MEDICAL APPLICATIONS OF GENETIC TECHNOLOGY

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- Humans have been manipulating DNA in the laboratory since the early 1970s, with the creation of the first transgenic mouse in 1974
- Since the completion of the human genome project in 2003, researchers have had access to more information about genes and disease than ever before
- This increase in knowledge has led to a boom in new genetic technologies that read, manipulate and even edit the human genome, with the aim of improving health
- These technologies are already being applied to diagnose rare genetic conditions, discover a person's risk of developing inherited illnesses, and develop targeted treatments
- In the future, genetic technologies could dramatically lower rates of inherited conditions in the human population, and revolutionise how we treat diseases like cancer

Reading and analysing DNA

- **Genetic testing** involves identifying changes (known as variants) in a person's DNA that are associated with a disease or risk.
    - -Genetic tests usually analyse single genes, or parts of genes
    - -Genetic screening (testing large numbers of people) began in 1966. Now newborns are tested for around 30 conditions.

Genomic testing is analysing large parts (or all) of a person's DNA to find variants that might be associated with a genetic condition. It is becoming a more widespread alternative to single gene tests

- -Genomic testing can be used both to diagnose genetic conditions, and to identify disease risks in healthy adults. This information can guide treatment or prevention.

- Analysing the DNA of tumour cells has enabled scientists to develop **targeted cancer therapies** to inhibit specific proteins present only in cancer cells
    - -One of the first, imatinib, was released in 2001. This drug blocks a protein produced from the fusion of two genes, which occurs in some types of cancer.

Reproductive technologies

- **Pre-implantation genetic diagnosis** involves genetic profiling of an embryo created using in vitro fertilisation (IVF), prior to transferring it to the uterus and allowing it to develop normally.
    - -First clinical application was published in 1990
    - -Can help couples who are at increased risk of passing genetic conditions on to their children
    - -Only those embryos that do not have the genetic condition being tested for will be selected and transferred to the uterus
    - -Has the ability to lower rates of many genetic conditions in the population

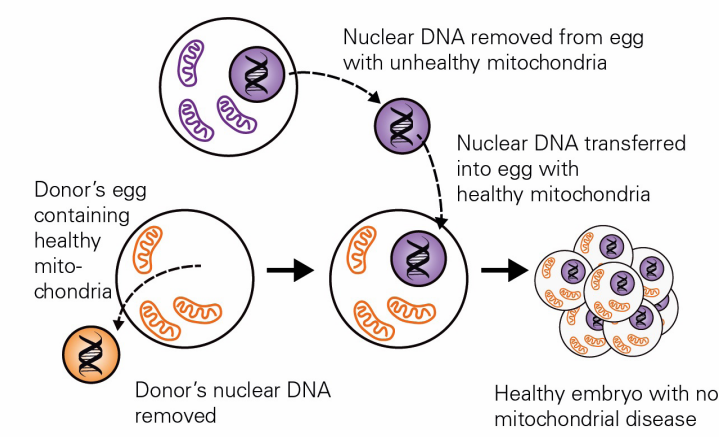
- **Mitochondrial replacement therapy** is an expansion of IVF techniques that could prevent mothers passing mitochondrial diseases on to their children

  -Mitochondria have their own genome, and during early development it is the mother's egg cells that contribute mitochondria to the embryo

  -In mitochondrial replacement therapy, a donor egg with healthy mitochondria has its nucleus removed and replaced with nucleus from the mother. IVF then produces an embryo that contains nuclear DNA from both parents and healthy mitochondrial DNA from the donor (see diagram).

  -Controversial because these DNA modifications can be passed on through generations. Such changes are referred to as "germline" modifications.

  -In 2015, United Kingdom became the first country to legalise the technique



Mitochondrial replacement therapy

Adapted from Australian Mitochondrial Disease Foundation

Genes as medicine

- **Gene therapy** involves introducing DNA into cells to treat or prevent disease

  -First gene therapy trial was in 1990. Early trials resulted in dangerous side effects caused by the viruses used to get genes into cells

  -In 2017, a 13-year old boy became the first person in the US to receive an FDA-approved gene therapy for an inherited disease. The therapy was called Luxturna, which treats a rare inherited eye disease by delivering a modified copy of the RPE65 gene to cells in the retina using an engineered virus.

- CRISPR-Cas9 is a bacterial enzyme system that is used for **genome editing** – directly changing the DNA sequence of genes

  -CRISPR-Cas9 was first harnessed for genome editing in human cells in 2013

  -CRISPR-Cas9 has not yet been used in human trials, but there is a great deal of excitement surrounding its application to human health

  -Researchers successfully edited viable human embryos using the technique in 2017, but there are huge ethical issues with embryo editing such as this – changes to genes at the embryonic stage would mean a change that reaches all cells in the body and is able to be passed on to children

Further Reading

Genetic and genomic testing

http://www.genetics.edu.au/publications-and-resources/facts-sheets/fact-sheet-15-genetic-and-genomic-testing

https://www.garvan.org.au/research/kinghorn-centre-for-clinical-genomics/about-kccg/what-is-clinical-genomics

Preimplantation genetic diagnosis

http://www.genetics.edu.au/publications-and-resources/facts-sheets/fact-sheet-29-preimplantation-genetic-diagnosis-pgd

https://www.nature.com/scitable/topicpage/embryo-screening-and-the-ethics-of-human-60561

Mitochondrial replacement therapy

https://www.newscientist.com/article/2107451-everything-you-wanted-to-know-about-3-parent-babies/

https://www.mito.org.au/wp-content/uploads/2016/03/Mitochondrial-Donation-Briefing-Paper.pdf

Gene therapy

http://www.genetics.edu.au/publications-and-resources/facts-sheets/fact-sheet-23-gene-therapy

https://www.yourgenome.org/facts/what-is-gene-therapy

https://theconversation.com/car-t-therapy-works-for-some-blood-cancers-but-can-we-make-it-work-for-brain-tumours-100125

Gene and embryo editing

https://www.broadinstitute.org/what-broad/areas-focus/project-spotlight/crispr-timeline

https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting

https://theconversation.com/scientists-edit-human-embryos-to-safely-remove-disease-for-the-first-time-heres-how-they-did-it-81925

https://theconversation.com/explainer-crispr-technology-brings-precise-genetic-editing-and-raises-ethical-questions-39219