Personalized medicine

Heidi Britton[1]; Alvin Qiu[2]
Citation: UBCMJ. 2017: 9.1 (3)

To some clinicians, the concept of personalized medicine may not be a new one. When evidence–based data emerge that support stratifying patients to potentially improve outcomes, medicine has historically adapted practice and protocols accordingly.

However, with the development of next generation sequencing and other technologies, an era of molecular–level precision medicine is emerging, and at some institutes, has already arrived. The Human Genome Project increased the affordability of sequencing technologies, spurring exploratory genomic research, and led to the development of applied clinical genomics. Patient–specific imaging, gene expression, metabolites, proteins, lipids, and other biomarkers offer potential new means of guiding and fine–tuning treatment and prevention in specific diseases.

Cancer is one such disease, and precision medicine is often used as a synonym for the buzzword "oncogenomics", or characterization of cancer–related genes. Massively parallel sequencing technologies have made clinical genetic testing more accessible to clinicians, and allowed for further exploratory and clinical research. Rather than a "minimum hit" phenomena to oncogenesis, cancer is now thought to be a highly complex disease, involving multiple signalling pathways, heterogeneous mutation patterns, and unique genes in every individual. In BC, eligible patients can be referred for genetic testing of the *BRCA1/BRCA2* tumour suppressor genes, with mutations predictive of breast, ovarian, and several other cancers, and associated with 5-10% of all breast cancers.[1] Circulating tumour DNA (ctDNA) is found in around 50% of patients with stage I cancer and is being actively investigated for its potential utility in detecting and even quantifying occult early–stage or relapsing disease.[2-4] Featured in this issue, is an article by researchers at the BC Cancer Agency, where close to 900 cancer patients have been evaluated through the BC Cancer Agency's Personalized Oncogenomics program.

There are many other avenues of precision medicine at earlier stages of development. Pharmacogenetics approaches provide genetic information, which can be utilized in choosing patient–specific medications and dosing regimens. Substantial fundamental work attempts to bring stratification to the individual, aiming to distinguish cells in an individual by their surface chemistries, and to design methods for targeted drug or gene delivery tailored to that individual.

With vast data output, current and future challenges include data interpretation, data storage, how to interpret variants of unknown clinical significance, and proving causality given such a complex system. Targeted gene screens or exome sequencing are currently preferred over whole genome sequencing for their speed, cost–effectiveness, and their capability to reduce discovery of variants of unknown significance. The exome is 1-2% of the genome, yet contains around 85% of Mendelian disease–causing pathogenic variants and many disease–predisposing variants.[5] Mathematicians, computer scientists, biostatisticians, and basic and clinical researchers are addressing these challenges, and success will depend largely on data sharing and collaboration—e.g., through consortia such as the Cancer Genome Atlas.

To move a technology from bench to bedside, scientific validity must be rigorously proven and coherent public policy and guidelines developed. Regulatory boards, such as the US Center for Disease Control, are developing frameworks to evaluate clinical genetic tests focusing on protection of patient confidentiality, clinical and analytical validity, data ownership, and critically, how to manage accidental genetic findings that are deemed significant but do not affect treatment, prevention, or outcome.[6]

This UBCMJ issue includes a microcosm of the breadth of 'personalized medicine': Coutin & Nislow discuss cell–to–cell heterogeneity as a critical consideration in patient variation to drug response, while Lo presents a method to supplement traditional biochemical methods for diagnosing dyslipidemias with targeted lipid sequencing panels. Shopsowitz discusses the challenges of targeting cancer cells with nanoparticle gene therapy, with the ultimate aim the provision of highly personalized treatments based on the patient's specific mutations and cell surface markers. Kosyakovsky reviews emerging research on the microbiome in health and disease. Altogether, these contributors present some of the most active areas of research in precision medicine, ranging from the fundamental science to the front lines of clinical practice.

References

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[1]MD Program, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada
[2]MD/PhD Training Program, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada

Correspondence to
Heidi Britton (heidibritton@outlook.com)
Alvin Qiu (alvin.qiu@alumni.ubc.ca)