Reading Genomes

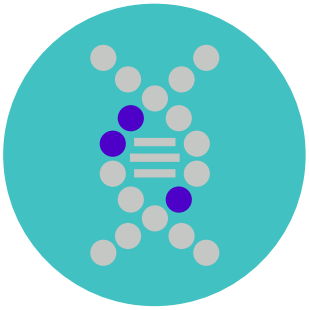
In the last two decades, there has been an amazing leap in information and insight into our human genome. This scientific advance has been enabled by new technologies, which can 'read' or 'sequence' the more than 6000 million letters in a person's genome – their entire genetic make-up – in days, rather than years.

In 2003, the Human Genome Project was completed and a 'reference' human genome sequence was published: the result of a $3,000,000,000 international effort. This data provided a global infrastructure for biology: researchers around the world could access a common collection of data, and overlay information about DNA variation and function.

Just over 10 years later, a genome sequencing technology company called Illumina, Inc. announced that their new machines could sequence 350 whole human genomes per week, at a base cost of less than 1000 US dollars per genome. The Garvan Institute of Medical Research in Sydney was one of the first institutes in the world to acquire this new technology.

What can you learn from a sequence?

Genomic technologies offer the potential to use personal genomic information to guide medical treatment. Genomic medicine has the potential to transform healthcare because all diseases have a genetic component -- from inherited disorders to complex diseases such as cancer and diabetes.



How could health-related DNA variants be used?

- To speed up diagnosis of existing genetic disorders
- To accurately characterise complex disease
- To guide treatment or predict a person's survival
- To better use pharmaceuticals and avoid adverse effects
- To identify new therapeutic targets and design/ develop new therapies
- To better understand biological pathways
- To make reproductive decisions
- To estimate risk of developing disease

What are the issues?

A person's genome contains information that:

- is both unique and shared with family
- can identify a person and their relatives
- may be of interest to others (eg. insurers, employers)
- is mostly stable throughout a person's lifetime.

This creates a unique set of ethical, legal and social challenges to address when adopting genomic technologies.

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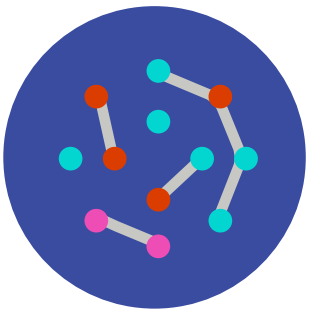
Personal Genome Project: Background

The Personal Genome Project (PGP) is a project dedicated to creating a totally unique scientific resource. The project involves recruiting people to have their entire genome sequenced and to have their results, together with personal data about their health and their lives, made publicly available online.

Who are the participants?

The first 10 people to have their genomes sequenced by the PGP are called 'the PGP 10'. The PGP 10 were recruited in the USA in 2007, and included the genetics professor who founded the PGP (Dr George Church), and a mix of men and women of different ages.

The project aims to recruit a total of 100,000 people worldwide, from a diverse range of genetic, social and environmental backgrounds. Theoretically, anyone who meets the eligibility requirements (e.g. being at least 18 years old) can volunteer to participate. So far, the project is up and running in the USA, UK and Canada. There have been discussions about a PGP Australia. The idea is to create a resource that researchers worldwide can use to advance our collective understanding of genetics, biology, and health.



What does being part of the PGP involve?

People can sign up online to be part of the PGP. When they sign up, they consent to have their entire genome sequenced and shared on the internet. They give samples of their blood, saliva, and skin cells, and provide detailed information about their health and lifestyle.

Giving consent to have your genome sequenced

People who sign up for the PGP are doing so on the basis that it's not anonymous, that information about them will become publicly available, and that any researcher anywhere can use their data.

The people running the PGP take informed consent very seriously. Every participant is required to take an exam to show that they understand the risks and protocols involved, and to score 100% on that exam.
However, some people believe that this type of test doesn't capture whether a person is informed enough.

What kinds of results are people getting?

People who have had their genomes sequenced are getting some results that have serious implications for their health. For example, a young woman found out she has an increased risk of Alzheimer's disease. A grandmother found out she has a high risk of breast cancer. A middle-aged journalist found out he has a genetic predisposition to a rare heart condition.

Who has access to the results generated by the PGP?

The results of the PGP are available online for anyone to access (see https://my.pgp-hms.org/). The intention is to make the results accessible to scientists world-wide so they can use the data for their research. In reality, though, anyone with access to the internet can see the results.

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HOW COULD SCIENCE TEACHERS USE PERSONAL GENOMES?

For Science teachers, the PGP provides an excellent example of 'Science as a Human Endeavour'.

The PGP involves everyday people who have chosen to have science and technology applied to their lives in a very personal way. This goes beyond the scientists who generate and interpret the data, and puts a human face on the science.

Where could the PGP be included?

PGP-related activities would be ideal for including in a Year 10 Genetics unit, specifically linking to:

ACSHE192 Advances in scientific understanding often rely on technological advances and are often linked to scientific discoveries; and

ACSHE230 Values and needs of contemporary society can influence the focus of scientific research

How could students explore the topic?

There are many different ways students could explore the topic and apply their knowledge and understanding.

Students could research information about the PGP and imagine they are a counsellor asked to advise to someone thinking about having their genome sequenced… what would they tell them?

Working in groups, students could take on the role of different characters and give their opinion of the PGP as part of a role play e.g. someone thinking of having their genome sequenced, their child, their employer or insurer, their doctor or their partner.

Students could construct a PNI (positive, negative, interesting) chart for the PGP.

Students could discuss whether or not they would have their genome sequenced, and if so, under what conditions?

A list of medical reasons for having your genome sequenced could be compiled.

Student could be given scenarios about people finding out they have particular medical conditions, then discuss what actions or life choices they would take.

Useful resources

The PGP – what it is, how to participate, using PGP data: http://www.personalgenomes.org

GENOME: The Future Is Now. Three 6-8 min webisodes about the first people to participate in PGP:

https://www.youtube.com/watch?v=mVZI7NBgcWM
https://www.youtube.com/watch?v=2r9DpthvNKM
https://www.youtube.com/watch?v=mgXAO8pv-X4

Nova Science Now: Personal Genome Project (3.5 min) https://www.youtube.com/watch?v=YbDgxZWyAZQ

New York Times article 'My genome,My self' by Steven Pinker (one of the PGP 10): http://www.nytimes.com/2009/01/11/magazine/11Genome-t.html?_r=0

Article about potential impacts on the families of people who make their genomes public: http://genomesunzipped.org/2010/10/why-public-genomics-is-not-a-purely-personal-decision.php

Pioneers of Personal Genome Sequencing playlist from Open Humans Foundation: https://www.youtube.com/user/PersonalGenomesOrg/playlists

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PGP Profile 1: Rosalyn Gill

Rosalynn Gill was one of the first ten Personal Genome Project participants (PGP9). Hers was the first fully public genome of a human female. Each of these participants have shared their genomic and medical information with the world

Where do I find her data?

Rosalynn's information is on the personalgenomes.org site as hu034DB1. Her public profile can be found at https://my.pgp-hms.org/profile/hu034DB1

Background?

Rosalynn was 45 years old in 2007 when she had her genome sequenced. She had to consider how her decision to be sequenced and release the information to the world would affect her children. She had some concerns about a family history of cancer and cardiac disease, but wanted all of the information.

Resources

A video about her background and her approach to this project can be found in

GENOME: The Future is Now WEBISODE 2 (https://www.youtube.com/watch?v=2r9DpthvNKM)

and further interviews are available in the personalgenomes.org youtube channel and playlists.

Genome report | Insufficiently evaluated variants | Coverage | Gene Report | Metadata

Show likely pathogenic and rare (<2.5%) pathogenic variants | Show all

Show All entries Search:

Variant	Clinical Importance	Impact	Allele freq	Summary
APOE-C130R	High	Well-established pathogenic Complex/Other, Heterozygous	14%	This is generally known as the ApoE4 allele of ApoE and is associated with increased risk of Alzheimer's. 20-25% of individuals are heterozygous for this variant, and 1-2% are homozygous. Data from Khachaturian et al. suggests an average 7% of all individuals developed Alzheimer's by the age of 80; when this is split by ApoE4 status: 10% of ApoE4 heterozygotes (3% increased attributable risk), 40% of ApoE4 homozygotes (33% increased attributable risk), and 5% of non-carriers (2% decreased attributable risk). Notably, their model suggests 70-75% of people would eventually develop Alzheimer's by the age of 100 regardless of ApoE4 genotype (and 25-30% are resistant, regardless of genotype), but that ApoE4 variants shift the disease onset to occur significantly earlier (4 years earlier for heterozygous carriers, 13 years for homozygotes).
SCN5A-G615E	High	Uncertain pathogenic Dominant, Heterozygous	0.029%	Rare, reported to be associated with long-QT syndrome (can cause syncopal spells, sudden death as a teenager / young adult), but observations are scattered may have some publication bias.
MTR-P749S	High	Uncertain pathogenic Unknown, Heterozygous	0.10%	Unreported, predicted to be damaging. Other recessive missense mutations in this gene cause methylcobalamin deficiency.

PGP Profile 2: Steven Pinker

The Personal Genome Project (PGP) recruits people to have their entire genome sequenced and to have their results, together with personal data about their health and their lives, made publicly available online. Steven Pinker, author and Harvard psychology Professor volunteered to be one of the first recruits (PGP6).

Steven's data can be found here https://my.pgp-hms.org/profile/hu04FD18
He wrote a long read for The New York Times about his experience
http://www.nytimes.com/2009/01/11/magazine/11Genome-t.html

MAGAZINE | My Genome, My Self

Magazine

My Genome, My Self

By STEVEN PINKER JAN. 7, 2009

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PGP Profile 3: Colin Smith

Colin Smith, a genomics professor from England, was the first participant of the UK arm of the Personal Genome Poject. Colin is an advocate for “open consent” and making genomic and health data publicly available. He donated his information to contribute to understanding of the human genome.

Colin’s information is on the personalgenomes.org.uk site as uk4CA868. His public profile can be found at https://my.personalgenomes.org.uk/profile/uk4CA868.

His profile includes raw data from online genetic testing company 23&me, a report from whole genome sequencing, and a report from analysis of DNA methylation.

You can read Colin’s thoughts on donating his genome in this article from The Conversation https://theconversation.com/why-i-donated-my-entire-genome-sequence-to-the-public-83741

or hear him talk about it in this 2.5min clip https://www.youtube.com/watch?v=6gLa6I04hTc

- Possibly Harmful Traits

Mag.	Identifier	Genotype	Summary
3.2	rs2981582	(T;T)	1.7x higher risk of ER+ breast cancer
3	rs1800460	(A;G)	(TPMT*3B) impaired drug metabolism
3	rs4244285	(A;G)	Poorer metabolizer of several popular medicines...
3	rs6920220	(A;G)	1.2x risk Rheumatoid Arthritis
3	rs7754840	(C;G)	1.3x increased risk for type-2 diabetes
3.0	rs1142345	(A;G)	TPMT*3C . impaired drug metabolism
2.5	rs11190870	(T;T)	Possibly even more increased risk of scoliosis
2.5	rs1121980	(C;T)	1.67x risk for obesity
2.5	rs1154155	(G;G)	2.5x increased risk for narcolepsy
2.5	rs13266634	(C;T)	Increased risk for type-2 diabetes
2.5	rs1421085	(C;T)	~1.3x increased obesity risk
2.5	rs2254958	(C;C)	1.61x increased risk for Alzheimer’s
2.5	rs339331	(T;T)	Prostate cancer risk
2.5	rs3780374	(A;G)	Substantially increased odds of developing V617...
2.5	rs7574865	(G;T)	1.3x risk of rheumatoid arthritis; 1.55x risk o...
2.4	rs1143679	(A;G)	1.78x increased risk for SLE
2.4	rs7966230	(G;G)	Slightly lower levels of plasma VWF
2.2	rs2231137	(G;G)	~1.5-3x increased risk for ischemic stroke
2.2	rs944289	(T;T)	2.6x increased thyroid cancer risk
2.1	rs1219648	(G;G)	1.64x risk for breast cancer
2.1	rs1329428	(G;G)	2x increased risk f
2.1	rs17077540	(A;G)	1.6x major depres
2.1	rs2231142	(A;C)	1.74x increased go
2.1	rs241448	(C;C)	2.14x increased ris
2.1	rs2420946	(T;T)	1.64x risk for brea