

# The role of genetics in medicine: A future of precision medicine

Detailing the current role of genomics/genetics in medicine and expanding on its future applications and implications.

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**A**lexis and Noah Beery were misdiagnosed and mistreated for cerebral palsy for 14 years, until genetic sequencing led to a proper diagnosis of dopa-responsive dystonia in 2010 and cured them of the symptoms that had plagued their childhood.<sup>1</sup> However, despite the power of genetic sequencing in medicine, it is still emerging in translation and is reserved for certain subsets of patients. Sequencing the first human genome was a 13-year international collaborative effort costing US\$3 billion.<sup>2</sup> Today, it can be completed for US\$1000 in under 24 hours<sup>3</sup> due to advancements in biotechnologies. This opens the door to the exciting prospect of routine whole-genome sequencing (genomic sequencing) for the standard patient, bringing forth an era of precision medicine, which tailors the prevention and management of illness to an individual patient using their detailed genomic data in combination with their environment, lifestyle, and background.

## Current uses of genetics in medicine

Prenatal screening tests are the most widely offered genetic tests across North America, whereby fragments of placental DNA fragments drawn from maternal blood are sequenced for genetic abnormalities. In recent years, cancer therapy has focused on using tumor-specific antigens<sup>4</sup> elucidated by sequencing as the targets of biologic therapies. For example, ado-trastuzumab is a monoclonal chemotherapy combination drug that has reduced the 3-year disease-free remission rate of HER2-positive breast

cancer by 11.3% from the prior standard of treatment.<sup>5</sup> Let us not forget that the sequencing of factors VIII, IX, and insulin were the foundation of pharmacologic management of hemophilia and diabetes respectively.

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Pharmacogenomics, the optimization of drug response in relation to genetics, is another promising emerging field and is a cornerstone of current genetic medicine. Ivacaftor is a potentiator of the CFTR channel and is the most effective cystic fibrosis medication on the market; however, it is only applicable to the 4% to 5% of the patient population who are homozygous for the *F508del* mutation.<sup>6</sup> In Canada, genetic testing is offered to patients only under specific circumstances, such as having a lineage of Huntington disease or a high index of suspicion for *BRCA1/2* mutations. Otherwise, patients may access fee-based genotyping through private biotechnology companies such as 23andMe<sup>7</sup> that profile patients' genomes for specific genes of interest. Whole-genomic sequencing is currently not widely available for typical consumers outside of specific research circumstances. Nevertheless, genomics has its place in current medicine and is poised to expand vastly in the next decade.

## The future of genomics in medicine

Clinician leaders visualize two primary future roles for preventive whole-genome sequencing:

1. As a noninvasive screening test for preventive medicine.
2. As a test to improve diagnostic capabilities.<sup>8</sup>

In effect, similar to how the identification of *BRCA1/2* mutation carriers led to prophylactic mastectomy and oophorectomies, early detailed genomic data would lead to valuable insight into future disease risks spanning diverse specialties from oncology<sup>9</sup> to psychiatry<sup>10</sup> and would aid in their prevention. In order to accomplish this feat, there is a worldwide push for "big data" in genomic medicine, where millions of reference sequences, individualized patient factors, and phenotypic expression are collected and coalesced into a multifactorial database and

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algorithm where individually sequenced genomes can be compared. To reach this goal, President Barack Obama launched the National Institutes of Health's All of Us campaign in 2015, mandating the collection of 1 million sequenced genomes, complementing environmental factors, and demographic information from US citizens.<sup>11</sup> Currently, over 600 000 have been collected.<sup>12</sup> This is a multinational effort; countries such as the United Kingdom and China have launched similar initiatives. The Global Alliance for Genomics and Health (GA4GH) predicts 60 million genomes will be sequenced worldwide by 2025. Just as radiological imaging has increased the positive predictive value of suspected diagnoses based on clinical signs and symptoms, and has decreased the rates of exploratory surgical procedures, genomics in medicine is poised to augment this further and add another layer of confidence to diagnostic approaches.

### Conclusion

It is exciting to hypothesize how the expanding role of genomics in medicine will impact our understanding and classification of disease. Perhaps purely clinical diagnoses such as trigeminal neuralgia, major depressive disorder, or atopic dermatitis will reform in light of underlying genetic origins. Ultimately, this will better classify our understanding of illnesses and improve treatment strategies and research.

Lastly, we cannot turn a blind eye to the barriers to precision medicine. With much of the world's population still deplete of basic resources and health care, genomics and precision medicine would primarily be a resource for developed countries in the next decade. The ethics of storing identifiable genetic information, the rights of patients to knowledge of such data, and the potential effects on stakeholders at all levels of health care are additional complex issues. However, given the current funding status and international attention garnered by precision medicine and genomics, it will certainly have its place in the future of medicine. ■

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### Competing interests

None declared.

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