TELUS Talks Health

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Personalization paradigm: what molecularly tailored medicine means

> "It's far more important to know what person the disease has, than what disease the person has."
> **– Hippocrates**

The topic of personalized medicine is attracting a lot of attention in the scientific community and raising controversial questions about healthcare privatization and data privacy, as well as its cost-benefit. Indeed, personalized medicine represents a whole new paradigm of diagnosing and treating disease and, as such, comes with many as-yet unresolved concerns.

This article takes a step back and instead considers some of the basics. It aims to serve as a primer on the promise of personalized medicine, the most prevalent ways that it is starting to be applied, what's driving its emergence, and what this fundamentally means to the future of medicine and healthcare.

Understanding an individual's molecules changes everything

A few vignettes to help set the stage:

- A 67-year- old woman battling colon cancer learns that her tumor has recurred and that conventional treatments will no longer be effective. Her condition is terminal. At the same time, the cancer research team sequences her tumor and discovers that it is over producing a specific protein that can be controlled with an existing medication for high blood pressure. The medication is prescribed and the cancer disappears.
- A 40-year-old man must prepare to broach funeral arrangements for his 7-month-old son who suffers from Leigh Disease, a rare neurometabolic degenerative disorder that results in pain, neuro motor degeneration and eventually death. He receives a call from a research team indicating that his son's disease can be traced to a metabolic disruption that can be treated.
- A 41-year-old woman with severe Rheumatoid Arthritis is pondering whether to start taking Azathioprine, understanding that there is a rare but severe potential adverse reaction involving suppression of her bone marrow that could be fatal. She is given the option to have a test from a local start-up to check for the gene variant that causes this complication before treatment.

These three stories share one common thread: They all illustrate how our new molecular understanding of disease at the individual level can provide cures, save lives and avoid potentially devastating adverse reactions.

These stories also highlight the first three areas of personalized medicine – oncogenomics, rare disease and pharmacogenomics – that are breaking through into conventional medicine with impressive results.

Progress in these fields is providing exciting glimpses into a new clinical world where diagnosis and treatment will come from a molecular understanding of disease and treatment at the individual level, rather than the traditional broad-based population level

Unprecedented data volumes that hold untold opportunity

This massive change is only just at its outset and is being powered by the convergence of multiple technologies. Computing power, gene sequencing, biosensors, nanotechnology, machine learning, big data and 3D printing, when applied to health, will provide the ability to understand it at a molecular level for each individual. The resulting data set available for analysis will be unprecedented in terms not only of volume (1-2 terabytes per person), but also scope, and ultimately uses.

This data will come from:

- **Genome** – the complete set of an individual's DNA including all of their genes – representing more than 3 billion DNA base pairs
- **Transcriptome** – the complete set of RNA transcripts produced by the genome at any one time
- **Proteome** – the complete set of proteins that are expressed by an individual at any one time
- **Metabolome** – the complete set of metabolites present within an individual at any one time
- **Microbiome** – the complete genomic information for the microbes that live inside and on the human body – approximately 100 trillion cells.
- **Physiome** – the physiological dynamics and characteristics of the individual, as measured through sensor technology
- **Anatome** – the individual's unique anatomical characteristics digitally represented through advanced medical imaging

With new abilities to capture and analyze this data, healthcare will be transformed through a precise understanding of how health outcomes are influenced by genetics, environment, diet and lifestyle on an individual basis. This understanding will result in new opportunities to treat, predict and prevent disease and, at the same time, build continuous feedback between health outcomes and the molecular changes that precede them.

Changing how we understand disease

This new personalized paradigm will change the way that disease is understood.

Traditionally diseases have been characterized by the physiological effects they have on a population. For many diseases, especially complex chronic diseases, there are multiple molecular causes that result in similar physiological signs and symptoms. For example, even in a rare disease like Leigh's Disease there are dozens of genetic variants causing multiple, different neurometabolic breakdowns that all clinically result in the condition that presents to a clinician as Leigh's Disease.

For a disease like Type II Diabetes there may be hundreds of different molecular causes, each with a different set of treatment options. Without the ability to differentiate at an individual level, current medical therapy applies a one-size-fits-all approach and treatment options are studied across these heterogeneous disease populations.

The impact of one-size-fits all treatments is quite varied. Some may work extremely well for one molecular variant of a disease, but may not work for others or can even be harmful. In fact, only half of the population will respond to most medications. This variability can be avoided when clinicians have an understanding of the molecular underpinnings of a disease for an individual patient. In personalized medicine only treatments that are certain to benefit the individual are prescribed.

The transformation of medicine from one-size-fits-all to a personalized approach will allow doctors to be more precise, predictive and ultimately preventive in their practice.

Three gates to personalized medicine

Personalized medicine is not yet an established paradigm and there are a number of gating factors that will need to be cleared before this vision becomes a reality. Interestingly, technology is not one of these gating factors. The current state and exponential progression of the underlying technologies actually bodes well for a near-term realization of personalized medicine.

Instead, the three challenges, in increasing order of difficulty will be:

1. **Complexity** – much of current health data is incomplete. Data from sensors will come from contexts we do not yet understand, and our ability to share information usefully between multiple systems is inadequate. Finally, we simply do not know what to do with much of this data (yet).
2. **Regulation** – the legal frameworks for ownership of the data and algorithms derived from this data needs to be fully clarified internationally. The privacy and security mechanisms to allow robust but secure sharing and secondary use of data need to be expanded, and laws to protect individuals against discrimination must be enacted.
3. **Culture** - in a matter of years, conventional medicine paradigms will be turned over completely and patients will demand treatments based on diagnoses derived from computer algorithms – healthcare professionals will need to adapt to roles that are dramatically different to what they have historically done.

These challenges, rather than the technology, may be the biggest obstacle in the way of personalized medicine. Early recognition of the changes required and engagement of a broad set of stakeholders will be essential to enable the appropriate system changes necessary for society to realize the benefits of this new and profound way of understanding health.

At TELUS Health we are tremendously excited about the potential for personalized medicine to transform health care for Canadians and look to work with other stakeholders to overcome the potential barriers to this exciting future. The realization of personalized medicine is one embodiment of our mission to turn information into better health outcomes by connecting consumers, healthcare providers and enterprises.