A genome project for Māori and Pasifika: charting a path to equity in genomic medicine for Aotearoa

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Ever since completion of the human genome project nearly two decades ago,[1] the application of genomic medicine has promised a great deal. Over the past decade, this promise has begun to be realised. The ability to affordably sequence all 20,000 genes in the human genome, a process called whole exome sequencing (WES), and more recently to sequence entire human genomes, is changing the way genetic diseases are diagnosed or understood.[2]

Genome wide association studies (GWAS), using methods that provide genotypes for hundreds of thousands of single nucleotide polymorphisms (SNPs) throughout the genome, have identified thousands of genetic variants that contribute to many complex traits (from Alzheimer's disease to zinc levels in serum).[3] The genes and regulatory circuits identified by GWAS are radically improving our fundamental understanding of human development, physiology and disorders, and opening doors to the repurposing of drugs or development of novel treatments.[3,4] There now seems little doubt that our expanding knowledge of human genomics will steadily change the way we understand, diagnosis, manage, and perhaps ultimately prevent, the common illnesses that have the greatest impact on human suffering and healthcare costs.

However, a fundamental concern that may limit the widespread, equitable application of genomic methods in New Zealand is the relative dearth of detailed knowledge about the nature and frequency of specific genetic variants that may influence the health and well-being of Māori and Polynesian people. While we all share essentially the same genome, the precise patterns of genetic variation that can be discerned in every individual are shaped by the environments in which our ancestors lived, and the migratory journeys they undertook. Our genomes therefore not only embody and reflect our ancestries and ethnic origins, but they also influence our health, and to a greater or lesser degree chart the course of our lives. How then to ensure that genomic medicine has equal value for all New Zealanders, regardless of their ancestral histories?

In order to answer this question, it needs to be appreciated that genomic techniques all depend for their success on the mass sharing of genomic data derived from large cohorts, in public or controlled-access databases, that provide detailed information about the identity and frequency of genetic variants (mainly SNPs).[4] The majority of these data are, however, derived from European, Asian and African populations.[5] And therein lies a potential problem for people whose ancestors voyaged the oceans and founded Aotearoa, and for many more recent migrants to this country. Although many findings in genomic medicine will be equally applicable to all people, it is also clear that there will be some significant genetic differences of medical relevance that may be of greater importance to those of Māori or Polynesian descent. Two important examples are SNPs that affect the function of the pharmacogene *CYP2C19*[6] and the *CREBRF* gene,[7] which influences body mass index. While the existing genome databases may be sufficient to enable genomic medicine applications based on genetic variants shared by all New Zealanders, the relative paucity of baseline genome data

for Māori and Polynesian people will limit development of applications tailored to people of these ancestral origins.

A viewpoint paper in this issue provides a robust blueprint to address this challenge, by clearly laying down the rationale and ground-rules for an ambitious plan to develop a repository of genomic data drawn from Māori and Polynesian volunteers.[8] The key elements of this proposed framework are that governance and management will be led by Māori and Pacific representatives, the work will be informed by cultural concepts and values, it will be acknowledged that DNA storage, utilisation and interpretation is a culturally significant activity, and that the primary use of the data generated should be to drive improved understanding of the genetic contributors to health outcomes of Māori and Pasifika.

There is some very important context for the rationale suggested by Robertson et al.[8] While to some extent the approaches proposed in this paper may seem contrary to the principles of open science and extensive sharing of data (with participant consent) that have underpinned this first decade of medical genomics, it is important to remember that human genetics has a chequered history including major missteps that have engendered great mistrust amongst indigenous people around the globe.[8] Add to this the centrality of whakapapa (genealogy) to the Māori world view, the significance of DNA and genomic data as a taonga (treasure) linked to whakapapa, and the explicit obligations in the Treaty of Waitangi that the rights, interests and taonga of Māori be protected, and the foundations of this proposal become abundantly clear.

Many opportunities and challenges lie ahead in order to realise this promise of a "genome project" for Māori and Pasifika people. The opportunities include the Genomics Aotearoa platform[9] which provides an infrastructure and government funding for the proposed project; the work carried out to establish culturally appropriate guidelines for genomic research and biobanking in Māori[10]; and the database itself, which it is hoped, will drive discovery research that ultimately leads to improved health outcomes for its primary stakeholders. In addition, the scale of this project will provide opportunities for workforce development around the scientific and medical aspects of genomic data. Māori and Pasifika community leaders and education groups have done well to support training and development of many lawyers, business people, and doctors, but we need more scientists drawn from these communities who are versed in genetics, bioinformatics, and big data analyses.

On the other hand, challenges include garnering wide support for a national resource from the many Māori and Pasifika communities yet to be engaged, generating the genomic data on-shore and ensuring its storage in a secure and culturally appropriate manner, and establishing procedures that maximise the health gains from these data while limiting the perceived risks posed. The last of these would seem to present the greatest challenge, but once overcome, will be the greatest source of opportunity. The framework proposed by Robertson et al,[8] provides a clearly stated and culturally appropriate path to a future where genomic medicine will contribute to reductions rather than increases in health disparities, in Aotearoa/New Zealand.

Competing interests:
Nil.

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