deep insight and better knowledge of their current and future health status enabling them to purchase insurance accordingly. Non-disclosure and/or restriction in access to such risk-relevant genetic information will increase insurer's exposure to anti-selection and can have a significant impact on the efficient operation and sustainability of insurance markets.

Impact on claims

Genomic medicine has the potential to improve prognosis and clinical outcomes of many diseases in the future, and ultimately impact longevity. This could have negative consequences for certain books of insurance business, such as annuity business. Conversely, life and health insurance may benefit from lower mortality.

That said there is a behavioural impact of predictive genetic tests that could affect mortality outcome. It is plausible that genetic test results could motivate health-related behaviour change. It might increase motivation by reinforcing the belief that current behaviour, combined with a genetic predisposition, is putting a person at increased risk of disease. Alternatively, given a common perception that genetic risks are unchallengeable, it might decrease motivation by weakening beliefs that changing behaviour will reduce risks. Genetic risk information may also weaken belief in the ability to change behaviour - for example, among people who learn that they have a genetic vulnerability to nicotine addiction.

The earlier identification of disease through genetic testing could have a significant impact on Life and Critical Illness business although the magnitude of the impact is unknown. Diseases that would have never caused symptoms or death during a patient's lifetime will now be detected and treated. This will have an impact on the timing and incidence of critical health events and potentially increase number of claims.

Higher health care costs

As medications will be designed and prescribed for particular genetic profiles, it is likely that the cost of treatment per patient will increase. However, there is the potential that gains from early diagnosis, better treatment and disease management will offset the potentially higher cost of treatment.

Legal and reputational risk

The use of genetic testing information has created much debate because of its potential for unfair discrimination in employment and insurance. The use of genetic information is highly regulated in mature markets and increasingly subject to legislation in new markets which further limits private insurer's ability to select and manage risk. Agreement on reasonable self-regulation is vital in order to help balance the interests of consumers and preserve the ability of insurers to underwrite sustainable insurance products.



Glossary of some commonly used terms in genomic medicine

Mutation: Any alteration of a gene or genetic material from its natural state. Generally, mutations refer to changes that alter the gene in a negative sense causing the protein product of the gene to have an altered function.

Pharmacogenomics: Study of genes related to genetic controlled variation in drug responses.

Polymerase chain reaction (PCR): A procedure in which segments of DNA (including DNA copies of RNA) can be amplified using flanking oligonucleotides called primers and repeated cycles of replication by DNA polymerase

Single Nucleotide Polymorphism (SNP): SNPs are a type of polymorphism involving variation of a single base pair. Scientists are studying how single nucleotide polymorphisms, or SNPs (pronounced "snips"), in the human genome correlate with disease, drug response, and other phenotypes.

Genome Wide Association Study (GWAS): Is an approach that involves rapidly scanning markers across the complete sets of DNA, or genomes, of many people to find genetic variations associated with a particular disease. Once new genetic associations are identified, researchers can use the information to develop better strategies to detect, treat and prevent the disease. Such studies are particularly useful in finding genetic variations that contribute to common, complex diseases, such as asthma, cancer, diabetes, heart disease and mental illnesses.

Get more definitions here: [https://www.genome.gov/glossary/index.cfm?](https://www.genome.gov/glossary/index.cfm?https://genomicscience.energy.gov/glossary/index.shtml?)
<https://genomicscience.energy.gov/glossary/index.shtml?>



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