industryinsights
Health care

Gene genie almost out of the bottle

The rapid development in understanding how the human body works at the cellular level is creating a potentially huge new industry that may revolutionise global health care – and the cash is pouring in, **writes Angela Jameson, Foreign Correspondent**

LONDON // Have you ever wondered what your DNA could tell you? Well, soon there will be an app for that.

The journey into the human genome is taking further great strides and the United Kingdom and its public healthcare system, the NHS, is right at the forefront.

A gene is a distinct stretch of DNA that determines something about who you are. Genes vary in size, from just a few thousand pairs of nucleotides (or "base pairs") to more than two million base pairs.

Genomics is a relatively new branch of science which uses DNA sequencing techniques and bioinformatics to sequence, assemble and analyse the function and structure of genomes (the complete set of DNA within an individual).

Looking at a person's genetic make-up can help to assess whether they are at risk from certain diseases and find the best course of treatment for them or suggest lifestyle changes.

This amazing science has only recently become possible due to an exponential decline in gene sequencing costs, faster processing techniques and large-scale government and pharmaceutical industry investment.

The science is stimulating a potentially huge new life sciences industry as well as major changes in health services.

According to a report by Deloitte for the UK Office of Life Sciences in October, the global genomics market is currently valued at about £8 billion (Dh42.19bn).

Analysts believe the market will grow rapidly, at about 15 per cent a year, as the cost of sequencing gets cheaper and governments and big pharmaceutical companies put huge investment into this field.

Sequencing a human genome now costs just US$1,345 compared with the $95 million it cost in 2001, according to the US National Human Genome Research Institute.

In the UK, the 100,000 Genomes Project was launched in 2012 with £200m of public money and is at the forefront of international research in this area. The project will sequence around 100,000 genomes from 70,000 people with rare diseases and cancer, and their families.

Dr Anna Middleton, the principal social scientist at the Wellcome Trust's Sanger Institute, who is working on a public engagement project for Genomics England, says the 100,000 Genomes Project research is pioneering and has huge implications for the NHS and patients.

"Treatment costs could be reduced but we are also taking away the diagnostic odyssey that some parents endure. After waiting [in the past] years for a diagnosis for their child, a whole genome sequence may offer this in a matter of months," she says.

The NHS is opening 11 Genomic centres across the UK which will give patients better access than ever to testing. But the test is nothing, Dr Middleton says, without sophisticated ways to interpret it. Clinical geneticists and bioinformatics experts are working hard on this and genetic counsellors, of which there are just 300 in the NHS, have to explain what the results mean in practical terms.

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The 100,000 Genomes Project should usher in a new era of personalised medicine but it should also generate research and business opportunities. For a start, Deloitte predicts that it will generate demand for formalised data interpretation companies.

Tom Slater, a fund manager at the Scottish firm Baillie Gifford has been investing in the genomics sector for five years, largely through the US company Illumina, which is a market leader in selling the machines that conduct genomic sequencing. "The possibilities that cheap genetic sequencing throws up are incredibly important for improving health care outcomes and taking cost out of health systems," he says. But he points out that there are still big challenges to overcome, particularly when it comes to the issue of collecting and sharing data.

Because the volumes of data are so huge, many analysts expect the big tech innovators – such as Google and Amazon – to become involved in this area, because they have the computing power and expertise to process such vast amounts of information. It is only by processing data on a huge scale that health professionals can begin to draw useful diagnostic patterns and predictors that can improve people's chances of beating diseases.

Last month, one of the UK's biggest pharmaceutical companies AstraZeneca said it would invest "hundreds of millions of dollars" over the course of 10 years, as it launched a huge effort to compile genome sequences and health records from two million people.

Astra says it will use the data to help drug development in all of its major disease areas, from diabetes to inflammation to cancer. It is partnering research institutions including the Wellcome Trust Sanger Institute, and Human Longevity, a biotechnology company founded in San Diego, California, by the genomics pioneer Craig Venter.

AstraZeneca also expects to draw on data from 500,000 participants in its own clinical trials, and medical samples that it has accrued over the past 15 years. GSK, the UK's biggest pharma company, is investing £65m over the next five years in a new non-profit research centre in Seattle called the Altius Institute for Biomedical Sciences. GSK wants to better understand biology so it can discover more medicines, like every other drug maker. It also wants to quit wasting money on drug candidates that look promising in the lab but flop years later when given to thousands of real people.

GSK is betting that one way around the problem will come from "the living genome" or what some call the "dark matter" of the genome. These mysterious stretches in the genetic instructions do not contain genes that provide code for making proteins, but they do appear to provide important controls over what genes do in different cells, in different states of health and disease, and in response to different environments.

But collecting data on such an enormous scale raises significant ethical questions, which Dr Middleton is considering in two research projects. A project called YourDNAYourSay.org looks at attitudes towards big date and genetics, while if you wondered how you might start a conversation about genomics – and experts are certain an increasing number people will soon want to do so – then a series of amusing short films on www.GeneTube.org should help you to get a grip on the basics.

One of the reasons it is important that the wider public understand how their personal data is being collected is that lots of commercial companies are keen to do it, too. For instance, Apple has developed a software platform that helps hospitals or scientists run medical studies on iPhones by collecting data form the devices' sensors or through surveys.

Google also has a little-known life sciences spin-off called Verily. The company is now independent of the search giant, but its website has moved away from its original life sciences brief and says it is now focused on using technology to better understand health, as well as prevent, detect and manage disease.

Back in the UK, there is talk that a gene-sequencing specialist that was spun out of Oxford University 11 years ago could list on the London stock exchange this year, with a market value of up to £1bn. Oxford Nanopore Technologies has developed a proprietary technology for genetic sequencing. Its two instruments – GridION, for large scale projects, and MinION for smaller ones. The MinION is the size of a memory chip. Since its launch in 2005, Oxford Nanopore has attracted £251m of funding and its big investors include the listed fund IP Group and the star fund manager Neil Woodford's Woodford Investment Management.

Meanwhile, the Cambridge university professor who invented the world's most successful technology for reading DNA has secured $29m in financing for his latest venture. Shankar Balasubramanian is seeking to exploit epigenetics – nature's instructions for switching genes on and off. He founded Solexa in 1998, which was acquired for $650m in 2007 by Illumina, which used its technology to become the market leader for reading genes.

The potential of gene editing has pushed more than $1bn of venture capital investment into gene-editing companies in the past two years, according to Boston Consulting Group.

Crispr, as the editing technology is known, is already being used by British scientists to redesign livestock, including editing cattle DNA to stop them growing horns.

AstraZeneca has invested millions in Crispr and is using it to edit the genomes of mice and of human cells to pursue therapies for heart disease, cancer and other illnesses. It believes Crispr could slash billions off the pharma industry's research and development costs. It is hoped this, in turn, would be reflected in the prices of new medicines.

Novartis, which has signed two deals with the gene-editing start-ups Intellia Therapeutics and Caribou Biosciences, plans to use Crispr for engineering immune cells and blood stem cells, and as a research tool for drug discovery.

Editas Medicine, which is looking at rare eye disease, raised $95m through a float in the US in February, while Intellia raised $108m in its own IPO this month. It develops treatments for cancer and liver disease.

Darren Griffin, a professor of genetics at the University of Kent, says the new treatments offer real hope: "Crispr technology is offering a range of exciting applications including treatment options for genetic diseases."

Silence Therapeutics is a UK biotechnology company that develops gene therapeutic technology based on RNA interference. RNA is the molecule responsible for controlling gene expression in nature. Gene expression determines what a cell is able to do.

Institutional investors including Henderson and Aviva have invested in Silence Therapeutics, but even its most advanced treatment – for pancreatic cancer – is still only in a clinical trial.

While it could still be years before investors see the sort of returns they hope for, few in the field doubt the coming genetics revolution in health care and its wider applications will affect every aspect of life, potentially changing humankind forever.

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The mysterious world of our cellular workhorses

Genes are often called the blueprint for life, because they tell each of your cells what to do and when to do it: be a muscle; make bone; carry nerve signals; and so on.

And how do genes orchestrate all this? They make proteins. In fact, each gene is really just a recipe for a making a certain protein.

And why are proteins important? Well, for starters, you are made of proteins. Fifty per cent of the dry weight of a cell is protein of one form or another. Meanwhile, proteins also do all of the heavy lifting in your body: digestion; circulation; immunity; communication between cells; motion; all are made possible by one or more of the estimated 100,000 different proteins that your body makes.

But the genes in your DNA do not make protein directly. Instead, special proteins called enzymes read and copy (or "transcribe") the DNA code. The segment of DNA to be transcribed gets "unzipped" by an enzyme, which uses the DNA as a template to build a single-stranded molecule of RNA. Like DNA, RNA is a long strand of nucleotides.

This transcribed RNA is called messenger RNA, or mRNA for short, because it leaves the nucleus and travels out into the cytoplasm of the cell. There, protein factories called ribosomes translate the mRNA code and use it to make the protein specified in the DNA recipe.

If all this sounds confusing, just remember: DNA is used to make RNA, then RNA is used to make proteins-and proteins run the show.

All the proteins in your body are made from protein building blocks called amino acids. There are 20 different amino acids used to make proteins, but there are only four different nucleotides in DNA and RNA. How can a four-letter code specify 20 different amino acids?

Actually, the DNA code is designed to be read as triplets. Each "word" in the code, called a codon, is three letters long. There are also special "start" and "stop" codons that mark the beginning and end of a gene. As you can see, the code is redundant, that is, most of the amino acids have at least two different codons.

Just about every living thing uses this exact code to make proteins from DNA.

Scientists first studying DNA sequences were surprised to find that less than 2 per cent of human DNA codes for proteins. If 98 per cent of our genetic information (or "genome") is not coding for protein, what is it for?

At first it was not clear, and some termed this non-coding DNA "junk DNA". But, as more research is done, we are beginning to learn more about the DNA between the genes, dubbed "dark matter", or intergenic DNA. Intergenic DNA seems to play a key role in regulation, that is, controlling which genes are turned "on" or "off" at any given time.

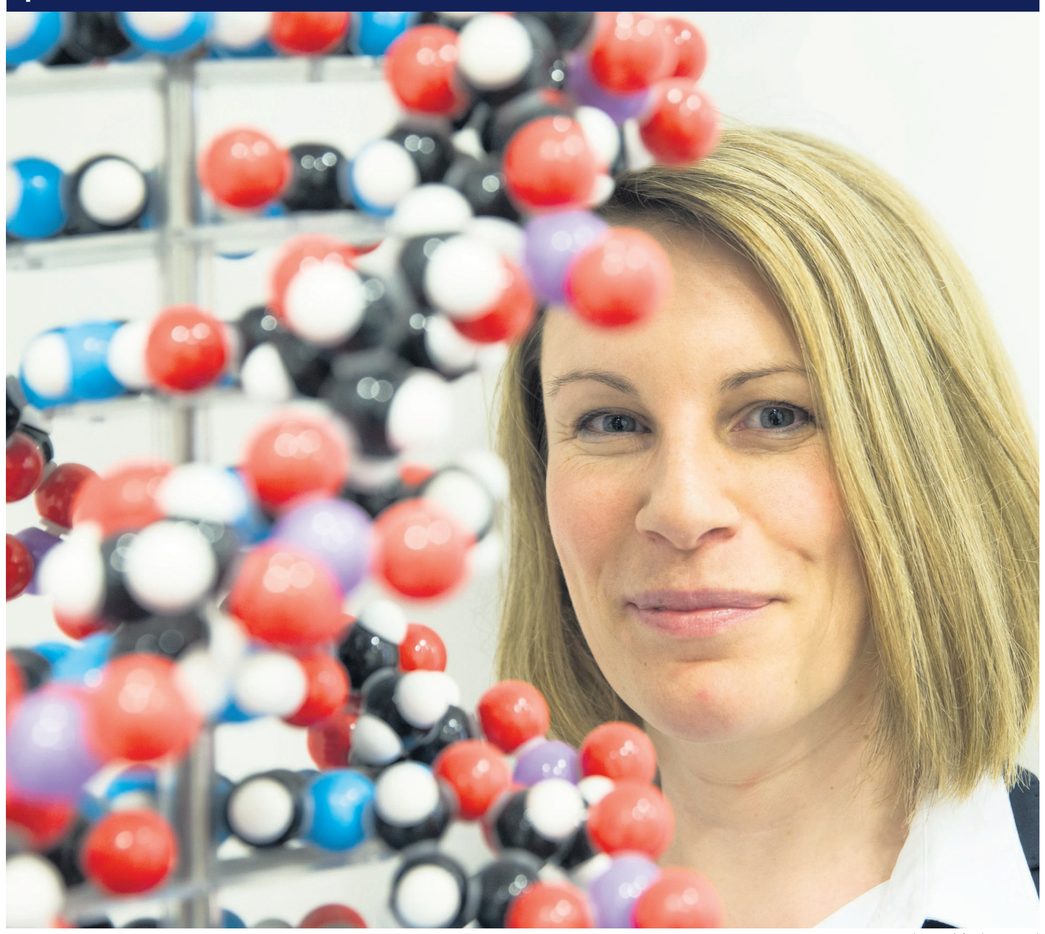
For example, some intergenic sequences code for RNA that directly causes and controls reactions in a cell, a job that scientists originally thought only proteins could do.

Intergenic DNA is also thought to be responsible for "alternative splicing", a kind of mix-and-match process whereby several different proteins can be made from one gene.

In short, it now seems that much of the interest and complexity in the human genome lies in the stuff between the genes ... so don't call it junk.

source: Stanford University department of genetics

q&a Dr Anna Middleton



Stephen Lock for the National

Revolution spurs a new era of considerations

The large-scale genome projects that are taking place around the world raise various ethical issues, which most people have never had to confront before.

How much would you want to know about conditions that you are predisposed to? Given that we have 20,000-plus genes, how much should doctors tell people about the genes they have?

Just because we have a gene that is linked to cancers or heart diseases does not mean we will suffer from those illnesses. With that uncertainty, do we really want to know what is genetically possible?

Additionally, how might commercial companies, including insurers, treat the information arising from genome sequencing, if they had access to it? How would our health systems cope if there was a rush of genetic testing for conditions for which they currently have no treatments? Dr Anna Middleton is the lead social scientist at the Wellcome Genome Campus in Cambridge, UK and is working on projects that look at these questions and the public's attitude to them.

Short, educational films on genetics are designed to provoke conversations in an informative, (and sometimes) amusing way.

They use clever graphics and animation to illustrate the scale of the issues and their importance. Here, Dr Middleton tells The National about her work.

How does your work help to educate the public about genomics?

I am currently working on two projects that are designed to engage the public with some of the social and ethical issues raised by genetics. These are very relevant in that genomic technology is on the verge of going mainstream. Apple has just signed a deal with Google-backed genomics company 23andMe, which will see 23andMe customers use their iPhones to share genetic data with researchers carrying out medical studies. However, the vast majority of the public don't yet know what they need to know about genomics. My first project YourDNAYourSay looks at data sharing and concerns you may have about handing over all your data, through a detailed survey and nine short films. The second project www.genetube.org features short films about how to start a conversation with people who do not know anything about this.

Why do we need to gather and store genetic data from hundreds of thousands of people?

The only way that we will unpick the power of genetics is by having access to very large data sets. We need to analyse these to interpret the implications for both serious conditions and the less serious things. Having large data sets is particularly valuable for working out if something rare is significant or not.

What is the role of consumer facing companies such as 23andme, Apple and Fitbit in genomics?

These companies are often interested in the recreational testing of healthy people. What is interesting is how the public might respond to the data sets they produce. We don't know if it is possible to improve your health through the collection of data, presumably people might change their gym workouts [for example] according to something they learn about their biology – but we don't know if that is the case and whether it can be sustained for the long term.

Is there a tension between the commercialisation of the data and the ambitions of public health programmes like the 100,000 genomes project?

The only way to benefit human kind is if we gather the data but where data gathering is led by commercial organisations there is a real tension there. The question is are we all in this together to improve human kind or not? If we are, then we should be making all this data shareable but it is more personal to you than an iris scan or a fingerprint. However, our fear over the big ethical questions should not scare us off the possibilities that widespread genome sequencing brings. Scientists and healthcare workers are working to cut across the barriers around the world, to make data sharing possible, across the profit and non-profit worlds. The key is for people to understand what it means and to make an informed decision about whether to participate or not. The challenge is to make the data sharing "safe" in ways that protect individuals – breaches of confidentiality must carry a firm penalty and what that looks like is still being worked out.

Angela Jameson

Region // Outlook

UAE among pioneers of a biological frontier

Genetics a growing sector in commercial medical research

Sananda Sahoo

In the Middle East, where the incidence of marriages between people descended from the same ancestors – termed consanguineous – is relatively high, the genetic sector is gaining importance in the medical and educational fields, according to officials and industry insiders.

Diagnostic laboratories and companies providing machines and gene testing kits are at the forefront of this sector in the UAE that is commercialising genetics research, which currently comes out of the universities and research centres worldwide.

About 30 to 40 per cent of marriages in the Middle East are consanguineous varying from one country to another in the region, according to Francisco Rodriguez, the general manager of Spanish company Igenomix UAE. Such marriages may give rise to recessive syndromes in the parents' children.

"The risk of having an affected child is considerably higher than in another ethnicities and countries," he says. "We are facing difficult cases with two or three diseases within the family and inherited, with difficult consequences such as affected children and sudden deaths."

Moreover, about 10 to 15 per cent of the total population in the Middle East is infertile, compared with the worldwide average of 10 per cent, according to Mr Rodriguez. This leads to assisted reproduction techniques and the rise in demand for genetic diagnosis.

Igenomix is one among the growing number of genetic diagnostic laboratories in the UAE.

The genetics industry in this country is built mostly around the companies that provide state-of-the-art machines and devices to conduct genetic tests in hospitals, and the diagnostics segment, that is, laboratories and clinics, for instance, that order and perform genetics tests.

More patients are now able to undergo genetic testing to detect diseases such as cancer, but also more routine daily tests such as for food intolerance.

Biotech companies that develop genetic medicines are yet to begin research and development in the UAE or the wider Arabian Gulf region.

"Once the product is available and the machine [to read the samples] is available, people will be able to use the services and help people make better decisions," says Marwan Abdulaziz Janahi, the executive director of Dubai Science Park.

Currently, the costs for genetic tests, for example for those relating to reproduction, can run into thousands of dirhams. Once the volume of patients develops further, the costs are expected to come down, he says.

Molecular diagnostics and personalised medicine is a small but a growing segment in the UAE on the back of the demand for fertility treatments, tests for inherited diseases such as thalassaemia, and prenatal testing such non-invasive prenatal testing for Down syndrome, among others.

At Dubai Science Park, where the latest genetic laboratory opened this month, there are about eight companies that provide the technology for genetic testing including Thermo Fisher Scientific, and five genetics laboratories among the 300 or so companies housed at the free zone.

The US biotechnology product development company Thermo Fisher Scientific opened its customer centre in Dubai in April last year. It also trains people on how to use the machines.

"Thermo Fisher Scientific enables its customers to conduct genetics research and clinical research by providing leading technologies, such as next generation sequencing and quantitative polymerase chain reaction platforms," says Colin McCracken, the vice president and general manager for Eastern Europe, Middle East and Africa at Thermo Fisher Scientific in Dubai. "These instruments are widely being used to today, particularly in oncology and infectious disease-related programmes."

Despite the relative youth of the segment, the genetic diagnostics market is getting crowded in the UAE.

"Now the market is more and more competitive, especially with the new tests such as next-generation sequencing [to study for mutations in specific genes]," says Fady Al Assaly, the spokesman at Alliance Global Group.

Governments in the Gulf region have been aware of the importance of genetic education and the industry for some time

Based in Dubai Science Park, Alliance Global Group, which opened in 2006, distributes laboratory machines and diagnostic kits in the local market.

Next-generation sequencing is used to improve success rate at fertility centres, and is also used at hospitals, private labs and veterinary centres.

Igenomix, for instance, performs about 200 prenatal genetic tests a month and the number is growing, according to Mr Rodriguez.

Last year in February, Igenomix opened its seventh office worldwide in Dubai Health Care City to provide reproductive genetic services, such as "carrier" genetic tests to screen for inherited diseases, to the Middle East.

Governments in the Gulf region have been aware of the importance of genetic education and the industry for some time.

In 2003, the Centre for Arab Genomic Studies was set up in Dubai to provide public awareness on genetic diseases in the region and to identify disease-causing genes in the Arab population, among other goals.

Some governments in the region, such as Saudi Arabia and Qatar, have also announced plans to sequence the whole human genome, a project similar to that of the Genomics England, owned by the UK department of health. The UK project, which was announced in 2013, aims to sequence 100,000 whole human genomes.

The Saudi Human Genome Project, also launched in 2013, looks to sequence the DNA, or the building blocks of a human body, for 100,000 Saudis. It was to be funded and organised by the King Abdulaziz City for Science and Technology.

The technology is there to record such data, but the question of what happens to the information and who owns it is critical, Mr Janahi says.

"But the bright side is that it has helped physicians to make better [clinical] decisions," he adds.

The Saudi programme aims to address the healthcare burden that the country faces from inherited diseases, which affect 8 per cent of births in the country, and the common genetic diseases such as diabetes, which affects more than 20 per cent of the population, through prevention and awareness and personalised therapies, according to the project.

Even though the commercial genetic sector is small in the region, there are a few challenges.

Competition from overseas companies and need for more education and awareness of genetic issues within the UAE are among these, according to Mr McCracken.

The legal issues such as who owns the results of genetic tests, whether it is the insurance companies, the employers, or the individuals themselves, are yet to be clarified in the UAE.

As Mr Janahi says: "It is a complex decision, and we still haven't reached that level, at this point we are still busy making sure we have the technology, and we use it in certain areas."

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The US biotechnology product development company Thermo Fisher Scientific opened a customer centre in Dubai in April of last year. Above, the company's HQ in Waltham, Massachusetts. Michael Fein / Bloomberg