# LEICA BIOSYSTEMS ARTICLE

## PRECISION AND PERSONALIZED MEDICINE

### Introduction

Precision and personalized medicine are terms used interchangeably. Personalized medicine is an older concept and has led to the idea that prevention and treatment have been created specifically for that patient. According to Genome.gov, "Personalized medicine is an emerging practice of medicine that uses an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease."[1] The President's Council of Advisors on Science and Technology defines personalized medicine as "the classification of individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment. Preventive or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not".[2]

The term precision medicine gained popularity with the 2011 report from the National Research Council.[3] Precision medicine is treatment or prevention approaches based on genetics, environmental factors, and lifestyle targeted to individuals or populations.[4] Precision medicine is a medical strategy or model for health care delivery that defines a disease at a higher resolution to enable the more precise targeting of disease subgroups with new therapies.[5] For the success of the precision medicine model of healthcare, it will need to rely on the patient, digital health, genomics, and other molecular technologies, data sharing, and data science.[6]

### Background

The human body contains trillions of cells. Within each cell nuclei are chromosomes responsible for transferring genetic information from one generation to another. DeoxyriboNucleic Acid (DNA) makes up the chromosome (and a small amount in the mitochondria) to control proteins to determine the structure and function of the body's tissues and cells. Protein consists of amino acids, and genes are part of the DNA that determine the amino acids' order that makes up the protein. When genes do not act the way they should, this is called a mutation or variant, which can cause illnesses or diseases.[7]




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There are approximately 6000 known genetic disorders divided into four categories, including[8]:

- Single-gene Mutation or Monogenic Disorder – one defective gene is present and inherited. Subcategories of a single-gene mutation are one defective gene in either parent (autosomal dominant); a defective gene from each parent (autosomal recessive); the defective gene is present on the female (X) chromosome (X-linked disorders). Examples of this disorder are hemophilia, cystic fibrosis, sickle cell anemia, and familial hypercholesterolemia.
- Multiple Genes Mutations or Multifactorial Inheritance Disorder – This disorder is the mutation of multiple genes and the effects from the environment. Examples of this disorder are heart disease, diabetes, Alzheimer's disease, arthritis, and cancer.
- Chromosomal Changes – Chromosomal abnormalities such as the number and structure can cause disease. Examples of this disorder are Down and Turner syndromes.
- Mitochondrial Mutations – This disorder is the mutation in the non-nuclear DNA. of the mitochondria. Examples include myoclonic epilepsy and mitochondrial encephalopathy.[9]

Genetics and genomics are similar concepts. Genetics is an older idea and concerned with a single gene.

Genomics deals with a broader scope encompassing all genes. According to the NIH National Human Genome Institute, genomic medicine is a subset of precision medicine emerging using molecular information about individuals to guide their clinical care.

Jeanette McCarthy, Ph.D., MPH, explains that precision medicine uses genomics across the lifespan – from preconception to adulthood. Some examples include:

- Preconception Carrier Screening – testing to determine the potential of having a child at risk for a genetic disorder such as cystic fibrosis, sickle cell anemia, or Tay Sachs. There are commercial tests now available for 100 disorders
- Prenatal diagnosis – identification of fetal DNA in the maternal bloodstream to test for chromosomal abnormalities
- Diagnosis for rare diseases in children – a few examples are Cat Eye Syndrome, Lichen Planus, and Rotor's Syndrome
- Adulthood – genetic testing in breast and colon cancer[10]

## Genomics and Cancer

The cancer process shows that genes mutate to cause unlimited cell growth. As the cell growth remains unchecked, it becomes a tumor. Human genome sequencing (decoding the DNA) has allowed for a closer look at the tumor cells. Tumor cells have mutations, and these variants are different depending on the

type of cancer. Each person's cancer is unique, and why some traditional therapies, such as surgery, chemotherapy, and radiation, may not be effective.[11] Identifying the cancer driver mutations in the tumor cells through genome sequencing (Next-Generation Sequencing) will allow for more targeted treatments.[12]

The Cancer Genome Atlas Program, set up by the US National Cancer Institute (NCI), molecularly characterized over 20,000 primary cancer and matched normal samples spanning 33 cancer types. This data has already led to improvements in the prevention, diagnosis, and treatment of cancer.[13] An excellent example of this is that ten years ago, lung cancer was either diagnosed as small cell or non-small cell, but today 30 genetic mutations are considered.[14]

Building on the Cancer Genome Atlas Program, in 2020, the Pan-Cancer Analysis of Whole Genomes (PCAWG) Project analyzed entire tumor genomes for 38 types of cancer. The PCAWG project was able to find at least one driver mutation in about 95% of the tumor samples, which could allow more cancer patients to receive a drug that targets the protein made by that driver gene. The PCAWG has begun to develop a database of 100,000 patients so that physicians can use it to determine the best treatment based on the patient's tumor genome type.[15]

## The Benefits of Precision Medicine

In 2003, sequencing of the first human genome occurred. This technology is in the early stage of being implemented into clinical medicine. Benefits of implementation include:

- Ability to use patient's genetic and molecular information as part of their medical care
- Improvement of choosing the treatment that works best for specific patients
- Increased knowledge of the underlying mechanisms which various diseases occur
- Better approaches to preventing, diagnosing, and treating diseases
- Integration of electronic health records in patient care to access medical data easily[16]

## Obstacles for Precision Medicine

The young field of Precision Medicine continues to evolve, although it does have challenges. Some of these challenges include:

- Cost – The Precision Medicine initiative will cost millions of dollars. Technologies for sequencing DNA, designing databases for large amounts of patient data, and developing targeted treatments will be expensive.[17]
- Amount of data needed – to promote discoveries and improvements in precision medicine, it is essential that information collected in a dedicated database can be accessible worldwide to process and interpret the growing volumes of data rapidly.[18]

- Insufficient technologies – To move the Precision Medicine initiative forward, this will involve designing new tools to collect, analyze, and share large medical data sets. Once the data is collected, artificial intelligence will need to collate and interpret the data.
- Limited knowledge – The area of precision medicine is rapidly developing, and clinicians may find it problematic to keep up with new treatment options. Multiple molecular diagnostic tests are available, making it difficult to determine the proper test for the patient. Genomic reports include large amounts of data, and clinicians may find it challenging to interpret the information and prescribe treatment options.[19]
- Gaps in research – Precision Medicine is growing and changing rapidly. Large randomized clinical trials may no longer be an option to generate the evidence needed to show an improvement in patient outcomes.[20]

## Closing

Precision Medicine is advancing rapidly. For example, in 2015, in the United States, as part of the National Research Agenda, President Obama announced a government-funded initiative called "All of US" with plans to enroll 1 million Americans. This project was created to share data generated over ten years from genomic sequencing, electronic medical records, and reported personal information to increase the understanding of disease biology, pathogenesis, and advance precision health care. Global Initiates are also underway in many countries.

Precision Medicine will change the way clinicians are practicing medicine. Today, most patients with the same disease receive the same drug at the same dose at the same time. In the future, and with the advancements of precision medicine, patients will receive targeted treatments based on their genomic mutations with a higher likelihood of success, fewer adverse events, more prolonged survival, and improved quality of life.[21]

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