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Professor Mattick is well known for showing that the majority of the human genome is not junk but rather specifies an RNA regulatory system that organises our development. He has published over 300 research articles and reviews, which have been cited over 70,000 times. His work has received editorial coverage in Nature, Science, Scientific American, New Scientist and the New York Times. He also developed one of the first genetically engineered vaccines and established one of the world’s first facilities capable of sequencing human genomes for $1,000, along with one of the first clinically accredited centres for whole genome analysis in healthcare.

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Cover image: Genetic research and biotech science concept. Human biology technology on abstract digital background. Colour manipulated from original: iStockphoto/ipopba.
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Biotechnology is the next industrial revolution, with the potential to rival others in its social and economic impacts. The pace of change is accelerating, and biotechnology is becoming an information industry with digital deliverables. The analysis and manipulation of genomic information is transforming life sciences research and all of the biological enterprises—healthcare and medicines, agriculture and farming, natural products, and environmental management—among the most important and fastest growing sectors of the global economy.¹

The value of two genetically engineered pharmaceuticals equals that of the total agricultural production of Australia. As with the electronics revolution, biotechnology will create new and unexpected applications, opportunities and threats, based on genetic data, genetic engineering, biosensors, bionic devices, organic nanostructures and biochemical principles.

There is a once-in-a-generation opportunity for Australia to be a foundational player in this major industrial transition, capitalising on our long-term investments in biomedical science, agricultural R&D and high-quality healthcare systems. Within a decade or two, all being well, there will be hardly any medical research program, healthcare encounter or health economic decision that won’t depend on or make reference to genomic, clinical, pharmacological and smart-sensor data.

The provision of that information requires the development of infrastructure for the collection of data and secure databases. It will also require advanced analytical software and point-of-care reporting systems that are yet to be built, which will have huge value and can be exported to the world. Biodata will also be used in many other spheres, including customs, quarantine, the protection of commercial rights, quality control, provenance, security and policing. Clearly, privacy and security of this data are essential.

Genetic engineering can now be done with speed, sophistication and precision that were unimaginable just a few years ago. It will improve the efficiency, quality and range of biological production, while at the same time reducing environmental footprints. Artificial intelligence operating on genomic and physiological data will accelerate discovery and create new intellectual property and products for the Australian biotechnology, pharmaceutical and agrifood industries. Genomic data and computer simulation will accelerate drug and vaccine development and place Australia in a stronger and more secure position in our economy, health and quality of life.

However, while we have the technical infrastructure and human capital, Australia currently lacks a vision for what its healthcare system and bioeconomy could look like in 20 years and a strategic plan to achieve that vision, especially in gathering and integrating genomic, clinical and physiological data.

The benefits of this vision and plan need to be proselytised with the community, and social, ethical and legal issues need to be addressed from the outset. There are national security issues, vulnerabilities and sensitivities to consider. The plan needs to be resourced by the astute and coordinated application of funds that are available to the Medical Research Future Fund, rural R&D agencies and public–private partnerships. Computer programming, bioinformatics and big-data analysis skills should be taught as core components of science and engineering degrees, and advanced capacities in those areas should be built into all biomedical and biological research institutions as well as all health, agricultural and environmental management enterprises and security agencies.
INTRODUCTION

Biotechnology dates back over 6,000 years to the domestication of wheat and the use of yeast for fermentation, but has entered the province of human design and invention as a consequence of the gene cloning, gene manipulation and genome sequencing revolutions of the past 50 years. While often thought of in terms of drug development and genetic engineering, biotechnology is fundamentally becoming an information industry with a universe of applications.

The speed of change is accelerating, and biological technologies are intersecting with optical technologies, nanotechnologies, advanced computing and artificial intelligence to create possibilities that were, if not beyond imagination, well beyond feasibility just a few years ago.

The diversity and complexity of life on Earth are, literally, amazing. Now humans have acquired the ability to read the genetic programming and analyse the structure of the molecules of life—how cells work, how we’re different from each other, and what makes a lime different from a lemon. Life has evolved the most exquisite nanotechnologies—protein machines that can bind oxygen and almost any other type of molecule; trap photons to turn carbon dioxide and water into carbohydrates; detect electric fields or sound waves and turn them into visual images; pump ions; facilitate the entry of viruses, bacteria and parasites into cells; and make molecular motors that spin or contract to trap prey, exert force and move.

There are also lateral applications. Understanding the principles of information storage in the human genome and the marriage of organic and inorganic chemistries will revolutionise computing and detection systems. Bionic devices will restore the loss and extend the range of human capabilities. The list goes on, and the potential to harness and expand the sophistication of biological systems from the molecular to the macro level is evidenced by the fact that we’re yet to emulate the sensitivity of canine olfactory receptors or the natural tactile sensitivity and finesse of the human hand in robots—but we will.

In this paper, I canvass current and foreseeable developments in biological technologies and information in four key areas, which intersect, and their potential and the strategic considerations for enhancing Australia’s health, economy, security and quality of life:

- genomics, big data and precision healthcare
- gene therapy and genetic engineering
- pharmaceuticals and vaccines
- bionic and biometric devices.

I don’t attempt to provide comprehensive coverage of these domains—that would be impossible, short of a report that is an order of magnitude larger. Rather, I canvass the landscape to apprise non-experts of the opportunities and issues and to inform strategic policy.
Life is the product of information, which is encoded in DNA and its related form, RNA. That information specifies an organism’s systems for gathering energy and raw materials, manufacturing organic compounds and programming cell and developmental biology. DNA and RNA are linear strings of four letters, or ‘bases’—A, G, C and T (or U in RNA)—strung together on a sugar-phosphate backbone. DNA is double-stranded—the iconic double helix—and one strand is the complement of the other (A pairs with T or U, and G pairs with C), thereby allowing replication. RNA is (usually) single stranded. It is copied from DNA in the process of gene expression and functions as a template for protein synthesis and as the regulator of differentiation and development.

The human genome comprises about 3.3 billion base pairs of DNA, which is, in raw computational terms (‘bits’ or ‘bytes’ of information), smaller than the Microsoft Office software program but powerful and sophisticated enough to direct the development of an organism that can run marathons, compose music and design spacecraft.

Humans vary in their genetic programming by about 0.1% (3–4 million DNA sequence differences), which is the basis of our physical and, to some extent, psychological diversity, as well as our different susceptibilities to various diseases and disorders. Human genomes differ from those of chimpanzees by 1% and by greater amounts from other mammals, more distantly related vertebrates, and so on. Cognitive programming takes up an increasing proportion of the genome as intelligence increases and requires the superimposition of molecular plasticity for the organism to be able to gather environmental information and learn. At the other end of the scale, bacteria contain an eclectic repertoire of genes capable of metabolising almost any organic substance, while viruses pack into a capsule enough genetic information in a few thousand bases to infect and replicate inside host cells, often with devastating consequences.

The genetic information revolution started in the 1970s with the development of enzymes that enabled DNA to be precisely cut, pasted (‘recombined’) with other DNA and grown (‘cloned’) inside bacterial cells. Methods were subsequently invented to replicate DNA rapidly in test tubes, and it has become a trivial task to isolate and amplify any specific gene or stretch of genes from any organism. This capacity in turn enabled the development of DNA sequencing technologies, which culminated in the Human Genome Project at the turn of this century.

Generating the first human genome sequence (a compendium assembled from different individuals) took 13 years and cost US$1 billion, and was a major milestone in human history—it gave us the ability to read our own genetic inheritance, although only a small part of it made sense.

At that time, DNA sequencing technology was evolving rapidly, at much the same speed as computers—following the famed Moore’s Law (see Figure 1), which holds that speed and capacity double and costs halve every 18 months. This changed and went hyper-exponential in 2007 when a new technology was introduced—a brilliant mix of DNA, chemical, optical and nanotechnologies, acquired from the UK start-up company Solexa and developed

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* DNA is the genetic material in all cells and many viruses. Some viruses, such as HIV and coronaviruses, package their genetic material as RNA, which is converted back into DNA in host cells.
by Illumina Corporation in San Diego—which allowed billions of DNA molecules to be sequenced in parallel by replicating them with fluorescently labelled bases.'

Figure 1: Cost per human genome, 2001 to 2019 (US$)

Source: 'The cost of sequencing a human genome', National Human Genome Research Institute, no date, online.

Other technologies have also entered the market, such as the semiconductor-based Ion Torrent system from Thermo Fisher Scientific. Other technologies have also entered the market, such as the semiconductor-based Ion Torrent system from Thermo Fisher Scientific.

By 2014, it became possible to sequence an entire human genome in a few days for just US$1,000.† The price decline has since slowed because of limited competitive pressure, and the price is currently about US$600 per genome but is likely to fall again with the advent of new sequencing technologies based on protein nanopores and high-resolution optics. Presently, around 6 terabases ($6 \times 10^{12}$) of sequence can be generated in two days by one person on one instrument (Illumina NovaSeq 6000) for a few thousand dollars. This exceeds by a factor of 40 the approximately 23 gigabases that were generated for the first draft human genome sequence.

Oxford Nanopore has developed a sequencer that measures the electrical charge disturbance caused by DNA transiting through a protein nanopore. One version of the sequencer is about the size of a harmonica, plugs into a computer USB port and can be used in the field, as it was to great effect during an Ebola outbreak recently (Figure 2). This technology is cheap and portable and is democratising the acquisition of genomic data.‡

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* This generates enormous amounts of data—the latest machine yields up to 20 billion sequence ‘reads’ and 6,000 gigabases of DNA sequence per run (about 2,000 human genome equivalents), but has the disadvantage that each sequence read is short, requiring high-density coverage of the fragments (usually 30×) to assemble a relatively complete sequence.
† One of the first of these instruments was installed at the Garvan Institute of Medical Research in Sydney.
‡ The Oxford Nanopore sequencer generates very long sequences (more than 1 million bases), which makes genome assembly much easier.
Newer sequencing systems, such as that being developed by XGenomes in Boston, promise to be able to sequence a human genome for US$100 using compact ultra-high-resolution microscopes, such as those being developed at the University of New South Wales (UNSW). Suppliers of existing technologies also promise to be able to reduce the cost of human genome sequencing to US$100, mainly by reducing reagent costs, although they’re seemingly in no hurry to do so, which provides a window of opportunity to get ahead of the curve by anticipating the road ahead.

The ability to sequence genomes at high speed and low cost is leading to an avalanche of information about the differences between individuals and species and their evolutionary history, relationships and molecular toolkits. This work includes the 1,000 Plant Genomes Project, the 10K Vertebrate Genomes Project and the Earth BioGenome Project, which aims to characterise the genomes of all of Earth’s animal, plant, fungal and protozoan biodiversity over the next 10 years. A quirky example is the publication in 2019 of the genome sequences of all butterflies in North America. Much of this information will be made available online.

The global sequencing market is predicted to grow from over US$10 billion in 2018 to around US$25 billion by 2023, with a compound annual growth rate of around 20%. Extrapolation to entire populations for both base genome data and diagnostic sequencing in cancer, and the use of sequencing in agriculture and other domains, will lift the market size to trillions of dollars, even before the value of the information and the provision of analyses are taken into account.

China is taking a strategic approach. It has established the Beijing Genomics Institute (BGI) in Shenzhen. BGI has acquired technology that rivals Illumina’s by purchasing a US competitor, although it is also defending several patent infringement lawsuits from Illumina. While ostensibly privately owned, BGI is operating at such a scale that it is likely to be state-subsidised, potentially able to gather genomic and other data from research institutions worldwide, including those in Australia. BGI also has a forensics arm known as FGI (Forensic Genomics International), which performs prenatal genetic testing in Australia, as do some local laboratories using US technology.

Personal genomic information is among the most valuable—and sensitive—assets on the planet. This also extends to the genomic information of all life. BGI understands this.
The practical applications and therefore the economic value of this data and the growing biological information economy are enormous. And they’re ideal for constructive exploitation by an advanced mid-sized economy such as Australia’s, which continues to be heavily dependent on primary (agricultural and mining) production and which urgently needs to be diversified and strengthened by developing other industries with high growth potential, such as those based on medical and biological knowledge. As Australia seeks to build its economy in a post-pandemic world, directing resources and effort to this growth area makes economic and strategic sense.

**Precision healthcare**

Healthcare ranks alongside food, energy, shelter, finance, transport and communication as the most important parts of the global economy. Indeed, health is the foundation of any economy. The sector is also growing rapidly—the prosperity gained from increased efficiencies in agriculture, mining, manufacturing and service industries is expended on lifestyle and health, with health eventually taking precedence over all others.

Healthcare is one of the last industries to enter the digital age, whereupon it will be transformed from *ad hoc* crisis management to strategic wellness management by personal genomic information and physiological data from smart sensors. There will be inertia and resistance from established structures and vested interests, requiring creative disruption and purposeful investments to overcome them. The most obvious source of interest and investment is the public and private health insurance sector, whose main driver is to reduce costs while improving outcomes, but the sector is under chronic financial strain. Nonetheless, this is one of the few areas where Australia might be able to leverage its comparative advantages at a time of rapid change and (therefore) great opportunity by developing global health information services that not only transform health, healthcare and health economics but also transcend the tyranny of distance.

Every aspect of health is strongly influenced by genetic factors. As surprising as it may seem, even individual vulnerability to infections by parasites, fungi, bacteria and viruses—such as malaria, polio, coronavirus and tuberculosis—is affected by personal genetic differences. Infection is, of course, dependent on being exposed to a pathogen in the first place, but its severity and course or even our awareness that it has happened are determined by idiosyncrasies in our immune system and our general state of health. If everyone is infected by a given pathogen, the subset that will become seriously ill or die isn’t random. This includes susceptibility to the Covid-19 virus, the severity of the symptoms, or both, although advanced age and comorbidities such as diabetes, hyperglycaemia and heart conditions are also major factors. It’s not genes versus environment, but both.

Likewise, while susceptibility to complex diseases such as diabetes, heart disease and cancer is heavily influenced by environment and lifestyle, those extraneous factors usually lead to disease only in genetically susceptible individuals. There are many people who are obese or smoke heavily who don’t contract diabetes or lung cancer, respectively, and, while at increased environmental risk, have low genetic risk.

Some people who smoke get emphysema and others don’t. Individuals with mutations in the alpha-1 antitrypsin gene, which protects the lungs from irritant-provoked immunological damage, are at high risk of emphysema and should be counselled not only not to smoke but also not to work in dusty environments, such as mines or bakeries. A recent US–Australian study showed that 7% of people with defects in a gene that predisposes to cancer have incipient early-stage tumours that they’re unaware of, which could easily be removed by surgery, but are otherwise ticking away like time bombs until they metastasise, and the system then has to throw the bus at them to try to save the person’s life. Identification, targeted advice and regular screening of at-risk individuals would save a lot of heartache and a lot of money.

* An exemplar is cardiovascular disease: over the past 40 years, death rates from cardiovascular disease have massively declined relative to other causes of mortality, with concomitant extension of lifespans, due to the shift from crisis management to wellness management.
† Including clinical geneticists, who will resist the democratisation of genomics and its use in all branches of medicine.
‡ This would not require Australian access to genomic and sensor data from other jurisdictions, but rather the provision of software and systems that can be used locally.
Complex diseases, such as Alzheimer’s disease, Parkinson’s disease and other neurodegenerative disorders—increasing problems in an ageing demographic—as well as neuropsychiatric disorders, which play havoc with the lives of younger people and those under economic and emotional stress, also have strong, albeit as yet not well defined, genetic components. The relevant genetic variants have proven hard to pin down by genome association mapping but are likely to be revealed as population-scale genome sequencing accelerates in the years ahead, as costs come down and national programs ramp up.

This knowledge will allow not only better diagnosis and earlier intervention to head off disease but also the identification of the biochemical pathways disturbed in these conditions and rational approaches to rectifying such disturbances, including new targets for drug development.

In late 2018, the UK announced the genome sequencing of a minimum of 1 million and a stretch target of 5 million people (approaching 10% of its population) in the following five years. The US ‘All of Us’ project will likewise sequence a million or more people in the next five years and is planning to integrate that information with electronic health records. China is reported to have the ambition to sequence 100 million genomes or more by 2030. Unfortunately, no such national ambition or program has yet been articulated in Australia; some ‘demonstration’ projects that involve genetic testing in rare diseases and cancers have been funded, but at a much lower scale and with less strategic organisation than necessary if Australia is to be a major player in the field.

Diagnosis, treatment and elimination of ‘rare’ diseases

Around 3% of the population are affected by developmental or intellectual disorders, often both, due to mutations in protein-coding genes, many of which have devastating impacts. Well-known examples are cystic fibrosis (defective salt transport), thalassaemia (defective oxygen transport) and Huntington’s disease (defective nerve cells). While these disorders are easily recognised from symptoms and family history, there are thousands more, which are individually rare but collectively common, that arise from damage to other genes. Such ‘rare’ diseases are estimated to result in over 10% of all hospital inpatient expenses in Australia and, in the case of those causing intellectual disability, an average of over $250,000 in annual healthcare and social support costs.

Genome analysis is transforming our ability to identify the genes responsible for these ‘rare’ diseases, with success rates of 50% and rising, giving closure to families desperate to know the nature of the problem, enabling renewed reproductive confidence and informing optimal treatments, sometimes with transformational outcomes.

Genome analysis is now, or soon will be, the first line of diagnosis of any serious condition of unknown origin—it will be the standard of care. It will be aided by more sophisticated phenotyping, such as the CliniFace initiative in Western Australia, combining the faces and voices of children and families to better diagnose rare disorders. Moreover, as the international databases grow, genetic disease diagnoses will become increasingly automatic, and at least some conditions will be repaired by gene editing and gene therapies (see below).

It’s also likely that pre-conception screening will greatly reduce the occurrence of genetic diseases in following generations. Genome analysis allows the identification of the approximately 1 in 15 couples at high risk of having a child with a severe genetic disorder and the consequent mitigation of that risk, reducing the incidence and burden of such disorders in the community, and bringing enormous reductions in costs and family distress.

This is an area that could benefit enormously from strategic thinking in relation to both health and health economics. While genome analysis is still relatively expensive, it may be much more cost-effective than current modalities—the often fruitless diagnostic odysseys that families have to endure and the health system has to pay for—even without considering the millions that are saved over a lifetime in those cases in which the diagnosis has led to an effective treatment, which is sometimes as simple as a dietary modification or a repurposed drug.

Most hospital genetic clinics and rare-disease research projects prefer the use of cheaper forms of genomic analysis called ‘panel’ or ‘exome’ sequencing, the latter of which polls just the 1% of the genome that encodes proteins. This is a false economy, not for the clinicians or the researchers, who are constrained for funds and have no incentive to
think or act strategically, but rather for the healthcare system. A whole-genome sequence not only gives a much higher rate of diagnosis but also provides a near-complete compendium of genomic information, including about risks for other conditions that may strike later in life and about adverse or non-responses to pharmaceuticals, which can be used to optimise that individual’s life journey.40

Strategic thinking in the application of genome sequencing and analysis, which may be prompted by an immediate problem but has lifetime value, would not only save money in the long term but also build the national genomic estate and the future of genomic medicine.49 The UK and China have established national genomics and health data centres,50 and the US is attempting to federate such data,51,52 but Australia is yet to do so.53 There’s a good case for initiating the acquisition of population-wide genomic data by replacing the Guthrie test (a neonatal heel-prick that polls a number of genetic conditions and is routinely carried out at birth)54 with whole-genome sequencing, although the value proposition would have to be well explained.

Cancer

Cancer is now the leading cause of death in higher income countries.55 One rapidly growing application of genome analysis is cancer diagnosis, in which the identification of the underlying ‘driver’ mutations is leading to extraordinary improvements in outcomes by identifying the correct treatment or likely response to pharmaceutical and immunotherapy, leading to substantial increases in life expectancy and, sometimes, permanent remission. Good examples are the recent cases of two children in Sydney, one with a thoracic sarcoma (connective tissue cancer) that was so large it could not be removed and was crushing her lungs, and the other suffering multiple metastases from a glioma (brain cancer), almost certainly fatal. The mutations driving their cancers were identified by genome sequencing, and both children were successfully treated with drugs specifically developed to block the activity of the aberrant proteins produced by those mutations and are apparently now disease-free.56 Beyond anecdote, the federally funded Australian Genomic Cancer Medicine Centre57 has doubled cancer response rates and progression-free and overall survival in patients who receive a matched therapy based on genomic tumour profiling,58 replicating data from multiple international studies.59-66 Genomic data also allows not only much more efficient but also new models for drug development and clinical trials that are particularly well suited to Australia’s circumstances and assets (see below).

It isn’t hard to envisage that the patient demand for such diagnostics and targeted treatments will rise rapidly and that genome sequencing of tumours will also become the expected standard of care. Indeed, it will be unethical not to offer this option. It may also be the cheaper option, despite the high costs of on-patent drugs, due to the reduction in adverse responses endured with blunderbuss chemotherapies. And, again, prior knowledge of risk, based on the genomic identification of inherited mutations in cancer-related genes, will enable more cost-efficient screening and effective early intervention.

From illness to wellness

It seems certain that, as the costs of genome sequencing and analysis continue to decline (as they will), personal genome sequences will be progressively incorporated into health records and be used to anticipate and take early mitigating actions to prevent disease and enable the identification of and regular screening for timely surgical interventions in those at high risk of cancer. This should also change insurance dynamics for the better (see below).

Genome analysis will also avoid a substantial fraction of adverse reactions to prescribed medications, sometimes fatal, which account for 4–10% of hospital admissions67-70 (and up to 30% of all hospital admissions in the over-65s)71 and most readmissions in advanced economies.72 Genomic analysis can also improve the efficacy of prescriptions, many of which are currently medicinally useless because of underdosing of individuals who are fast metabolisers of the drug, the wrong choice of drug for their innate physiological attributes, or misdiagnosis of the underlying condition.73,74 For example, the anticoagulant clopidogrel is ineffective in many patients, and toxic in others, due to natural variations in the genes encoding the enzymes that metabolise drugs.75 Differences in the rates of clearance of drugs mean that their circulating concentration is high in some people, leading to toxicity, and does not reach
therapeutic levels in others—a problem at both ends of the spectrum and a particular issue in the polypharmacy of the elderly.76-78

Genome data will also transform drug development and rescue useful drugs that failed clinical trials. At present, pharmaceutical companies are faced with the dilemma of selecting a dose that shows sufficient benefit and sufficiently low toxicity to acquire approval—a one-size-fits-all approach when no one is average. Genome sequencing of participants in clinical trials enables better stratification, higher success rates, earlier fulfilment of phase 3 milestones,79,80 more accurate prescription of drug and dose, reduced adverse reactions, improved efficacy, and large savings in both pharmaceutical development and healthcare costs.81

Population-scale genome sequencing will also identify a host of other rare—and not-so-rare—but avoidable conditions. For example, 3 in 4 people per 1,000 have an undiagnosed genetic condition that causes high levels of ‘bad’ cholesterol (called familial hypercholesterinaemia), which, if not identified and treated, leads to a high risk of coronary heart disease in later life.*

One in 10 of us will end up in hospital at some point in our lives because of a simple genetic condition that can be identified ahead of time from a genome sequence and in many instances easily avoided. A high proportion of cardiac arrests in the young have genetic causes (structural and arrhythmogenic heart abnormalities),83 which can be identified by genome analysis and prevented by a pacemaker or appropriate drug treatments, or even by the avoidance of strenuous competitive sports. A case can be made that all unexplained sudden deaths that don’t involve misadventure should be subject to a genomic autopsy, if for no other reason than to alert surviving family members to their potential risk, test their genomes for the presence or absence of the damaged gene and, where required, institute preventive measures. Genomic sequencing may also avoid false prosecutions for unexplained child deaths.84

There are immense opportunities to apply genomic information to the diagnosis and treatment of chronic conditions with unknown causes. For example, chronic pain is one of the most common, distressing and burdensome forms of disability (around 20% of Australians are experiencing it at any one time)85 and is listed among the conditions with the highest disability burden, according to the 2016 Global Burden of Disease Study.86 One underlying cause is histamine intolerance, which occurs in about 1% of people because of a defect in the production of the enzyme diamine oxidase. This results in a range of inflammatory symptoms, including chronic (most commonly gastrointestinal) pain, asthma, migraine and eczema, but is frequently, if not usually, undiagnosed.87,88 This condition can be identified by genome analysis and then simply and effectively treated with a low-histamine diet and enzyme supplementation.89 Similarly, migraine headaches associated with specific genetic variants in enzymes that protect against excess levels of catecholamine neurotransmitters and hormones can be alleviated by reducing the dietary intake of inhibitors,90 while migraines associated with other genetic variants are treatable with vitamin supplementation,91 but such treatments are not indicated without genomic information.

Genome analysis may also be used to more accurately anticipate and mitigate individual risks of complex disorders such as diabetes, high blood pressure and other cardiovascular disease using ‘polygenic risk scores’.92 It will allow automatic high-resolution blood typing and transplantation donor matching, among many other things.

Finally, genomic analysis can be used to track infections, as is being done presently with Covid-19, by identifying idiosyncratic pathogen genome changes that characterise particular outbreaks, as well as identifying natural inherent human host genome variations that partly determine whether individuals succumb to the infection in the first place and subsequently have specific complications, or are asymptomatic.

Thus, genomic analysis will empower a huge shift from practising medicine according to the mythical ‘average’ person, unaware of personal genetic factors, to tailored individual ‘precision’ medicine—summarised as the

* In the UK, 50% of males and 30% of females with undiagnosed familial hypercholesterinaemia will have developed coronary heart disease by the age of 55.82
4 Ps: predictive, preventive, personalised and participative—in what’s arguably the biggest advance in healthcare since sanitation.

Data from the internet of things

The health impact of genomic information will be further enhanced by intersecting it with physiological and environmental data from smart sensors that detect heart rate; blood pressure; temperature; circulating levels of glucose, biomarkers or prescribed drugs; the amount a person moves each day; gait changes (indicating the possibility of physical and neurodegenerative disorders); sleep–wake patterns; and so on. Such sensors are increasingly built into personal devices, including smartphones and ‘fitbits’, as well as into wearable patches or implantable devices. More than a million health and wellbeing apps are available from the Apple and Google app stores, and many of them are linked to internal or external smart sensors. There are even apps that can detect respiratory disorders, including Covid-19, based on the cadence of the voice, breathing patterns and coughing. Ingestible sensors are even being placed into pills to monitor medication usage and compliance and physiological responses. While the companies concerned have struggled to gain traction, there’s an inevitability about the trajectory of the intersection between healthcare and the internet. Smart-sensor data is far richer than, and can enormously add value to, clinical and pharmaceutical records, as it supplies, agnostically, real-time physiological data that can be interrogated and analysed for disease identification, stratification and the value of interventions. Little, if any, of this data is being harvested by the national healthcare system.

Some of these issues have been canvassed in a recent report from the Australian Academy of Technology and Engineering, the recommendations of which include mandatory use of electronic health records and the incentivisation of the adoption of wearable monitors. The benefits are clear, but some may be concerned about the potential for negative interplay, which can and will be exaggerated, and the opportunity may be compromised unless there’s proactive and transparent presentation of the value proposition and safeguards.

Data integration for research and health management

Software can be developed to alert us and our physician to early warning signs of genetically at-risk conditions, such as elevated blood sugar levels, high blood pressure and movement changes, but this requires the construction of a data ecology that permits the integration of genomic and phenotypic data.

That won’t happen overnight, as there’s a lot of soil to till technologically, organisationally and socially. Efficient, clinically accredited sequencing facilities are required, as are secure databases with controlled access and blockchain-type data security, and software suites that automatically analyse genome sequences for variations of known medical significance and report them in context-dependent ways to clinicians at the point of care, along with recommended actions based on published evidence and national guidelines, with clickable links to primary sources and further information. The provision of this curated information to doctors, nurses and patients will be simplified and doesn’t need bespoke genetic counsellors (as is often claimed), except in cases of severe familial disorders.

The provision of integrated, evidence-based genomic and physiological data to busy clinicians, along with recommended actions linked to national guidelines, will revolutionise the quality, effectiveness and delivery models of healthcare, leading to improved community wellness, quality of life and national productivity and the greater efficiency of stressed healthcare systems. It’s hard to imagine any clinical encounter or personal or systemic healthcare decision being made in the future without consulting genomic and physiological data analyses. Much of the value of this information will be realised in primary care—the GPs make the initial diagnoses, write the prescriptions and issue referrals, so accuracy at this level has enormous flow-on benefit. At a hypothetical $5 per provision, this amounts to a revenue stream approaching $1 billion per year in Australia alone—a cost that would be

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* There were 150 million patient encounters with GPs in Australia in 2016. There were also many hospital and other health-related encounters.
The availability of millions of individuals’ genomes with matched clinical information and physiological data from smart sensors will also transform medical research. Much is being made of the application of machine learning and artificial intelligence to big datasets, but the challenge is to assemble the big datasets in the first place. Once that’s done—routinely and automatically—it will be possible to compare any set of environmental and genetic parameters against disease incidence and progression and to tease out the factors involved. This will put discovery into warp drive and render the reductionist approach that has dominated medical research since the 1950s largely obsolete. In fact, it’s hard to envisage many future medical, health or biological research investigations that won’t use big-data analysis.

This new data ecology will create new health information services and pharmaceutical products. It will also challenge many of the existing structures in healthcare, health policy and regulation and create new structures and enterprises.

Imagine the healthcare setting and encounter of the future. Genome sequences will be routinely incorporated into personal medical records and automatically analysed, in conjunction with other clinical and physiological data, to inform the person concerned and healthcare professionals (subject to patient approval) of genetic variants that have healthcare implications, normally limited to those that have substantial risk and are actionable. The same data will be queried in context-dependent ways, for example in conditions such as pregnancy or high blood pressure or before travel into areas with particular disease risks. The release of data from child genomes will be limited to those conditions for which preventive action or treatment is required or desirable prior to adulthood, after which all of the information will be made available to the individual with their informed consent. No pharmaceutical prescription will be made, nor will it be ethical to do so, without reference to pharmacogenomic indices in order to ensure the correct selection of drugs (increasing numbers of which will be developed from genomic analyses) and the optimal dose to treat the underlying condition.

This is the much better, more informed and more efficient healthcare system that Australia should be planning for. It’s also an engine for economic growth, high-value digital exports and increased prosperity, as well as a path for safeguarding the security of our population’s health.

Realising this once-in-a-generation opportunity will require a bold strategic vision and strategic investment in the acquisition of genomic data, the provision and deployment of smart sensors by healthcare providers, the establishment of integrated genomic, clinical, pharmaceutical and sensor databases, and the development of analytical modules and distribution channels to make maximal use of the information. Creating positive change and overcoming resistance from the status quo will require sophisticated policy analysis, measures to mitigate risks, and regulatory frameworks that must be incorporated from the start. It will also require proselytisation of the benefits and an informed public discussion to understand the enormous promise. It will need to proceed in a way that achieves that promise and, while recognising vulnerabilities and risks, manages them in a transparent and effective way that maintains public confidence.

* Some insist that it isn’t appropriate for citizens to have access to genomic information, in case they worry, take inappropriate action, or both. That’s neither respectful of personal rights nor politically sustainable. Therefore, it’s important that the analyses provided be of high quality from a trusted (national) source, with clear links to further information and recommended actions that are evidence-based and in accord with national best practice guidelines. The value of the democratisation of this information will be to permit and encourage greater personal provenance over the maintenance of health.

† Some serious conditions, such as Huntington’s chorea, are not treatable, but individuals may still elect to know their risk, and be entitled to do so.
The local landscape

Australian research institutions, universities and, to some extent, clinical genetic laboratories have been quick to adopt new technologies in DNA sequencing and analysis. Substantial core facilities are available at the Australian Genome Research Facility (headquartered in Melbourne with branches in other capitals),102 the Ramaciotti Centre for Genomics at UNSW103 and the BGI facilities at the QIMR Berghofer Institute in Brisbane.22

However, despite the technical capability to sequence genomes, the research and clinical diagnostic sectors are not well equipped to embrace the new genomic and big-data ecology. Many biomedical and biological research laboratories don’t have sufficient bioinformatic skills (although that’s improving), let alone big-data and artificial intelligence capability. Data science and informatics should be an obligatory component of any science degree, but that isn’t the case in most Australian universities. Universities and other research institutions need to build such expertise and work together with government and industry to create not data pools but data lakes for analysis.

Strategic vision isn’t common in clinical circles and health departments in Australia. The dearth of it poses a risk to Australia being a substantial player in, and beneficiary of, the genomic–big-data revolution, despite our quite substantial precompetitive strengths. Provinciality and fragmentation are handicaps—especially in a federation with separate state and territory health departments. Most clinical genetic analysis in Australia is carried out in hospital-based paediatric services* (and some adult genetics clinics) that focus on diagnosing serious developmental and intellectual disabilities, mainly using limited panels or ‘exomes’;† the data from which has some diagnostic utility but little long-term value for broader health management40 and is rarely consented and incorporated into national health records for wider use. In any case, provincial hospital genetic laboratories don’t have the wherewithal or the bandwidth to conduct comprehensive genomic analysis at scale.

The problem is compounded by a risk-averse culture and the distortion of the public discussion by kneejerk privacy concerns that are raised or amplified by the media without accompanying analysis of the benefits and risks.‡ The value proposition of such data, and its protections, hasn’t been well sold to the Australian public, who tend to be sceptical when government is involved. For example, the Australian Digital Health Agency, set up as the national repository of clinical and pharmaceutical data, initially struggled to gain traction, although its acceptance and use are increasing (over 80% of GPs and pharmacies now use the system, and more than 2 billion records have been uploaded).105

In any case, more attention needs to be paid to obtaining the social licence to collect, protect and use personal biodata, including genomic data, for health and research purposes.§ One important ingredient may be to ensure that citizens are given control over who has access to their data, with exceptions (for example, for criminal investigations or the identification of remains) subject to judicial oversight, while allowing it to be de-identified and aggregated for research purposes.

How are we to build the infrastructure to collect and analyse genomic and sensor data? The local investment environment is limited in resources, lacking in confidence, or both, because of limited leading-edge biotechnology business experience in Australia, so we can’t look to the private sector to build the ecology of the future (although it may contribute), as the infrastructure needs to be developed and managed as a resource for the entire health system. Capabilities at most state-funded genetic laboratories are grossly inadequate for a big-data world. They have poor computational facilities, restrictive security practices and overstretched IT staff and have no time to plan for a digital ecosystem future.

* For example, the Victorian Clinical Genetics Service.104
† The protein-coding regions of the genes only.
‡ The dearth of objective analysis and the abundance of sensationalist and just-so stories in the media, often reflecting the underlying ideology of the writer, are a serious threat to the development of good public policy in Australia. More attention to balanced reporting and reasoned position papers are required.
§ The Australian Digital Health Agency does not currently include a facility for incorporating genomic data.
A few Australian companies are developing genomic analysis capability, and at least 18 offer such services globally. Most are relatively new. Genome.One was established at the Garvan Institute to undertake clinical diagnosis in genetic disorders and cancer and for ‘wellness’ but struggled and eventually failed, lacking cash flow, unlike enterprises abroad that have greater working capital to build their portfolio while the market develops. A spinout company, Pryzm Health, has developed innovative patient self-reporting interfaces to complement genomic and conventional clinical information and is partnering with the US-based healthcare provider Sanford Health and with BGI in China.

Other incipient companies are developing genetic analysis and pharmacogenomic/wellness testing in Australia, but they’re also struggling, mainly because the market is limited, while Medicare reimbursement doesn’t extend to genome analysis beyond serious genetic disorders. A few local companies are offering limited genetic diagnosis of cancer, but most such work is done overseas through local portals. There are also experimental cancer genome analysis projects supported by the Australian Government and philanthropy.

In such circumstances, there’s a case for government to act as an impresario to accelerate, facilitate (by the augmentation of private activity, the deployment of non-monetary government resources, or both) and, where necessary, to fund the construction of what’s been described by Nicholas Gruen, using genomics as the exemplar, as ‘emergent public goods’.

A trusted national resource?

The fragmented landscape of genome analysis enterprises and state-based genetic services suggests that the only practical approach to the implementation of precision health care in Australia is for the federal government to establish a central facility that:

- develops evidence-based, well-curated and continuously updated genome interpretation, integrated with information from clinical records, smart sensors and patient self-phenotyping
- suggests recommended actions linked to national guidelines and best practice publications
- can be accessed (with patients’ permission) by accredited healthcare professionals.

Such a comprehensive data analytical service would constitute a major public good and an extremely valuable asset, the software and analytics of which could be exported to other jurisdictions (or will have to be imported, if Australia is slow off the mark). As I’ve noted, at $5 per provision, the economic potential is enormous, beyond that obtained from improvements in national health from a more sophisticated, less wasteful and more accurate health management system.

The Medical Research Future Fund (MRFF) provides around $1 billion annually for health-related R&D activities beyond investigator-initiated projects funded by the National Health and Medical Research Council, but increasingly seems a wasted opportunity.

The MRFF funds a range of ad hoc clinical genetic ‘demonstration’ projects grouped under the banner of the Genomics Health Futures Mission, but the potential of this serendipitous war chest is compromised by the lack of an overarching vision and strategic plan for, and corresponding investments in, the organised acquisition of genomic data; the development of software for its automated analysis and integration with phenotypic data; interrogation by artificial intelligence; and provision of the information to researchers, health system managers, healthcare practitioners and citizens.

* Akin to clinical decision-support systems such as UpToDate (online).
Other applications of genomics integrated with big data

Genomic analysis has wide applications in animal and plant breeding, and its power is enhanced by the advent of precise genetic engineering technologies. In Australia, most of this work is done by CSIRO, universities and state departments of primary industry, funded in large part by rural R&D corporations, whose funds derive from government-matched levies on production. This has placed Australia at the forefront of the drive for efficient and high-quality agriculture and food production, although improvements could be made by the establishment of joint reference databases, such as for mammals or grasses (wheat, sugarcane, oats, rice, corn, barley, sorghum, millet and rye) that share genetic features. Again, a more strategic and coordinated approach would be valuable.

Genomic data (‘DNA fingerprinting’) has been used for many years for the confirmation or elimination of suspects in criminal investigations. The growth in DNA databases and our increasing knowledge of genotype–phenotype correlations allow individual identification through the prediction of physical features, ethnic origins and even surnames (through Y-chromosome comparisons in patrilineages). The iconic example is the identification of the Golden State serial killer in the US by the similarity of his DNA fingerprint to that of a relative. The same approach of familial searching has been used to identify a rapist in South Australia and a killer in Queensland. Genomic data can increasingly predict facial features (and height) to near identikit resolution and will ultimately extend to other characteristics, including voice—a capability that’s inevitable with the growth and integration of DNA and photographic/biometric databases, such as the Australian ‘national facial biometric matching capability’ database.

At least one company offers genetic genealogy (the identification of suspects by matching to a close relative) and a forensic DNA phenotyping system—with funding support from the US Department of Defense—that predicts ethnic ancestry, eye colour, hair colour, skin colour, freckling and face shape in individuals from different backgrounds, including mixed ancestry, in some cases to quite specific subpopulations and geographical locations. This capability is being embraced by Australian police forces and presumably security agencies, and regulatory frameworks are under discussion. Naturally, this also raises privacy concerns and encourages the search for new ways to protect the data using blockchain and cryptographic approaches to genome ‘cloaking’.

DNA analysis can also be used to check identities; protect commercial rights (by ‘barcoding’ proprietary plant varieties, breeds or microbial cultures); and confirm the provenance and track the origins of pathogens, foods and other biological materials, including contraband. Further, manufactured goods, including explosive devices, bear DNA traces of the human participation in their manufacture.

National and social security

The national security implications of genomic data are substantial. A genome is the ultimate personal identification. If the DNA profiles of all citizens are available, police and security agencies are far better able to identify and track criminals and foreign agents.

There are legitimate privacy and security concerns, and there will need to be strict restrictions and controls on access. Personal genetic data can be highly sensitive, for example, for the ~1% of the population who differ genetically from standard males and females, although the acceptance of gender diversity is improving rapidly. It can also be used maliciously in other ways, for example, to expose nonpaternity without permission—a risk that

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* Voice ID is being adopted by banks and taxation departments for personal identification in phone conversations.
becomes increasingly implicit even in innocent analysis. Thus, there’s potential for hacking genomic databases and the subsequent coercion, recruitment and extortion of individuals in many contexts.

The social implications of genomic data are also significant, including the potential for or fear of genetic discrimination and genetic exceptionalism, although these problems can be addressed by community discussion and appropriate legislation. Some of the issues have been covered in the 2003 Australian Law Reform Commission report on genetic privacy (Essentially yours). As the report noted:

“The major challenge … [is] … to find a sensible path that meets twin goals: to foster innovations in genetic research and practice that serve humanitarian ends, and to provide sufficient reassurance to the community that such innovations will be subject to proper ethical scrutiny and legal (and other) controls.”

Australia is fortunate to have both its public and private health insurance community risk-rated, and therefore independent of individual genetic or social circumstances. There’s a widespread and reasonable concern, however, that genetic risks revealed by genomic data will increase premiums or limit coverage in life and employment insurance—as is presently the case if there’s a family history of, for example, heart disease or cancer. This has been the subject of a recent Australian Government inquiry, and the Financial Services Council (the peak body for Australian life insurers) has introduced a moratorium on requiring the disclosure of genetic tests up to certain financial limits, similar to the system in operation in the UK.

Contrary to expectations, the opposite may apply. For many, including insurers, knowledge of individual risks will reduce those risks greatly, for example by the installation of a heart pacemaker or the prescription of medications that reduce cholesterol, or more regular cancer screening of those at high risk, which will change actuarial calculations in favour of all parties. On the other hand, or in any case, it may be simpler to legislate against genetic discrimination in life and employment insurance, as in Canada and some other countries. Better still, compulsory superannuation may provide the opportunity for a community risk rating to be applied by requiring large superannuation funds, if not already doing so, to include unconditional life and disability insurance.

* There’s also a strong case not to report genetic risks that are not ‘actionable’ (that is, for which there is no mitigating treatment), such as Alzheimer’s and Huntingdon’s diseases, unless the individual requests such information, as some do.
Genomic information is the raw material for genetic engineering. Genetic engineering, as opposed to the genetic selection practised since time immemorial in the agricultural, animal breeding and fermentation industries, has its roots in the manipulation of genes in microbial hosts during the 1970s to produce pharmaceutical products such as human insulin. The technical complexity of genetic engineering in plants and especially animals is much greater and has largely been limited to introducing gene sequences that confer viral or insect resistance or disable particular genes, such as those involved in ripening, to extend the shelf lives of products.

The ease and precision of genetic engineering have been transformed with a discovery that came out of left field (in another example of the beautiful serendipity of research and how rapidly the landscape can change), in this case of a viral defence system in bacteria that’s been adapted to allow DNA changes, insertions or deletions in the genome of any organism.

This system is called CRISPR, an acronym derived from the characteristics that were first noticed in strange repeated sequences in bacterial genomes. The technological innovations that have ensued have been extraordinary; the latest enabling relatively error-free insertion by RNA guide molecules of any desired sequence at any specific position in the genome (termed ‘prime editing’). CRISPR is now being widely used to alter genomic information in research, human medicine, pastoral animals, agriculture and industrial biotechnology.

**Human gene therapy and repair**

CRISPR prime editing has been shown to correct the genetic causes of the inherited genetic disorders Tay–Sachs disease and sickle cell anaemia and has the potential to correct the majority of known genetic variants associated with human diseases. There are also other systems, less efficient but nonetheless effective, for gene editing using engineered sequence-specific DNA binding proteins.

Such genetic repairs are mainly confined to those that are feasible to undertake after birth by, for example, the reintroduction of engineered blood cells or injection into affected tissues, such as the eye. In many if not most genetic disorders, the damage is already done, although some are amenable to lifesaving treatments, including dietary modification or supplementation. It’s possible that in future damaged genes may be repaired in embryos but, in practical terms, many if not most debilitating monogenic disorders will be simply avoided, once genomic sequencing is routine, by preconception screening and subsequent embryo selection in at-risk couples to avoid those that are compromised, as commonly occurs at present with chromosomal disorders such as Down syndrome.

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* CRISPR = clustered regularly interspaced short palindromic repeats.
† Such selection is independent of other characteristics and, at least for recessive genes, doesn’t appreciably change the allele frequency in the population, which allays concerns about longer term unintended consequences. Genetic disorders in the heterozygous state confer resistance to diseases, such as cystic fibrosis (resistance to cholera) or sickle cell anaemia and thalassaemia (resistance to malaria).
Genetic engineering of virulence or replication genes in human viruses has been undertaken for many years to make them suitable as gene therapy delivery vehicles or attenuated vaccines. Ex vivo genetic engineering of patients’ immune cells, notably synthetic ‘chimeric antigen receptor’, or CAR T-cell therapy, is being used successfully to target antigens present on haematopoietic (blood) cancer cells and shows promise for solid tumours. CRISPR has also been successfully used to eliminate the HIV retrovirus from the genome in mice, and there have been promising results in a human patient.

There has been one case of so-called germline editing, carried out in China, to alter a gene in embryos to confer resistance to HIV-AIDS. This has been widely condemned and prompted international efforts to restrict human reproductive engineering.

Our ability to make sensible changes to the human genome, or the genome of any complex organism, is limited by our currently poor knowledge of genomic information, especially the genetic factors associated with complex traits such as athletic or musical ability, personality and logical or creative intelligence, among the many dimensions of human biology and diversity. In most cases, we don’t know the identity of the specific genetic variations involved and, in any case, most have minor effects and operate in networks, in which a benefit in one dimension may be a handicap in another. While there’s no doubt that humans will ultimately have sufficient knowledge to guide their own evolution, that day is a long way off, even if it does engender much debate in the interim.

**Genetic engineering of microbes, plants and animals**

Things are of course simpler in other organisms, but genetic engineering is still largely limited to simple subtractions or additions of genes or suites of genes.

Gene subtraction includes the deletion of the ‘poll’ gene for horns in cattle, the disabling of the myostatin gene, which negatively regulates muscle growth to increase muscle mass (meat yield) in merino sheep, goats and pigs, and the deletion of specific genes in pigs to obtain resistance to viral gastroenteritis and porcine respiratory and reproductive syndrome.

The addition of new capabilities is the ambition of the nascent field of ‘synthetic biology’, or ‘genome printing’, and is based on the demonstration that complete viral and even bacterial genomes can be assembled in the test tube and inserted into a blank viral capsid or cell to create a viable organism. This means, in theory, that any new type of bacteria or virus, with new genetic circuits, can be designed in silico and made viable in any reasonably well-equipped laboratory. The construction of synthetic animal and plant genomes from scratch is not yet possible, and may never be possible, although it may be possible to reverse-engineer existing species to recreate extinct ones or make new ones.

Designer changes can and are being made across the board, with increasing range and sophistication. The addition of new genetic capabilities has led to the development of new strains of animals, plants, yeasts and bacteria with better growth rates, new metabolic capabilities and enhanced disease resistance, among many other characteristics.

Examples include the introduction of the biosynthetic pathway for beta-carotene synthesis in ‘biofortified’ or ‘golden’ rice, bananas and potatoes to increase vitamin A content (lack of which causes blindness in an estimated 250,000–500,000 children annually), and ‘purple’ rice, which has been engineered to produce the antioxidant compounds found in blueberries, although take-up has been dogged by largely irrational campaigns against genetically modified plants. The introduction of the bacterial insect ‘Bt’ toxin into cotton, corn and other crop plants has, in fact, led to massive reductions in insecticide use, with far less collateral damage to other insects in the ecosystem, and with no evidence of harm to human health or the environment. Some 99.5% of cotton

* Developed at the Queensland University of Technology.
† More than 200 Bt toxins are naturally produced by the soil bacterium *Bacillus thuringiensis*, cultures of which are sprayed on plants in ‘organic’ farming.
Plants have also been engineered for resistance to a wide range of viruses and to control ripening (to extend shelf life), flowering time and plant architecture in many fruit and horticultural species, including tomatoes, strawberries, apples, kiwifruit, grapefruit, watermelons and cucumbers. As with human genome sequencing, China is investing heavily in genome editing for crop improvement.

In animals, examples include the introduction into cattle of a gene that confers resistance to tuberculosis and the introduction of a growth hormone gene (from Chinook salmon) into Atlantic salmon, which enables the salmon to grow faster and to reach the same size with 25% less food. Trials are underway to insert or modify sex determination genes to bias sex ratios in the beef and dairy sectors, as well as in poultry, silkworms and pest control.

Such designed modifications increase the efficiency and quality of food production, as well as reducing waste and environmental damage. The future will also bring a universe of bio-innovations, including bacteria engineered to produce, for example, spider silk, which is stronger per unit weight than high-tensile steel, as well as other biomaterials for industrial and medical applications, such as tissue regeneration.

**National and social security**

The immediate concern for national security is the use of genetic engineering for bioterrorism or state-sponsored harm.

Bacteria can be easily engineered, even in a backyard laboratory, to carry lethal toxins, but they’re difficult to disseminate and relatively easy to contain.

Not so with viruses. The topic du jour is the concern that the virus that causes Covid-19 may have originated in, or at least escaped from, a laboratory. That might or might not be the case, but it was almost certainly not designed there, if for no other reason than that we don’t yet know enough about the idiosyncrasies of the proteins in viruses that allow them to infect human cells. Therefore, it’s essentially impossible at present to design specific genetic changes to that end, even if the technology for engineering viral gene sequences is straightforward.

On the other hand, it may be easy to isolate virus variants that can infect humans by selection for growth in cultured human cells, although this often causes the attenuation of virulence. It’s possible to make existing viruses more lethal by engineering in genes that attenuate immunological responses, although such viruses may also be less contagious.

In any event, it’s almost impossible to prevent the spread of new natural, selected or purposely engineered viruses that have high infectivity, except by national quarantine, which comes at considerable economic and social cost, and the development of vaccines or treatments, which takes time. As Covid-19 demonstrates, such viruses may be by far the biggest threat to national security, as broadly defined, and an easy weapon for adversaries that have different values from ours. The protection against this is the development of rapid-response capability, including the fast-tracking of vaccines and antiviral drugs.
A new generation of pharmaceuticals was ushered in with genetic engineering, which enabled the production of protein therapeutics in recombinant bacteria. Those therapeutics included insulin (previously obtained from the pancreases of pigs), erythropoietin (EPO) and other previously impossible-to-manufacture proteins, such as growth hormone (accomplished in part by John Shine, the current president of the Australian Academy of Science).\(^{179}\)

A sobering comparison is that the 2019 value of just two of those products, insulin and EPO (approximately US$43 billion),\(^{180}\) rivalled that of total Australian agricultural production in the same year (about US$42 billion).\(^{181}\) This again indicates the extent of the financial opportunity presented by biotechnology.

Genetic engineering has also transformed vaccine development. CSIRO and universities have developed recombinant-DNA-based vaccines against bacterial\(^{182}\) and viral pathogens, most famously Gardasil, a vaccine against human papilloma virus that protects against cervical cancer,\(^{183}\) by Jian Zhou and Ian Frazer at the University of Queensland. This capability is also an important part of the national defence against pandemics.\(^{184}\)

**Rational drug design**

Drug design and development have progressed enormously over recent decades through a combination of advanced chemistries, the development of vast natural and synthetic chemical libraries, high-throughput genetic screens and cell-based assays, knowledge of the atomic structure of protein targets, and computer-aided drug design.

A typical protocol is to first identify a target protein that would be desirable to block, such as a rogue fusion protein that leads to uncontrolled cell growth, or a pain receptor, by basic research into normal or abnormal processes. An increasing number of such targets are being identified by genomic analysis.\(^{80,185}\) The protein can be produced from cloned genes, its structure can be determined and then tested against chemical libraries or selected compounds that are designed to bind the functional part of the protein, followed by fine-tuning of those showing good activity.\(^{†}\) Alternatively, chemical libraries can be tested against cultured cells, bacteria or parasites, for example, to identify those that block their growth, followed by target identification.\(^{186}\)

Such approaches have led to a new generation of targeted anticancer drugs, among many others, with enormous commercial value. They have also led to many antiviral compounds, some of which have been spectacularly successful in, for example, suppressing HIV-AIDS\(^{187}\) and curing hepatitis C.\(^{188}\) One of the first and most emblematic examples was the development by the Melbourne company Biota, in collaboration with CSIRO, the Australian

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* Erythropoietin is used to bolster red blood cell production in people undergoing chemotherapy or otherwise suffering anaemia and (illegally) to bolster oxygen-carrying capacity in endurance athletes.

† The libraries may be derived from natural sources, such as spiders, snakes or cone shells that have evolved to block particular pathways in prey, or from libraries from marine microorganisms and other organisms that have been developed in many Australian laboratories. They may also be made synthetically. Most pharmaceutical companies have large compound libraries.
National University and the Victorian College of Pharmacy, of a drug, Relenza, that specifically binds an influenza virus surface protein and blocks infection.189

Such ‘rational’ (as opposed to compound-screening) approaches have also led to a new generation of drug discovery companies that use artificial intelligence, operate entirely in silico,190 and outsource drug testing to online companies that specialise in flexible automated experimentation.191 The latter may change the current model of experimental testing by eliminating operator error, hidden variables and expectational bias, which are likely to be the reasons for the poor reproducibility of findings published by universities and research institutes.

Australia has advanced capabilities in all areas of drug development. We have major centres in Brisbane and Melbourne and substantial molecular cell biology and chemistry capability across the country. Australia is also a favoured place for clinical trials because of the quality of our healthcare system. However, our nation is currently only an early-stage drug developer and isn’t the base for a major pharmaceutical company, simply because we don’t have institutions with sufficient resources to play in the big league.

Or do we? Australia’s largest biotechnology company, CSL, which was initially established as a federal agency to produce penicillin in World War II and now specialises in serum and vaccine products, had ~US$8.5 billion in revenue in 2019 and a market capitalisation of ~$150 billion.

The Walter and Eliza Hall Institute recently sold part of the royalty rights to an anticancer drug, developed by the process referred to above, to a wholly owned subsidiary of a Canadian pension fund for US$325 million.192 Australian superannuation funds are the repository for ~$2.7 trillion193 of forced and voluntary savings and are bound by law to optimise shareholder (contributor) returns. This, and their lack of technology domain knowledge, makes them inclined to invest primarily in so-called blue-chip stocks, banks and mining. However, the value of healthcare stocks has risen far faster than that of the rest of the market (by 500% over the past decade),194 pre-Covid-19, and is likely to do well in future. Moreover, while more volatile high-technology stocks yield higher capital gains than the All Ordinaries Index over time,194 although they require a portfolio approach, the Australian superannuation industry could expand the capital available for new high-tech businesses in Australia and improve their performance at the same time. Such investment could be encouraged by the recent billion-dollar valuations of three Australian biotech companies that successfully completed phase 2 clinical trials.195

The major limitation on drug development,191 which particularly inhibits entry by smaller players, is the enormous cost and high (~90%) failure rate of clinical (safety and efficacy) trials in the post-thalidomide era, which amounts to approximately US$3 billion per approved drug.196 This causes several problems, which include the high cost of on-patent drugs to recoup investment but which also reduce their availability in most jurisdictions. The clinical trials also result in delays, which impose an opportunity cost in the form of lives lost in the interim.

A different model

The conventional hermetic isolation between industry and user–payer systems has created an unsustainable model for drug development. The fraction of GDP attributable to health is 18% in the US,197 rising year on year, and is estimated in Australia to reach $81.8 billion or 16.3% of government expenditure in 2020,198 in part because the costs of drug development must be recouped in markets. Ironically, government-mandated regulatory processes contribute to spiralling costs and inefficiencies in drug development, precisely at a time when rational drug development has the potential to transform health outcomes in a way not previously possible.

It’s possible to reimagine industrial drug development as a result of the evolution of targeted design linked to genomic information. Academia and industry are the engine rooms for drug development, but they depend on clinical leadership, access to patient populations and data from clinical trials. While drug development was based on empirical observation rather than biologically informed rational design, clinical trials couldn’t be regarded as a standard of care. However, rational drug development for genomic biomarkers has transformed the risk:benefit ratio for participation in clinical trials.
Consider phase 1 studies, in which the activity of new drugs is unknown and the primary purpose is to define a safe dose and schedule for efficacy testing. For empirical drug development, such as cytotoxic chemotherapy, the objective response rate (ORR) is estimated at 5%. Consistent with this, targeted therapies used in phase 1 studies without matching to the molecular target also have an ORR of 5%.52 However, genomically matched targeted therapies in phase 1 have an ORR of 30%.59,60,62 This means that genomically based drug trials are likely to be many times more efficient than the current model, all of which lead to major savings in cost and time and the expansion of the pharmacopoeia for precision medicine.

Consequently, participation in clinical trials now presents meaningful therapeutic options for patients with advanced cancers. However, the current trials participation rate in adults in Australia is about 7%. Arguably, increasing clinical trials participation rates to 20% of all cancer patients, and in any others in which targeted therapies are being trialled, would have a major impact on health outcomes, medical research and the development of a sustainable model for healthcare.

The health outcomes include more rapid and equitable access to novel therapeutics, which are otherwise only accessible out of pocket or at market costs to the system, and a better standard of data-driven, evidence-based clinical care. There would be improvements in the health workforce through training and exposure to research, greater engagement with the global and domestic pharmaceutical industry, collateral investment into research partnerships, and a shared risk model for drug development with industry.

This would build the life sciences economy by trading the market costs of drugs through the Pharmaceutical Benefits Scheme for genomic and clinical data generated by the expansion of clinical trials, making research and healthcare interoperable. This model exploits the assets of the Australian healthcare system: it’s data-rich, has an outstanding research reputation, has single-payer (government) control and comprises a relatively small ecosystem for drug development that doesn’t compromise its role as a major market or other markets abroad.
Australia has a strong history in medical devices and has produced a small cohort of particularly successful companies such as ResMed (now based in California), which manufactures and exports sleep improvement devices, and Cochlear, which produces bionic electro-acoustic implants for the restoration of hearing. Other groups are trying to develop gene therapies for hearing loss.

Bionic electrophotonic eye implants are under development for sight restoration in Victoria and NSW. Bionic hands responsive to implanted electrodes with sensory feedback are being developed in Australia and abroad.

There are exciting prospects for the development of 3D-printed body replacement parts and tissues involving a range of biological and inorganic components, including cartilage, hearts, and bones. Australia has dedicated research centres and facilities in this area in universities, CSIRO, hospitals and industry.

3D printing is also being used to mimic biological phenomena, such as iridescence with photonic crystals. Natural or evolved hybrid bioelectrical devices are being developed as highly sensitive single-molecule detection systems.

A number of Australian research laboratories are developing implantable devices and wearable biosensors, such as conductive polymers for non-metallic wireless medical implants, nanocomposite-based sensors to detect stresses, wear and damage in orthopaedic implants, wearable sunburn sensors and nanopatches for vaccine delivery.

The interplay between organic and inorganic molecules has almost unlimited potential, not only to repair damage, or to create new products, but also to enhance human capabilities as the fusion of biological, nonbiological and computer/data systems unfolds. In this paper, I can do justice to neither the range of initiatives underway or under development nor the imaginative potential of the field, but Australia’s medical industries and defence and security agencies should take notice, as they may well have already.
Australia’s security is underpinned by its economic strength, and there are many opportunities to build enterprises and capability in the biotechnology sector, which has huge potential for growth, health and economic benefits. Therefore, the urgent challenge becomes how to optimise the opportunities before they are realised by others, so that we aren’t once again importing technology and data analysis capabilities that we could well have developed ourselves.

Many of the opportunities—specifically in genetic engineering, gene therapies, drug and vaccine development, smart sensors and bionic devices—involve an interplay between research groups, venture capital and industry, so any strategic frameworks that assist that interplay are valuable. In particular, I suggest, we need to remove barriers to entrepreneurism (such as taxation on equity in startups before that equity is liquidated) for our talented scientists and engineers, develop a better informed and confident investment advisory sector, and use government and superannuation investment to capitalise on Australia’s strengths and supercharge the next generation of bio-industries.

The integration of genomic, clinical, pharmaceutical and smart-sensor data has the most transformational potential across all socio-economic indices, which is why it has occupied much space in this paper. It’s also the one objective and opportunity that can’t be achieved without a whole-of-government plan.

Embedded expertise in government departments and security agencies is also required for optimal strategic planning and prompt take-up in a rapidly evolving technological environment.
1. The Australian Government and the state and territory governments should consider, first and foremost, what’s possible and desirable and develop a bold vision of what the healthcare system and bioeconomy could and should look like in 20 years. They shouldn’t be dissuaded from pursuing that vision by the complainerati, vested interests, problem finders, short-term narrow thinkers and risk-averse managers, which together are the greatest challenge and greatest hurdle.

2. The federal, state and territory governments should develop an overarching strategic plan for the acquisition and development of infrastructure for integrating genomic, clinical, pharmaceutical, sensor and self-phenotyping data and for the provision of trusted online evidence-based analysis of that information and advice to healthcare practitioners and citizens (recommendation 8). The obvious sources of the necessary resources (including those required for recommendations 5–7) are the Medical Research Future Fund and public–private partnerships.

3. The federal, state and territory governments should be proactive in convincing our citizens of the personal and national value of big data in healthcare, using a model that combines political leadership with subject-matter expertise.

4. Smart sensors should be made available through Medicare and routinely installed in hospitals, clinics and other healthcare settings, such as aged-care homes.

5. Conversion to electronic health records should be mandatory for all healthcare providers receiving government support or reimbursement in Australia, as recommended by the Australian Academy of Technology and Engineering.99

6. Genetic tests should be progressively upgraded to whole-genome sequencing in order to build the national genomic estate—converting diagnostic expenses into an enduring strategic asset.

7. The Australian Government should establish secure national repositories for the storage and integration of genomic and phenotypic data for research and healthcare use. This de-identified data should be made available to researchers and health system managers around Australia. It could also be provided to external parties, such as pharmaceutical companies, under appropriate conditions in exchange for early access to expensive treatments or shared benefits.

8. The Australian Government should establish a central unit to assemble and supply evidence-based, well-curated and continuously updated genomic analysis, informed by clinical and other data and linked to national treatment guidelines, at the point of care. The cost of doing this will be trivial compared to other costs in the healthcare system, and trivial in relation to the cost reductions and healthcare improvements that it will enable. This capability can also be exported to other jurisdictions and generate huge revenue. All suitably accredited health professionals, including general practitioners, should be able to obtain a genomic report, pharmacogenomic advice, an early warning of an incipient disease, or any combination of that information, about a patient upon request. Citizens should also be entitled to access such information in the interests of caring for their own health, provided it’s conservative and actionable.
9. Australian security and police agencies should establish internal expertise in biotechnology and biodata analysis. They should have access to national genomic information under defined circumstances and subject to judicial approval and oversight.

10. Australian universities should provide training in computer programming and big-data analysis as a core component of all science and engineering degrees.

11. Australian research funding agencies and CSIRO should continue to invest in advanced genetic engineering and vaccine and drug development.

12. Australian superannuation funds should be encouraged to invest at least 1% of their resources into domestic start-up and early-phase enterprises (however best defined), or baskets of such enterprises, in high-tech and digital enterprises, especially in health.

13. Major investment funds and relevant government departments should consider establishing bio-intelligence units to keep abreast of opportunities and incorporate those opportunities into their strategic planning.
3. Figure obtained from ‘The cost of sequencing a human genome’, National Human Genome Research Institute, 2020, online.
11. J Shieber, ‘XGenomes is bringing DNA sequencing to the masses’, *TechCrunch*, 16 March 2019, online.
13. ‘MGI announces $100 genome; Illumina files patent suit’, *Bio IT World*, 27 February 2020, online; A Regalado, ‘China’s BGI says it can sequence a genome for just $100’, *Technology Review*, 26 February 2020, online.
17. BGI Genomics, online.
18. ‘Complete Genomics, BGI agree to $117.6M merger’, *genomeweb*, online.
20. Matthew Campbell, Dong Lyu, ‘China’s genetics giant wants to tailor medicine to your DNA’, *Bloomberg*, 19 November 2019, online.
21. ‘Global genomics giant establishes base at QIMR Berghofer’, QIMR Berghofer Medical Research Institute, 16 August 2021, online.
22. ‘About BGI Australia’, BGI Australia, 2020, online.
23. ‘Forensics’, BGI Australia, 2020, online.
See, for example, ‘Percept cell-free DNA prenatal test’, VCGS, 2020, online; ‘Generation: a new era in prenatal testing’, QML Pathology, 2020, online; ‘Frequently asked questions’, Sonic Genetics, no date, online; ‘Non-invasive prenatal testing (NIPT)’, Genomic Diagnostics, 2020, online.


‘Secretary of State for Health and Social Care announces ambition to sequence 5 million genomes within five years’, Genomics England, 2 October 2018, online.

National Institutes of Health, online.

‘Genomics and medicine’, National Human Genome Research Institute, online.

B Wang, ‘China’s $9.2 billion precision medicine initiative could see about 100 million whole human genomes sequenced by 2030 and more if sequencing costs drop’, NextBigFuture, 7 June 2016, online.

Mackenzie’s Mission, online; Department of Health, ‘Genomics Health Futures Mission’, Australian Government, 8 May 2020, online; ‘Bringing genomic cancer medicine home: major funding boost means rare cancer patients can access precision medicine trials in their home state’, news release, Garvan Institute, 18 July 2018, online.


Cliniface, online.


B Doble, DJ Schofield, T Roscioli, JS Mattick, ‘Prioritising the application of genomic medicine’, NPJ Genomic Medicine, 2017, 2:35, online.


See R Beery, ‘The Beery family whole genome sequencing success’, Genetic Alliance, no date, online. This was solved by a team led by Australian Richard Gibbs AC.

See ‘Alan’s story: a life-changing diagnosis through genome sequencing’, Garvan Institute, no date, online. This was solved by a team led by Chris Goodnow at the Garvan Institute of Medical Research.

50. ‘The dataset’, Genomics England, online; BiobankUK, online; National Genomics Data Center, online.


52. Genomic Data Commons, ‘GDC collaborations’, National Cancer Institute, 2020, online.

53. Some data is stored at the NCI at the Australian National University; ‘Thousands of genomes prepared for clinical use’, NCI Australia, 8 March 2018, online.


56. See ‘Ellie’s story: from intensive care to the playground’, Garvan Institute, 2 September 2018, online; ‘Minderoo Foundation’s $5 million donation to Zero Childhood Cancer will help kids like Jack beat brain cancer’, Children’s Cancer Institute, 15 May 2019, online.

57. Australian Genomic Cancer Medicine Centre, online.

58. D Thomas, personal communication.


60. DL Fontes Jardim, M Schwaederle, C Wei, JJ Lee, DS Hong, AM Eggermont et al., ‘Impact of a biomarker-based strategy on oncology drug development: a meta-analysis of clinical trials leading to FDA approval’, JNCI: Journal of the National Cancer Institute, 2015, 107, online.


62. TL Stockley, AM Oza, PL Bedard, ‘Molecular profiling of advanced solid tumors and patient outcomes with genotype-matched clinical trials: the Princess Margaret IMPACT/COMPACT trial’, Genome Medicine, 2016, 8:109, online.


66. RR Miller, ‘Hospital admissions due to adverse drug reactions: a report from the Boston Collaborative Drug Surveillance Program’, Archives of Internal Medicine, 1974, 134:219–223, online.


84. ‘Patricia Stallings’, *Wikipedia*, online.


90. K Eagle, ‘Toxicological effects of red wine, orange juice, and other dietary SULT1A inhibitors via excess catecholamines’, *Food and Chemical Toxicology*, 2012, 50:2243–2249, online.


92. AV Khera, M Chaffin, KG Aragam, ME Haas, C Roselli, SH Choi et al., ‘Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations’, *Nature Genetics*, 2018, 50:1219–1224, online.


95. ‘A smartphone app helping doctors and patients breathe easier’, Uniquist, online.

96. ‘New app collects the sounds of COVID-19’, news release, University of Cambridge, 6 April 2020, online.

97. Proteus, online.
References

102. Australian Genome Research Facility (AGRF), online.
103. Ramaciotti Centre for Genomics, online.
104. For example, the Victorian Clinical Genetics Service (VCGS); online.
106. 23&Me, online; Foundation One, online; Helix, online; Nebula Genomics, online; Veritas Genomics, online; Variantyx, online; Dante Laboratories, online; pieriandx, online; Fabric Genomics, online; Congenica, online; Genome Medical, online; PGDx (Personal Genome Diagnostics), online; CentoGene, online; Invitae, online; Circle, online; Fulgent Genetics, online; GeneDx, online; Omnigen, online.
109. For example, 23strands, online; Clear Sky Genomics, online.
110. myDNA, online.
111. Genomics for Life, online; Xing Cancer Care, online; GenomiQa, online.
112. Roche Foundation Medicine, online.
113. ‘Bringing genomic cancer medicine home: major funding boost means rare cancer patients can access precision medicine trials in their home state’, news release, Garvan Institute, 18 July 2018, online.
115. UpToDate, online.
120. A Regalado, ‘More than 26 million people have taken an at-home ancestry test’, *MIT Technology Review*, 11 February 2019, online.
127. C Curtis, J Hereward, ‘How accurately can scientists reconstruct a person’s face from DNA?’, *Smithsonian Magazine*, 4 May 2018, online.
128. See, for example, ‘NAB voice ID’, National Australia Bank, online.
130. Parabon Nanolabs, online.
131. D Box, ‘Queensland cops use DNA analysis to “see” suspect’s face’, The Australian, 27 September 2016, online.
143. R Stein, ‘Chinese scientist says he’s first to create genetically modified babies using CRISPR’, NPR, 26 November 2018, online.
165. M Niederhuber, ‘Insecticidal plants: the tech and safety of GM Bt crops’, *Science in the News*, Harvard University, 10 August 2015, online.
170. Yuanpeng Gao, Haibo Wu, Yongsheng Wang, Xin Liu, Linlin Chen, Qian Li et al., ‘Single Cas9 nickase induced generation of NRAMP1 knockin cattle with reduced off-target effects’, *Genome Biology*, 2017, 18:13, online.
172. A Quinton, ‘Meet Cosmo, a bull calf designed to produce 75% male offspring’, *UCDavis*, 23 July 2020, online.
179. ‘Profile: John Shine’, Australian Academy of Science, online.
189. ‘Case study: Relenza—the first effective flu-fighter’, CSIRO, online.
190. See, for example, Turbine, online. See, for example, Arctoris, online. The author is a non-executive director of this company.
192. KPMG, Super insights 2019, April 2019, online.
193. ‘Index charts’, ASX, 2020, online.
196. ‘US national health expenditure as percent of GDP from 1960 to 2020’, Statista, 2020, online.
198. ‘Hearing restoration with gene therapy’, Knowledge Exchange, University of NSW, 8 July 2019, online.
200. ‘Bionic hands that feel’, Knowledge Exchange, University of NSW, online.
202. NA Traugutt, D Mistry, C Luo, K Yu, Q Ge, CM Yakacki, ‘Liquid-crystal-elastomer-based dissipative structures by digital light processing 3D printing’, Advanced Materials, 8 June 2020, online.
205. See, for example, M Mellor, ‘This machine 3D prints bones for better, healthier implants’, Wired, 7 February 2020, online; ‘Bona fide bone substitute could revolutionise surgery worldwide’, University of Sydney, online; ‘CSIRO and Anatomics develop world’s first 3D-printed sternum’, Engineers Australia, no date, online; ‘Printing with biomolecules’, Knowledge Exchange, University of NSW, online.
206. See, for example, ‘ARC Training Centre for Innovative BioEngineering’, University of Sydney Nano Institute, online; N Paxton, ‘3D printing of bone’, Australasian Science, July 2019, online; Anatomics, online.


214. ‘Wireless medical device implants’, Knowledge Exchange, University of NSW, online.

215. ‘Sensing implant wear using nanocomposites’, Knowledge Exchange, University of NSW, online.

216. ‘A wearable sunburn sensor!’, Knowledge Exchange, University of NSW, online.

217. ‘UQ technology with the power to revolutionise global vaccine delivery’, Uniquest, 9 October 2019, online.
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<th>Acronym</th>
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<tr>
<td>AIDS</td>
<td>acquired immune deficiency syndrome</td>
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<tr>
<td>BGI</td>
<td>Beijing Genomics Institute</td>
</tr>
<tr>
<td>CRISPR</td>
<td>clustered regularly interspaced short palindromic repeats</td>
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<tr>
<td>CSIRO</td>
<td>Commonwealth Scientific and Industrial Research Organisation</td>
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<tr>
<td>DNA</td>
<td>deoxyribonucleic acid</td>
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<td>EPO</td>
<td>erythropoietin</td>
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<td>GDP</td>
<td>gross domestic product</td>
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<td>HIV</td>
<td>human immunodeficiency virus</td>
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<td>IT</td>
<td>information technology</td>
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<td>MRFF</td>
<td>Medical Research Future Fund</td>
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<td>ORR</td>
<td>objective response rate</td>
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<td>R&amp;D</td>
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<td>RNA</td>
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