Explore the ways in which contemporary genetics both challenges and underpins notions of human freedom, value and identity

"*Maps made places on the edges of the imagination seem graspable and placable*" - Abdulrazak Gurnah, *By the Sea.*

The Age of Discovery was intimately associated with the creation of maps. The exploration of New Worlds between the 15th and 17th century was part of a global process driven by advancements in maritime technology that fundamentally altered and connected human societies. The surviving medieval 'mappae mundi' that pre-date this period lay out for the modern viewer a world that is now almost unrecognisable; centered around the Garden of Eden, their stretched vellum skins are littered with mythical beasts and biblical events. By the end of the Age of Discovery, at the dawn of the Modern era, maps looked very different. New continents had appeared and mysterious sea creatures had been replaced with trans-continental trade routes. These new maps both reflected and shaped people's changing attitudes to the world and their place in it. Now, in the Age of Information, we are witnessing the mapping and exploration of a new frontier, the human genome, a process that promises to have just as revelatory and profound an impact as the discovery of new worlds.

On September 6th 2012 the Encyclopedia of DNA Elements (ENCODE) consortium published five years' worth of combined work from over 400 scientists aimed at understanding the way the human genome functions[1]. This work was deemed necessary after the initial mapping of the human genome by the Human Genome Project, published in 2001, revealed for the first time the 3.2 billion letters that make up a human genome. A landmark achievement, it finally laid out for all to see this hitherto unmapped isle which sits within the cells of every single human being. Knowing that within its code lay the biological blueprints for transforming a single cell into a fully functioning human being, its long sequence of As, Ts, Cs and Gs was frustratingly enigmatic. The ENCODE project, by looking at how the genome uses these letters to build and regulate genes in hundreds of different human cell types, is part of global efforts by scientists to understand how the genome works.

[1] The ENCODE Project Consortium et al (2012). 'An integrated encyclopedia of DNA elements in the human genome'. Nature 489, pp. 57-74.

Just as the natural world is not just for geologists, the genome is not just for biologists. While scientists continue working to find the biological meaning within our genome, different groups are already actively using developments from contemporary genetics to both support and challenge ongoing debates and narratives relating to a huge diversity of social, political and cultural issues. As a living record of our ancestry, the genome is being extensively studied by those interested in uncovering more about their ancestry, and in so doing has supported and challenged concepts of identity. Technological developments have opened up new possibilities for medical diagnostics and treatments, while the ability to read the genome of an embryo and screen for an ever-expanding range of genetically determined health risks raises the timeless question of how we should value and treat human life. This essay will discuss a few of these themes to demonstrate the enormous impact that contemporary genetics is having on modern society.

Identity

Despite, or perhaps because of, our incomplete knowledge of how it works, the genome has become a powerful cultural symbol. In an increasingly atheistic society the letters and lines wrapped around the double helix structure of the genome have become a 21st-century scripture. People are looking to it for information and guidance about who they are and where they come from. One of the most common uses of genetic sequencing technology has been to assist people who are interested in learning more about their ancestry. Tracing of family trees has long been a past-time, recently popularised by television shows such as '*Finding Your Roots'* and '*Who Do You Think You Are?'*. Many hope that by learning about their ancestry it can give them a sense of belonging and a stronger foundation to their identity, a cure for the isolation and anomie of modernity. DNA sequencing has the potential to provide much deeper roots than traditional approaches to ancestry, as genetic markers are able to directly match regions of a person's genome to those found in different populations going back tens of thousands of years, ultimately to a shared common ancestry in Africa.

Many companies now provide direct-to-consumer (DTC) genetic tests which promise to provide a detailed account of personal ancestry based on a DNA sample. The most well known of these companies is the California-based *23andMe*, the name referring to the 23

pairs of chromosomes carried by each potential customer. With over 150,000 genotyped members they claim to offer 'the most comprehensive DNA ancestry service in the world'[2]. For less than $300 *23andMe* will genotype approximately one million informative markers across a customer's genome. The rapid increase over the years in the number of markers that are used for these tests, combined with better statistical tools to analyse the data, has resulted in these tests being increasingly accurate in their ability to identify signals of ancestry in the genome[3]. However, interpretation of these tests remains a challenge. With each generation further back in time you go, the number of ancestors we have increases dramatically, making our ancestry a complicated patchwork rather than a single thread. Considering an individual genome, there is limited power for inference as genetic markers are usually shared between multiple populations with varying frequencies. This is why personal ancestry estimates are often given with wide confidence estimates as errors are always possible. Yet as Mark Jobling, a geneticist at the University of Leicester says, "if men have a Y chromosome that is more common in Scandinavia than England, they're convinced they're a Viking"[3].

Such one-dimensional interpretations of genetic information are inevitable as they are easy to digest (and market) and appeal to our desire for a clear and stable identity. However, contemporary genetic approaches have the potential to offer a much more nuanced view of identity if the focus is shifted from a search for certainties in individual narratives to a more global perspective. Evolutionary anthropologists attempt to trace the migrations of human populations by sampling and studying the frequency of genetic variants in different populations around the world. By looking at multiple genomes simultaneously, each of these unique records can be woven together to provide a startlingly detailed picture of human migrations. A recent study combined information from hundreds of thousands of genetic markers from hundreds of individuals from over two hundred populations to identify at unprecedented details the levels of admixture between different human groups[4].

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[2] www.23andme.com/ancestry/

[3] Callaway E (2012). 'Ancestry testing goes for pinpoint accuracy'. Nature 486, pp. 17.

[4] Lawson DJ, Hellenthal G, Myers S, Falush D (2012). 'Inference of Population Structure using Dense Haplotype Data'. PLoS Genetics 8(1): e1002453.

The genome, unlike a surname or nationality, is a unique aspect of our identity in its ability to directly connect us all to a shared humanity. People will always be interested to know where they come from and identity can be as much about what is different as about what is shared. Ancestry tests marketed at consumers capitalise on people's desire to know about their unique ancestry, and there is a place for this. However, it misses the opportunity for genetics to underpin a new concept of identity. Every person's genome is the product of two human beings coming together to produce a child, a process repeated over and over again for thousands of generations. We are brief custodians of this genome sequence which we inherit; then, adding a few new mutations of our own, we fuse it together with someone else's and pass it on to the next generation. The genome by its very nature is something that marks us out as unique while at the same time connecting us to the entire human story. By focusing on the global story of human migrations and our common ancestry from Africa there is the potential for a new concept of identity to emerge that encompasses human diversity and is at the same time deeply personal.

Freedom

Our genome, as a set of biological instructions for making a living human being, has raised several issues in relation to concepts of human freedom. Through decades of debate it has become the consensus that the combination of our genome and environmental influences interact to produce our morphology and behaviour. As the science writer Matt Ridley puts it in his book of the same name, we are a product of '*Nature via Nurture*'[5]. Much of the work in contemporary genetics centers around the identification of genetic variants that influence our phenotype, primarily through large-scale Genome-Wide Association Studies (GWAS), where large cohorts of individuals that do or do not possess a specific trait of interest are genotyped to look for variants in the genome that associate with this trait.

The majority of associations that are detected explain a fairly small amount of the observed variance within populations. For example, despite the extensive studies that have gone into the genetics of human height, genetic variants identified so far can only

[5] Ridley M (2004). 'Nature Via Nurture: Genes, Experience And What Makes Us Human'. Harper Perennial.

explain 45% of the observed variance[6]. The debate on the impact of genetics on notions of human freedom has often played out like a tennis match between the relative importance of genetic and environmental determinism. Perhaps the most salient issue facing current debates is not whether genetic or environmental influences are more important, but, given that we know there are genetic variants that can predict a person's risk of developing specific diseases or behaving in certain ways, what should we do about it and what are the implications for the concept of human freedom? Different countries are dealing with these issues in myriad different ways, which are partially a reflection of their underlying social values.

As research in genetics sheds light on ever more genetic variants that play a role on our phenotype and the availability of personalised genetic testing grows, so too do the consequences of the debate on how to regulate the availability of genetic information. Many predict that the $1000 genome will soon be a reality yet in many ways the legal and ethical frameworks for dealing with genetic information have not kept pace with technological developments. Despite the efforts of projects such as ENCODE, the ongoing deluge of data still far outweighs our ability to understand and interpret it. Many caution that our enthusiasm for the potential medical benefits of personalised genetic sequencing must be balanced with the dangers of premature diagnoses based on an incomplete understanding of the results, leading to unnecessary and potentially harmful treatments, a process known as the cascade effect[7].

In the context of these issues, the freedom to access personal genetic information has been widely contested. One of the most keenly contested issues is the right of individuals to have access to direct-to-consumer genetic tests. In the United States the situation varies between State, but generally there is limited or no specific regulation over the availability of DTC genetic tests, with over 60 companies (including *23andMe*) providing such tests. A survey of over 1000 customers of such services in the USA found that the majority were satisfied with their experience and were able to understand the results[8].

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[6] Yang J, et al (2010). 'Common SNPs explain a large proportion of the heritability for human height'. Nature Genetics 42(7), pp. 565-9.

[7] Deyo RA (2002). 'Cascade effects of medical technology'. Ann. Rev. Public Health 23, pp. 23–44.

[8] American Society of Human Genetics (2010). 'Direct from consumers: a survey of 1,048 customers of three personal genetic testing companies about motivations, attitudes, and responses to testing'. Science Daily [online], http://www.sciencedaily.com/releases/2010/11/101107213820.htm

In Europe the picture is quite different. Some countries have taken paternalistic measures including legal action to limit the availability of DTC tests. For instance, in Germany the Human Genetic Examination Act (2009) states that any 'predictive' genetic examinations can only be ordered and interpreted by qualified medical doctors. The aim of the legislation is "to protect human dignity and the individual right to self-determination via sufficient information"; however, in practice such laws prevent German residents from freely accessing the kinds of genetic information that are available from DTC tests to consumers in the USA. It has been argued that such laws are the result of conservative attitudes within the medical profession, which seeks to monopolise and control access to information of relevance to health and disease. However, a recent survey of attitudes towards DTC genetic testing in Europe found that 82.1% of the general public strongly opposed such tests, only marginally lower than the 87.3% of health-care professionals who were also in strong opposition[9]. This suggests that distrust of the information provided by such tests is deep-rooted and extends beyond the health-care professions. Nevertheless steps such as those taken by Germany to restrict access to genetic information seem ill-founded. Much of the apprehension towards personalised genetic testing is driven by a lack of awareness about the information provided by genetic tests and how to interpret them. This ignorance is not unique to the general public but is shared by health-care professionals, with research showing that primary-care physicians are not adequately trained to help patients interpret single-gene test results, let alone the results of whole-genome tests, which are a rapidly approaching reality[10].

This unpreparedness is an inevitable consequence of the rapid pace of technological advances and discovery in modern genetics. The solution is not to restrict access to such information, an approach that is likely to be untenable in an age where free access to information is considered a human right, but to increase efforts to educate people to give them the ability to understand and interpret genetic information. It has been argued that the results of genetic tests which show an increased risk of disease could lead to increased anxiety, akin to seeing the cards of fate laid out in front of you. However, so far all studies

[9] Mai Y, et al (2011). 'A critical view of the general public's awareness and physicians' opinion of the trends and potential pitfalls of genetic testing in Greece'. Per. Med. 8, pp. 551–561.
[10] Guttmacher AE, Porteous ME, McInerney JD (2007). 'Educating health care professionals about genetics and genomics'. Nature Rev. Genet. 8, pp. 151–157.

into patient responses to genetic tests have shown that these concerns are unfounded[11]. Even if such information can be a cause of anxiety, it should be weighed against the potential health benefits to the individual of knowing their risks and vulnerabilities. More than 100,000 people die each year from adverse drug reactions[12]; many of these people would certainly have benefited from knowing that there are certain drugs to which they are overly sensitive.

Arguments about the dangers of exposing people to too much knowledge are an example of the propensity for genetic exceptionalism to enter into the debate about the right to freedom of information. There is a persistent belief that genetic information is somehow different and more dangerous than the results of other health tests such as blood pressure or cholesterol levels, which in many cases actually have higher predictive power of future disease risk.

This tendency for genetic exceptionalism has many causes, one being a lack of knowledge about the relationship between the genome and health. The media often portray genetics as a universal panacea to disease, with recurrent headlines about the discovery of a gene for 'X' disease paving the way for a potential cure. Unfortunately, such stories are rarely founded in scientific reality. Their ability to grab public attention is a product of the strong metaphors and associations with which the genome is imbued. Seen as a blueprint for life, there is a sense that within the genome, if only we could understand it, is the potential to understand, explain and ultimately perhaps cure all negative aspects of the human condition.

This underlying feeling can be sensed in the response to the recent announcement that 80% of the human genome has been found to be, at some level, functional[13]. Although there was some criticism of this finding, centering around the loose definition of 'functional', many geneticists announced with a sense of satisfaction that the longstanding belief that most of the human genome was 'junk' could now finally be thrown out. The previous view - that most of the human genome is non-functional - has long been a source of discomfort. It can always be argued that any part of the genome which we describe as

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[11] Guttmacher AE, McGuire AL, Ponder B, Stefansson K (2010). 'Personalized genomic information: preparing for the future of genetic medicine'. Nature Reviews Genetics 11, pp. 161-165.

[12] Lazarou, J, Pomeranz BH, Corey PN (1998). 'Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies'. JAMA 279, pp. 1200–1205.

[13] The ENCODE Project Consortium et al (2012). 'An integrated encyclopedia of DNA elements in the human genome'. Nature 489, pp. 57-74.

junk is merely a mistake driven by our current state of ignorance. However, there is also a feeling that our genome, the blueprint for making us, should be well-designed. While this is an obvious expectation of believers in Intelligent Design, who see God's work in the genome, it is also a common belief among atheists and agnostics. A genome where everything has a function reinforces the idea that life has a purpose; it makes it easier to believe that there is a meaning to our existence. A genome full of junk that has accumulated through accidental mutations, duplications and retroviral invasions makes it that little bit more tempting to think the opposite.

Whatever meaning we derive from our genetic sequence, it should ultimately be treated like all other sources of personal information. By making it available to those who want it, providing them with the right education, and putting it in the appropriate context so that it is interpreted correctly, genetic information can be helpful. Limiting access to personal genetic information is not only a violation of people's freedom to learn more about themselves - ignorance of this self-knowledge may end up being far more harmful than the information that some recent legislation has been trying to protect us from in the first place.

Value

Assuming that human freedom of access to genetic information is protected, and spreads as it is predicted to, how might this impact human values? Alan Guttmacker, Director of the National Institute of Child Health and Human Development at the US National Institute of Health, has described two divergent scenarios[14]. On the one hand, personalised genomics could revolutionise medicine by providing individually-tailored risk profiles that empower people to do more to actively manage their own health. On the other hand, the rise in personal genetic information could lead to a '*Gattaca* effect', with information being used to further an agenda of social discrimination, with employers refusing to hire individuals with a high risk of serious disease, and a growing market for genetically modified or pre-selected 'designer babies'. While both these alternative are presented as illustrative extremes rather than likely outcomes, they demonstrate the

[14] Guttmacher AE, McGuire AL, Ponder B, Stefansson K. (2010). 'Personalized genomic information: preparing for the future of genetic medicine'. Nature Reviews Genetics 11, pp. 161-165.

potential for contemporary genetics to have a major impact on human society. Such developments necessitate urgent ethical reflection.

Nowhere is the potential impact of contemporary genetics more important and more in need of discussion than in relation to pre-implantation genetic diagnosis and fetal screening. By allowing parents and medical professionals to see the entire genome sequence of an embryo before implantation, there is an unprecedented opportunity to make decisions about a child's future based on its genetic information, which may have consequences beyond healthcare. Furthermore, recent advances in fetal genetic sequencing technology could increase the number of parents opting for fetal screening, by replacing invasive methods of screening that put the child's life at risk with non-invasive approaches such as sequencing the genome of a child from a mother's blood sample[15,16].

Modern genetics cannot escape the shadow of the 20th-century eugenics movement; eugenics being a bio-social movement which sought to improve the genetic composition of humanity. Many of the scientists who pioneered our current understanding of genetics through the development of the Modern Synthesis of evolutionary and genetic concepts were active participants in the promotion of the eugenics movement. One of the most notable examples, Sir Ronald Fisher, who was one of the key participants in the development of modern genetics and statistics and hailed by Richard Dawkins as "the greatest biologist since Darwin"[17], saw the promotion of eugenics as a social and scientific issue of utmost importance. He was instrumental in founding the Cambridge University Eugenics Society, campaigned for laws permitting sterilization on the basis of eugenics and, fearing that over-breeding by people of lower intelligence risked reducing human intellectual capacity, practiced what he preached by having eight children of his own. Although eugenics fell out of favor after the events of World War 2 showed the appalling misuse of genetics in Nazi Germany, it is often forgotten that the Nazis originally modelled their eugenics policy on Anglo-American policies which promoted forced sterilization of "undesirables"[18].

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[15] Ravitsky V (2009). 'Non-invasive prenatal diagnosis: an ethical imperative'. Nature Reviews Genetics 10, pp. 733.
[16] Fan HC, et al (2012). 'Non-invasive prenatal measurement of the fetal genome'. Nature 487, pp. 320-324.
[17] Dawkins R (2010). 'Who is the Greatest Biologist since Darwin? Why?'. Edge, http://www.edge.org/3rd_culture/leroi11/leroi11_index.html#dawkins
[18] Weindling P (2010). 'Genetics, eugenics, and the Holocaust'. In 'Biology and Ideology from Descartes to Dawkins', eds. Alexander DR, and Numbers RL. University of Chicago Press.

New technologies are paving the way for new ways to modify the genetic composition of the human population. The 20th-century eugenics movement was driven primarily by a top-down coercive approach aimed at improving the human condition. The modern use of genetic technologies to improve the genetic makeup of offspring is expected to be more of a bottom-up movement driven by the desire of individuals to produce genetically fit offspring. Some have argued that therefore an entirely different type of ethical debate is necessary to deal with the potential use of these new reproductive technologies, which Lee Silver, professor of molecular biology at Princeton University, has termed 'reprogenetics'[19]. However, taking a deeper historical perspective, one can see that the desire to produce maximally healthy and successful offspring is a universal feature of human individuals and societies that pre-dates the 20th-century eugenics movement. In the Classical Greek state of Sparta, new-borns were brought before the Gerousia, a council of elders, to decide if the baby should be reared or not. Those considered 'puny and deformed' were thrown into a chasm on Mount Taygetos to die[20]. While this is the most well-known early example of eugenics there is evidence that several other regions engaged in similar practices to remove children deemed unfit[21].

Another well-known and longstanding practice that continues to this day is the favouring by parents of offspring with a Y-chromosome, leading to sex-selective infanticide. In societies where cultural norms value males over females parents may benefit more from raising male offspring. Advances in pre-natal sex determination in recent times have made it simple to identify the sex of a child before birth. The exact number of fetuses that are aborted based on sex is hard to estimate and varies between countries but significant deviations from the expected sex ratio suggest that in China, for example, around a million female fetuses are aborted every year in a silent slaughter that was exacerbated by the imposition in 1979 of the one-child policy.

The methods to explicitly improve the genetic composition of a population that a Western audience are most likely to be familiar with are the practices of the 20th-century eugenics movement. The early practice, in the USA and some European countries, of

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[19] Silver LM (2007). 'Remaking Eden: How Genetic Engineering and Cloning Will Transform the American Family'. Harper Perennial.
[20] Cartledge P (2001). 'Spartan Reflections'. London: Duckworth.
[21] Buxton R (1999). 'From Myth to Reason?: Studies in the Development of Greek Thought'. Oxford: Clarendon Press.

castration of those catagorised by the government as mentally deficient was replaced, due to technological advances, by sterilisation, which was considered a much more palatable and less harmful procedure[22]. These government programs of sterilisation were frequently based on IQ levels, a thin veil that in practice, due to biases in the tests, meant the targeting of those of low social status and minority racial groups. They were the consequence of societies with deep social divides, and which saw intelligence as an innate sign of worth rather than the product of a beneficial environment. The top-down nature of these programs was an inevitable consequence of the technologies available. Nobody was going to volunteer to castrate or sterilise themselves.

This recognition that human societies have been practicing genetic selection of offspring long before the advent of modern technologies is not to say that therefore there is no need for new debate; on the contrary, it is to emphasise that the place for these new technologies must be seen within the larger perspective of longstanding and deeply-rooted human motivations. Societies impose cultural norms and individuals then act within these constraints to maximise their opportunities. Any attempt to consider the ethical issues associated with genetic practices and human values must therefore address both ends of the scale, the wider social pressures and the rights of the individual.

How will people and societies react to the availability of pre-implantation genetic diagnosis technology that allows them to know and perhaps, one day, modify the genome sequence of a future child? As we have already discussed, this will depend on the cultural values of the society in which the technology is available. In a culture that values men over women it is likely that such technology would be used so that parents could preferentially select the gender of their offspring. This would be a continuation of the old practice of sex-selective infanticide made more efficient by new technology. Something more novel would be parents selecting between embryos whose genetic sequence predicts the highest IQ. Such technology would allow goals of the 20th-century eugenics movement, which were previously only achievable through state intervention due to technological limitations, to be carried out through the individual choice of parents.

This inevitably leads to the fear of the 'designer baby'; once a term found in the realm of science fiction, it now seems more and more like an imminent reality. Despite many

[22] Larson EJ (2010). 'Biology and the emergence of the Anglo-American eugenics movement'. In 'Biology and Ideology from Descartes to Dawkins', eds. Alexander DR, and Numbers RL. University of Chicago Press.

people's aversion to the concept of designer babies, in one sense such a practice would only be a slight change from the genetic selection that people already practice when they choose a partner, and in doing so pre-select 50% of their future child's DNA. We defend an individual's right to chose a partner, so why not their right to chose between a few genetic variants that will make up a tiny percentage of the resultant child's genome? The negative feelings people have towards the concept of genetically manipulating embryos are in some ways akin to attitudes towards domestic crops and animals. Few people have a problem eating organically grown foods, even though the vast majority of these have been subject to artificial selection for favourable traits by farmers for thousands of years. However, these same people often refuse to eat genetically modified foods because of concerns about interfering with nature and 'playing God'. Such arguments are often based on fear, born out of a lack of understanding about the genetic manipulation that already occurs without any explicit intervention in the laboratory.

Perhaps a more credible criticism of the goal of genetic improvement is that it is dependent on the concept of Platonic idealism - that there is an ideal human form to which we should aspire. It requires one only to look between cultures, or a short distance back within a culture, to see that the physical and mental attributes which are most highly valued can vary greatly. Pedigree breeds of dogs serve as a warning against this genetic agenda, as efforts to create ideal forms of dog through breeding resulted in the subsequent emergence of many severe health conditions, due to excessive inbreeding and loss of genetic diversity in these populations. Humans already possess relatively low levels of genetic diversity, much less even that our sister species the chimpanzee, despite their much smaller population size, a consequence of the extreme bottlenecks that characterised the early demography of our species. In striving towards an ideal form of human there is the risk of destroying the diversity that is necessary to flourish.

Conclusion

Everyone wants their children to be healthy and happy. With developments in technology, new avenues are opening. How far are societies and individuals willing to go to further this objective? How far is it right to go? These ethical questions are in urgent need of being addressed by transparent public debate. To do otherwise would leave the development and application of these technologies in the hands of interested minority

groups who may not be acting in the general interest. This has happened before with reproductive technologies and should not be allowed to happen again. The conclusions of this debate will set the agenda for the moral and biological development of our societies.

The ethical and social issues surrounding developments in contemporary genetics can be as slippery to get a hold on as the twisting double helix. At the heart of the debate is the genome itself. Created by the fusion of two gametes, few acts are more universally considered sacred. The debates surrounding genetics are filled with contradictions. We believe in the sanctity of life yet we routinely abort fetuses because of inherited health conditions. We live in a society that values the individual's right to information yet countries pass laws restricting people's access to read their own genome. To talk about the genome and genetics is to talk about life itself. Notions of human freedom, value and identity are all inseparable from the scientific endeavor of genetics. Advances in genetics have the potential to do tremendous good, particularly in the field of medicine. However, there is also the danger that genetics can be used as a tool and a justification for stigmatization, discrimination and oppression. The moral and ethical implications of the genome are as diverse as the sequences themselves, rising out of the synthesis between our developing scientific understanding and the social circumstances surrounding and driving their discovery. As we move forward one thing is certain, we can expect the uses and abuses of contemporary genetics to change and mutate just as frequently as the genome itself.