EDITORIAL

Clinical Genomics Today

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From the discovery of the structure of DNA in 1953 to the completion of sequencing of the first human genome in 2003, the field of genomics has undergone rapid advancement and continues to do so with the advent of next-generation sequencing.[1] The popular media regularly reports new genetic findings, and genetic testing companies advertise directly to consumers, promising to unravel and to understand our genetic makeup. Likewise, 'personalized medicine' is now a buzz word in the mainstream media, pushing patients to ask their doctors about how 'pharmacogenomics' affects their medication profile. These new technologies have undoubtedly altered the landscape of genomics and will continue to transform patient care over the coming years.[2,3] But how will the era of 'personalized medicine' shape our practice as medical students, residents, and future health care professionals?

This issue of the UBC Medical Journal explores the fascinating and evolving field of clinical genomics, and contributes to the dialogue in this growing field on clinical practice. Our feature articles explore genomics education in the medical school curriculum (Friedman), and the integration of new genomic knowledge in clinical practice (Armstrong). Our other articles include an overview of drug matching to specific genomic biomarkers in cancer (Agha), an analysis of direct-to-consumer genetic testing (Dhillon), and an interview with UBC pharmacologist Dr. Stan Bardal on the study of pharmacogenomics (Aminoltejari).

That an individual's genetic signature can lead to disease has been long postulated and investigated, from the management of intestinal cancers to endocrine disorders. Newborn screening for genetic conditions, through chorionic villus sampling and amniocentesis, has revolutionized how we predict and prevent disease in those we cherish most. Similarly, we are now able to perform specific mutation testing, such as in the *BRCA* and *APC* genes, associated with breast and colon cancers, respectively.[4] Closer to home, the Treatable Intellectual Disability Endeavour in B.C. (TIDE-BC, Children's Hospital, www.tidebc.org) strives to further our understanding of the genetic causes for intellectual disability due to inborn errors of metabolism.[5] Intellectual disability (ID) affects 2.5% of the population, and often the cause is idiopathic. However, there are 81 types of ID, each due to a genetic defect that causes an inborn error of metabolism, which are potentially treatable. These treatments include vitamin and nutritional supplements that can prevent morbidities and significantly benefit a child's life, provided the correct diagnosis is made early enough postnatally and medical management appropriately directed.[5] This is but one example of how clinical genomics is able to radically change how we understand and treat disease, while there are many more areas where the genomics era is poised to offer radical alternatives in medicine.

Pharmacogenomics is another field where genetic discoveries can have significant implications on clinical care. Pharmacogenomics refers to the understanding and prediction of drug response for individual patients based on their individual gene profiles, and the appreciation of how the metabolism and excretion of medication for a given individual can ultimately affect efficacy and treatment choices.[6] Genetic testing is now more frequently done in clinical drug trials, and for medications such as warfarin and clopidogrel, this information is becoming integrated into clinical care. For example, the US Food and Drug Administration recently highlighted the importance of genetic tests to optimize dosing for patients on warfarin, given the demonstrated adverse effects occurring in patients with *CYP2C9* and *VKORC1* variants.[7] The Pharmacogenomics Knowledgebase (www.pharmgkb.org) is an additional resource, which provides clinically relevant information regarding the individual variation in drug response.[8]

While the positive impact of clinical genomics cannot be doubted, there remain important ethical and resource concerns that pertain to the widespread adoption of modern genetic methods in medicine. For example, early and extensive fetal genomic testing can be used inappropriately. Necessary pharmacogenomic testing for every individual can skyrocket already excessive health care costs. Furthermore, genetic companies that advertise direct-to-consumer (DTC) genetic testing without physician opinion or genetic counseling risk undermining the patient-doctor relationship.[9] And without background knowledge and expertise, interpreting results from genetic tests can be difficult, with a high chance for erroneous conclusions. The observed variability and poor regulation, as well as lack of standardization in DTC testing, means that some findings may have a low predictive value, while others may be wholly inaccurate.[10-12] Patients may find themselves alone when dealing with confusing information that may not be correct.

It is clear that genomics is already changing clinical practice, and will continue to do so. As health care trainees, professionals, and lifelong learners, we must understand and appreciate this rapidly evolving field, and the impact and implications of these new technologies. If used correctly, genetic technologies can be

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a pillar for risk stratification and disease prevention. It can be a cornerstone for treatment optimization and side effect reduction. Yet, the ethical, resource management, and regulatory concerns associated with these medical breakthroughs must be addressed. The age of genomics has arrived, and it is our responsibility to embrace these new technologies in an ethical and effective way, furthering the positive transformational impact they will undoubtedly have on the future of health care.

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