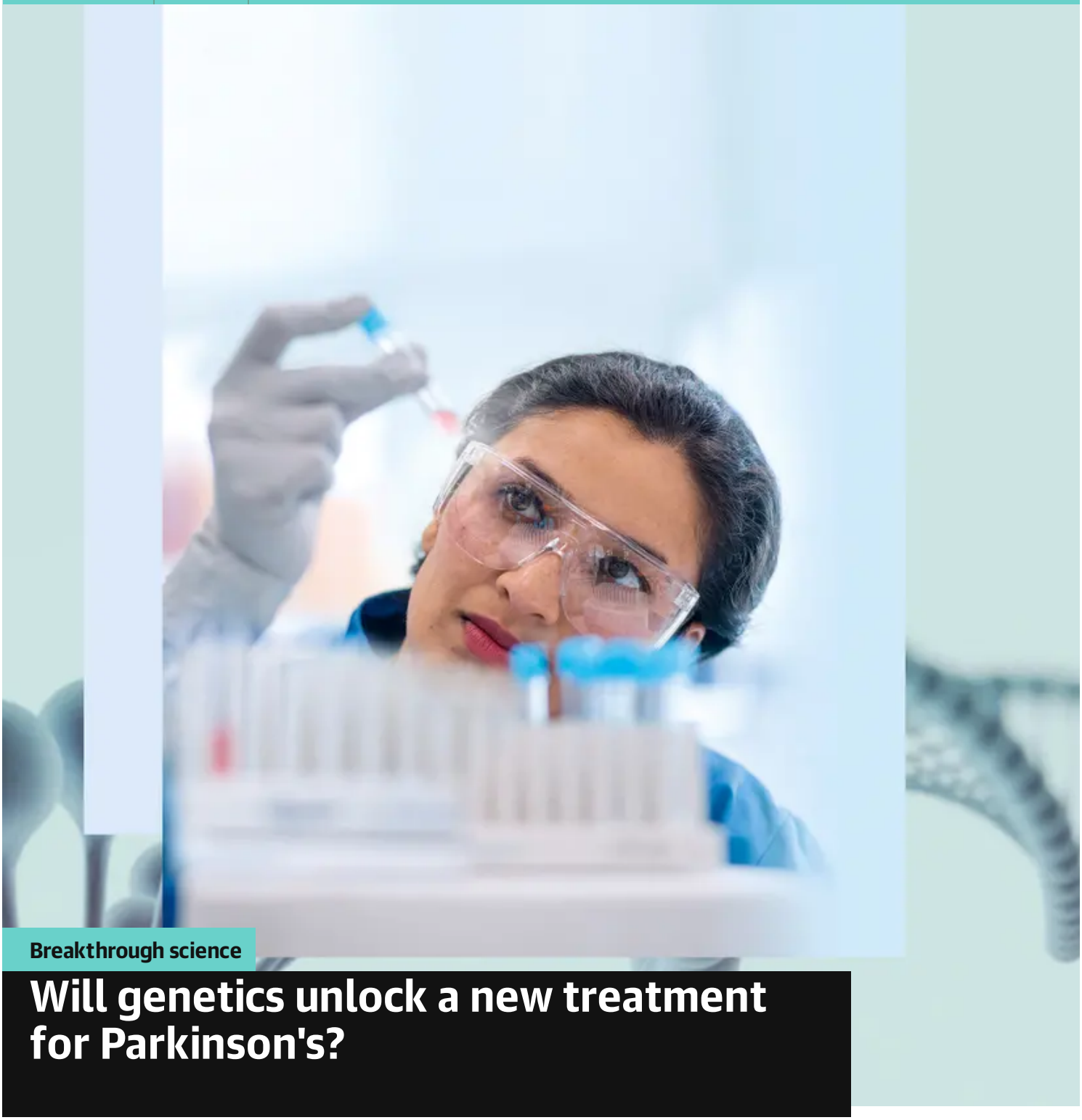

Breakthrough science

Will genetics unlock a new treatment for Parkinson's?

With scientists increasingly using genetics in drug research and development, GSK is collaborating in a new approach to tackle gene-carried Parkinson's disease

by Sue George

Main image: Composite: Getty/GSK

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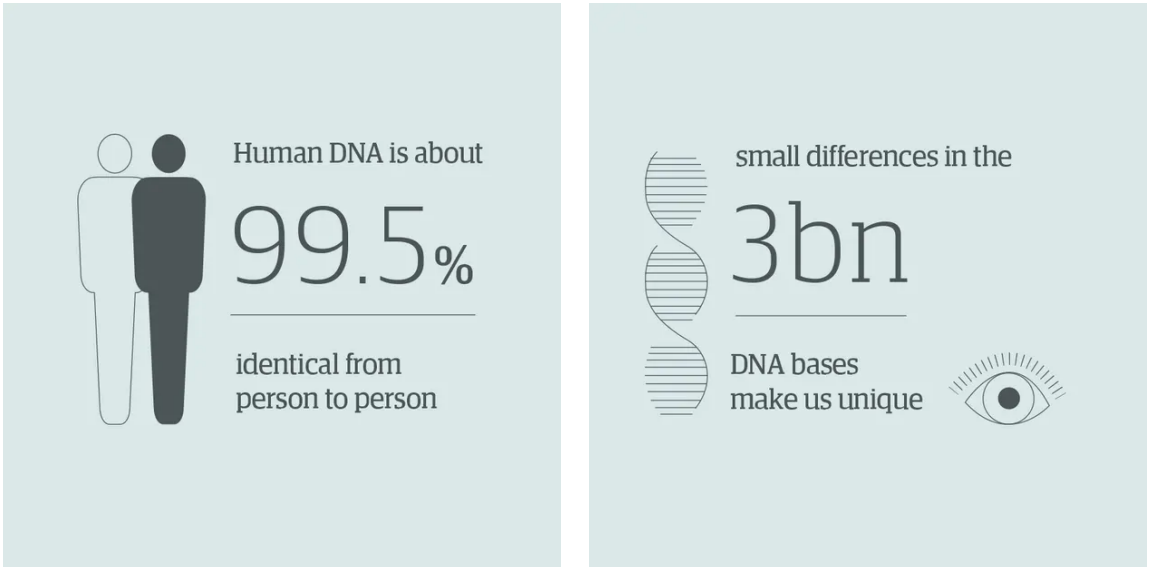
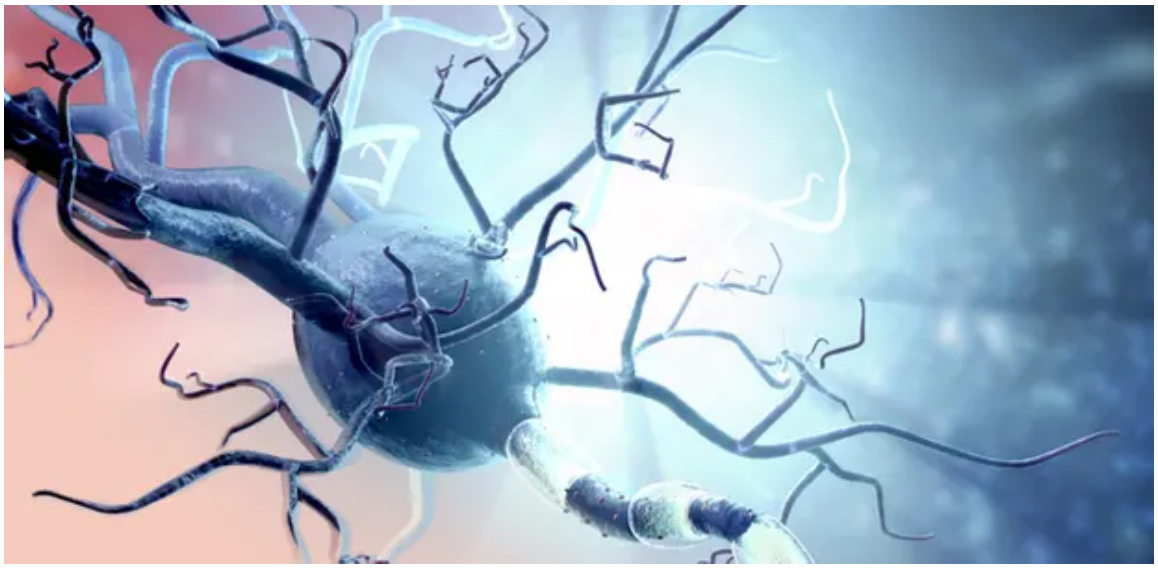
Rapid developments in the field of genetics since mapping of the human genome began in the 1990s have led to huge advances in our understanding of the causes of human diseases.

We now know that human DNA is about 99.5% identical from person to person. However, those small differences in the 3bn DNA bases that make up our genome are what make us unique.

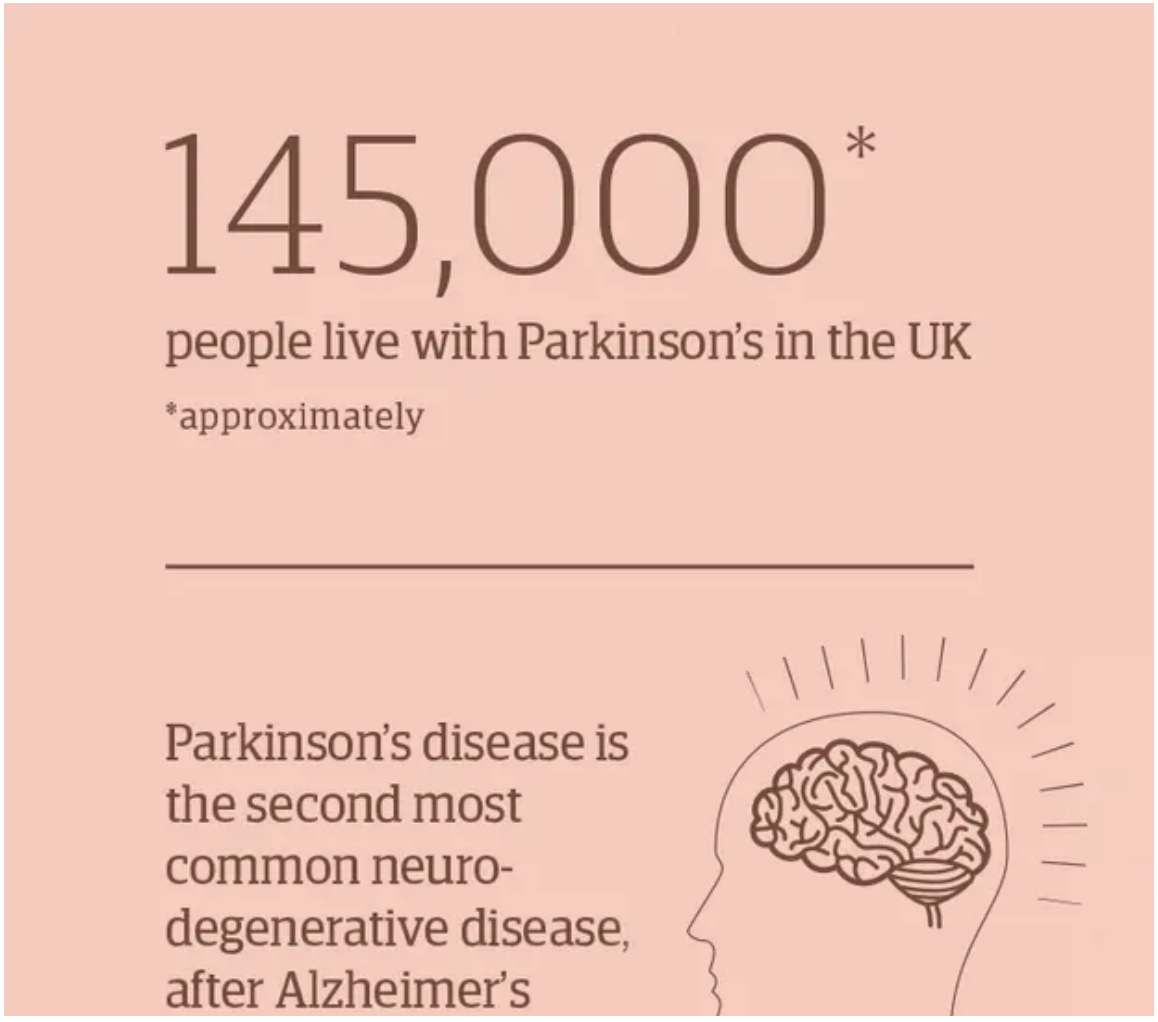


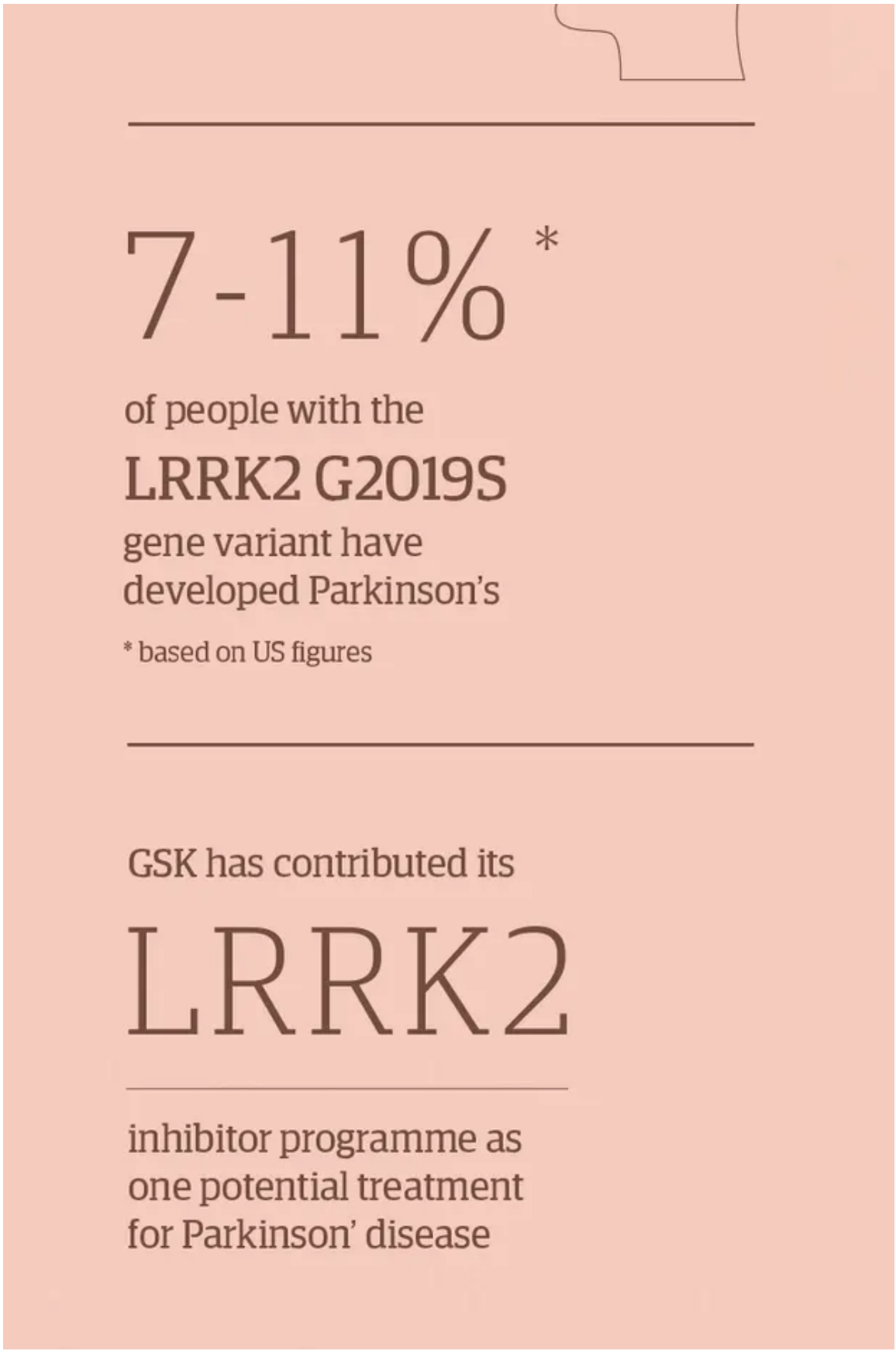
Genetic differences indicate whether we are more likely to have – for instance – perfect pitch, blue eyes, or a fear of heights. These tiny variants also influence our risk of getting a particular disease, and the sort of drugs that are likely to treat it most effectively.

As a result, scientists increasingly use genetics as a basis for drug research and development. But the fact that some variants of these diseases affect comparatively small numbers of people can have an impact on how easy it is to carry out this R&D.



Parkinson's disease, for instance, is the second most common neurodegenerative disease, after Alzheimer's. There are many people around the world with Parkinson's, including about 145,000 in the UK, but few of those cases have a genetic cause. When there is a genetic cause, it is most often the G2019S mutation in the LRRK2 gene.





In the US, there are about:

- A million people with Parkinson's disease.
- 135,000 LRRK2 G2019S carriers.
- 10,000-15,000 people with Parkinson's disease who are LRRK2 G2019S carriers.

These carriers would benefit from specific treatments, but developing them has often proved challenging. According to Matt Nelson, head of genetics, GSK, understanding genetics is key to increasing our knowledge of the causes of disease and will have a key role in developing effective new medicines. "Genetics provides us with a direct causal connection between particular genes, particular pathways and the diseases we are interested in treating," he says. Research indicates that drug research backed by genetic support is about twice as likely to lead to a successful medicine. "There is an exponential growth in our understanding and insights as to how genes influence disease, severity and progression. All of this can be very insightful when discovering new treatments," Nelson says.

"Approximately 90% of drug candidates fail in clinical development," says Carolyn Buser-Doepner, GSK's head of target sciences. "This high level of attrition after multiple years of research and clinical trials represents the greatest challenge and opportunity for pharmaceutical R&D.

"Genetic data can also inform on potential safety risks for a given drug target," she continues. "Collectively, these data are expected to improve target selection to allow for safer, more effective targeted medicines to be discovered."

This is why GSK has teamed up with 23andMe – a consumer genetics and research company – to discover new therapeutic drug targets, and consequently new treatments. GSK's $300m equity investment and four-year collaboration will also help identify patient subgroups and allow more effective identification and recruitment of patients for some clinical studies.

When a customer signs up for 23andMe's service, the company's state-of-the-art genotyping technologies measure more than 600,000 genetic variants in the person's DNA. Of the 5 million customers of 23andMe, more than 80% have opted in to allow their anonymised data to be used in research and to be recontacted. This consent has to be given explicitly, and can be withdrawn at any time. For the purposes of drug target discovery, at this time GSK will only have access to aggregated summary statistics from these analyses, not any personally identifiable details.

To enable work to start immediately, GSK and 23andMe have agreed to collaborate on GSK's LRRK2 inhibitor programme as a potential treatment for Parkinson's disease. This programme has the potential to progress quickly by leveraging 23andMe's consented customers who are aware of their LRRK2 variant as a result of the company's FDA-authorised genetic health reports. By recruiting patients with defined LRRK2 mutations, this programme has the potential to reach clinical proof of concept more effectively and efficiently.

Anne Wojcicki, CEO and co-founder of 23andMe, has a personal connection with Parkinson's disease; the father of her children has the LRRK2 mutation. As she said in her August Facebook Live video, 23 minutes with Anne: "We have thousands of customers with this mutation, and knowing there are a number of drugs in development specifically targeting [this], I am really excited about what we will be able to do. My hope is we will be able to have an impact on drug discovery and make something happen faster than it normally could."

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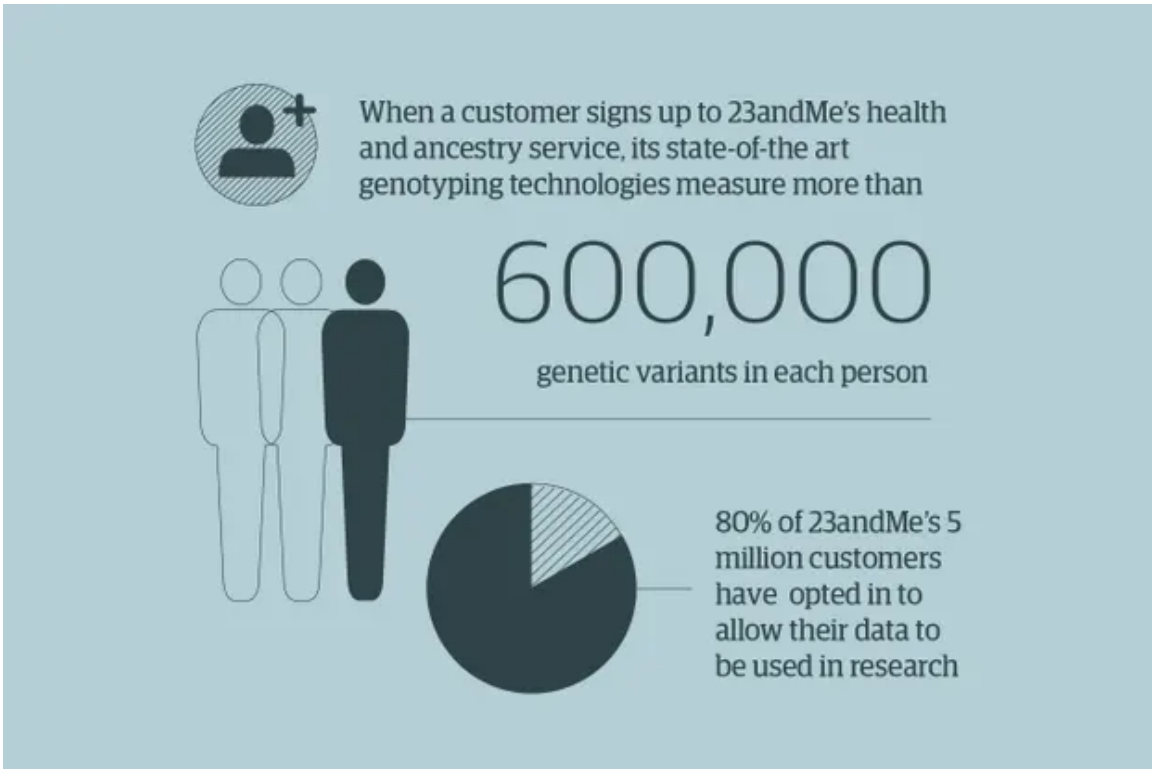
If, later in the drug development process, there is a good candidate medicine to treat Parkinson's patients with this gene variant, 23andMe scientists will be able to recontact the relevant customers, who may then be facing Parkinson's disease, to see if they consent to be part of a clinical trial in their area. This should greatly speed up the start of clinical trials.



GSK's collaboration with 23andMe is part of its new approach to R&D, which focuses on the immune system, genetics and advanced technologies. But this is not GSK's first large-scale work of this type. It is currently working with the UK Biobank – sequencing the genetic data from 500,000 anonymised volunteers. GSK is also part of a collaboration called Open Targets. This is developing an open-access search engine to search and evaluate the extensive genetic data that are already available.

There is certainly cause for hope about what genetics is likely to contribute to our future health and medical care. "We can all be excited about the tremendous new insights genetics is providing into what causes disease in humans and how genes might modify disease risks and progression," Nelson concludes. "Over the next 10 to 15 years, a new generation of therapies will be developed that are more efficacious, more effective and safer for treating disease."

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