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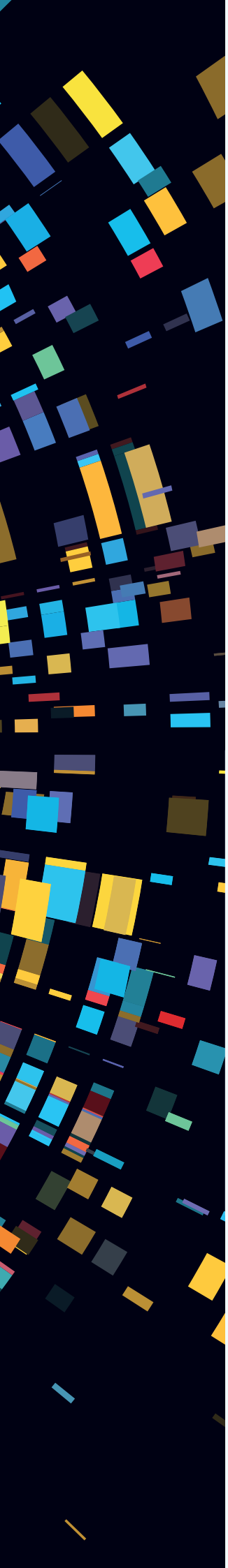
WHOLE GENOME SEQUENCING: EXPLORING THE CHALLENGES

Melody Redman and **Francis Sansbury** unpack a complex and rapidly expanding area of medicine.

key points

- Introduced in the UK in 2021, Whole Genome Sequencing is a new area of genetic testing with many applications, but which also raises many ethical and practical challenges.
- Because WGS can reveal much more information, it is both more clinically useful and likely to reveal unexpected issues and problems.
- Unpacking the human genome does not reveal who we truly are, and the authors remind us that our identity and the value of human beings transcends genetics; it is only to be found in our relationship with Christ.



The NHS introduced Whole Genome Sequencing (WGS) in early 2021 for a range of indications.[1] Further background reading on WGS and its several positive impacts is available in our blog on this topic.[2] Here, we focus on the potential challenges arising from WGS (though they may also apply to other forms of genetic testing) and then explore how we can apply a Christian worldview in this field.

what is Whole Genome Sequencing?

Our genome is our body's set of genetic information, including over 20,000 genes. Whole Genome Sequencing (WGS) aims to *sequence* all of someone's DNA, although an NHS laboratory would only *analyse* a small part of this. Often, a trio is used for WGS. This means testing the patient and both biological parents, which is helpful for interpreting the results.

the National Genomic Research Library and Big Data

Patients who undergo WGS in England are asked for permission for their genomic data to be added to the National Genomic Research Library (NGRL).[3] The NGRL stores WGS data and can also link this to the patient's wider primary and secondary care NHS records.

If a patient chooses to fully withdraw from the NGRL, their data will be removed from future research, but cannot be removed from research that is underway or has already taken place.

challenges:

incidental findings

WGS may reveal incidental or unexpected findings, such as adult-onset neurological disorders or cancer predisposition genes in children. Although NHS laboratories will not look for these, sometimes they cannot avoid seeing them.

variant classification and uncertainty

Genetic changes may be classified as a 'variant of uncertain significance' (VOUS/VUS), if there is insufficient evidence to know if the variant is a benign human variation or pathogenic. Further information (such as family segregation studies or research) may enable re-classification, but patients may be left with uncertainty. Families can find this uncertainty difficult. VUSs may be more common in different ethnic groups who have been under-represented in genetic testing.

revealing biological parentage

Because a trio would often be used (comparing the patient's sample to mum and dad), non-paternity or non-maternity can be identified. This unexpected information can cause complex ethical dilemmas and may not be disclosed if it is not relevant to the patient's care.

reproductive options

Couples may face challenging decisions about reproduction if they know their genetic status. There is some evidence that having genetic testing may help those who know their status, whether or not they opt for prenatal diagnosis.[4] Pre-implantation genetic testing involves the discarding of affected embryos.[5] Testing in pregnancy is often offered, particularly when a person plans to have an abortion if the baby is affected.[6]

> like Jesus, we must express compassion and walk with people who face these experiences

sharing information with close relatives

Obtaining a genetic result or an incidental finding may have implications for other family members. Should one's genetic information remain private to them, or should that information be shared where there are potential health impacts for others? This is a hugely complex area for individuals and for society. As clinical geneticists, whilst we seek to maintain the patient's confidentiality, we must also consider the potential risk and consequences to other family members if an individual refuses to share that information. A 2020 High Court Case (ABC v St George's University Hospital NHS FT) highlighted complexities around this balancing act.[7]

consent

For WGS, 'fully-informed' consent may not be possible.[8] Rather than using a 'consent form', NHS doctors in England use a 'Record of Discussion'[9] where we communicate types of situations such as complex, uncertain or unexpected results.

When the patient undergoing WGS is a child, usually someone with parental responsibility would complete the Record of Discussion to approve the test going ahead. Typically, parents can only consent to testing when the genetic variant would be of relevance during childhood. However, the test may reveal carrier status for recessive conditions or other incidental findings that are not relevant in childhood. How and when should these findings be communicated?

data security and access

It is crucial that genomic data is kept securely. There are also questions around access to this data – for ▶

example, should Genomics England be permitted to receive fees for using patients' data when for-profit companies conduct research?

inequities and inequalities

The dystopian near-future in the film *Gattaca*[10] shows a society where individuals are categorised and discriminated against based on their genetic composition. Polygenic screening of embryos is already available in the USA,[11] although the European Society of Human Genetics has called this an 'unproven, unethical practice '.[12]

There are already issues around equity within the devolved nations of the UK; the NHS Long Term Plan WGS aims relate to England only. There are also issues of equity worldwide.

applying the Christian worldview

God created human beings in his image,[13] and God knows us even before we are formed in the womb.[14] However, Scripture also tells of the fall[15] and that humanity is marred by sin.[16] The genomes of humans and other organisms have become corrupted, leading to death, disease, and decay. However, through Jesus, we have an eternal hope because he will return and, on that day, '*There will be no more death or mourning or crying or pain, for the old order of things has passed away*'. (Revelation 21:4) Whilst we are responsible for caring for our bodies, we must balance this with not becoming preoccupied with searching for future risks of disease or genetic perfection or believing that our identity lies in our genome.

Genetic conditions vary widely in the nature and severity of their effects. Many genetic conditions can cause great pain and suffering – both to the patient and to their loved ones. Families can experience feelings of guilt, fear for the future, and concern about other children or family members. Like Jesus, we must express compassion[17] and walk with people who face these experiences.

As with many technologies, genetic testing, including WGS, can be used for great good. For example, WGS can help reach a relevant diagnosis for the patient. However, it can also be used for purposes which many of us would regard as potentially harmful, such as testing a fetus for the presence of a condition to decide whether to end a pregnancy. We are all one in Christ Jesus, regardless of status or disability.[18] If we believe that life matters from the moment of conception,[19,20] then life should still matter, even if affected by a genetic condition. However, these decisions are highly emotive and complicated for families. God calls us to defend the rights of the vulnerable.[21] Jesus perfectly exemplified both how to be sensitive and compassionate and how not to compromise on sin.[22] The challenge for Christians is to do the same whilst protecting these most vulnerable of people.

We are also called to seek justice.[23] If an individual's ability to access insurance or healthcare were affected by their genetic blueprint, or if only the most genetically 'superior' embryos were chosen, this would introduce further inequalities into society. We must take care to safeguard against inequity and inequality.

> when we seek to build something monumental, we must carefully consider if this actually aligns with God's will

Understanding more about the genome may give us helpful insights into aspects of human health and disease, both on an individual and a societal level. 'Big data' can benefit the nation's health – such as by identifying modifiable risk factors for illness. But big data can also be used for commercial gain or other harmful purposes. There is so much that we do not yet understand about the genome. The Tower of Babel reminds us that when we seek to make a name for ourselves and build something monumental, we must carefully consider if this actually aligns with God's will.[24]

conclusion

The wider rollout of WGS in the NHS poses many potential opportunities and challenges.[25] Our genome is unique, but it is not where our identity lies. Humans are bearers of God's image. For believers in Jesus, our primary identity is as a child of God. We should seek to prevent any inequalities arising from new technologies. Where possible, we should contribute to policy-making and consultations. We should also walk alongside and show compassion to those experiencing the effects of a genetic condition or facing challenging decisions in this area. o

further reading

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