The Gene Genie

a crash course

by Marius Stuart, 15/02/18

Why this talk

- Because Biotech is one of the main up and coming industries and will have a major impact on all our lives
- And because next month's speaker, Prof. Simon Waddington will be telling us all about Gene Therapy and it may be useful to have a crash course in Genes and heredity beforehand

A couple of questions

- **Who am I?**
- **Daddy! Where do I come from?**

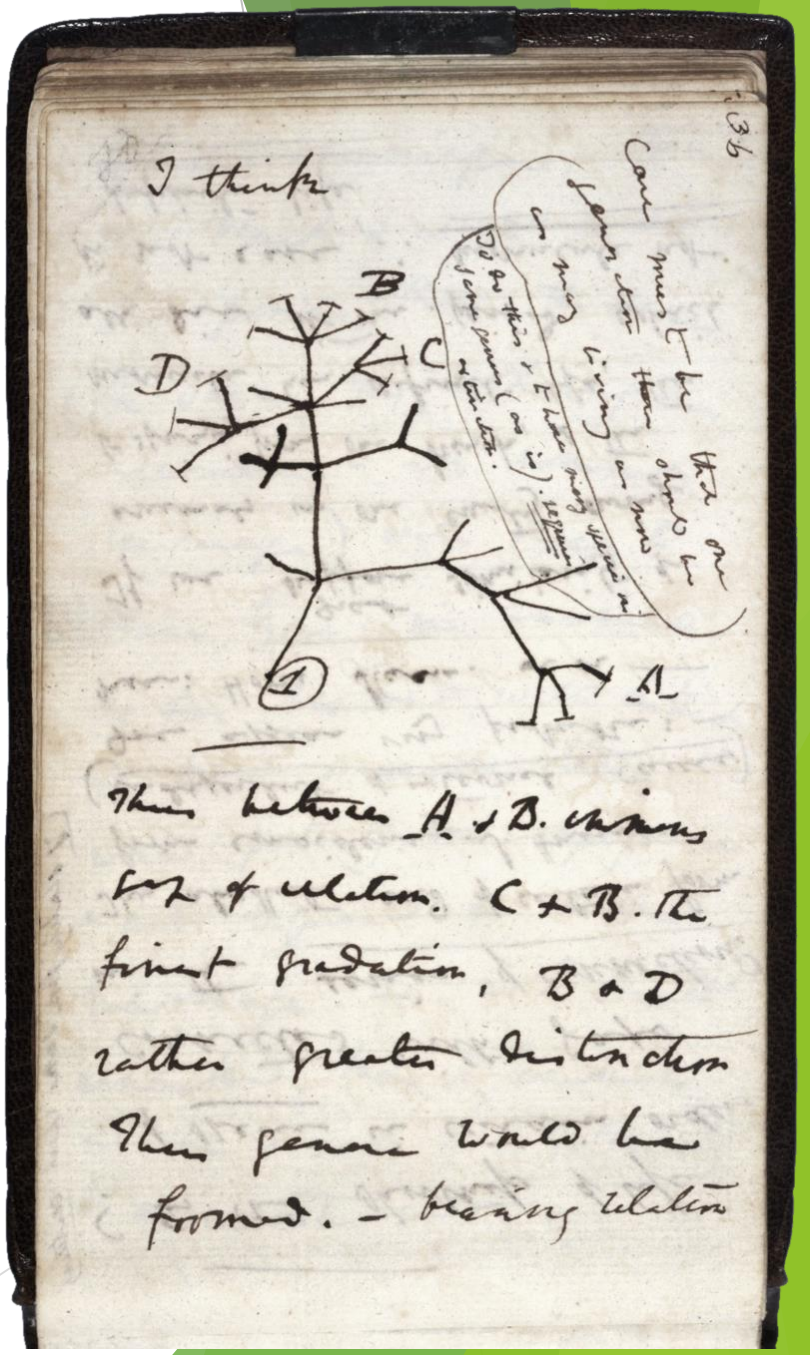
Have you ever asked yourself -

- Why do most animals look similar?
- Why are some very different?
- And the same goes for plants
- What stops us, or for that matter other animals, morphing into something else?
- How come children tend to have features similar to their parents?
- And what makes us individuals?
- What makes biological twins, triplets etc. look identical?
- But are they?
- And why are some diseases prevalent in some families but not others?

My Family

Charles Darwin

- Born 1809 and died 1882
- In 1831 at 22 years old he began Beagle voyages
- During voyages to South America he collected many contemporary as well as fossilised animal and plant samples
- In 1835 during the Galapagos Islands tour he scribbled down important observation "***Each variety is constant in it's own Island***"
- With the help of John Gould, ornithologist, two discoveries were made –
  1) Fossils discovered were just large versions of current specimens
  2) Assorted birds Darwin classified into different groups were in fact 12 different species of the same bird, finches
- In 1837 he conceived the idea of the "Tree of Life"



Heresy!

- The Tree of Life possibly explained the way different species could evolve without the need to invoke God's guiding hand
- But if it wasn't God what else could be causing this evolution?
- The first part to an answer was already being used by cattle breeders, the artificial selection of advantageous random traits i.e. Milk production etc
- A curate at Okewood Chapel in Surrey, Thomas Malthus provided a clue to why this may also apply in nature in a 1798 publication
- Survival due to beneficial mutations through feast and famine
- In 1858 Alfred Russel Wallace, naturalist, provided Darwin with competition
- In 1859 "On the origin of Species by Means of Natural Selection" was published

About the same time

- In 1843 a young man called, Johann and later known as Gregor Mendel was taken in by Augustinian Friars who inhabited a crumbling abbey in Brno, Czech republic
- He was ordained as a priest in 1847 and in 1848 began work as a parish priest
- He was not a great success and was sent to the University of Vienna in 1851 to try an get a degree in natural sciences but found Biology to be disorganised and lacked any underlying logic
- It was here he developed an interest in Heredity, **why or how did like beget like**?
- The likeness question had been around for centuries, so what was the mechanism?

The Likeness Question

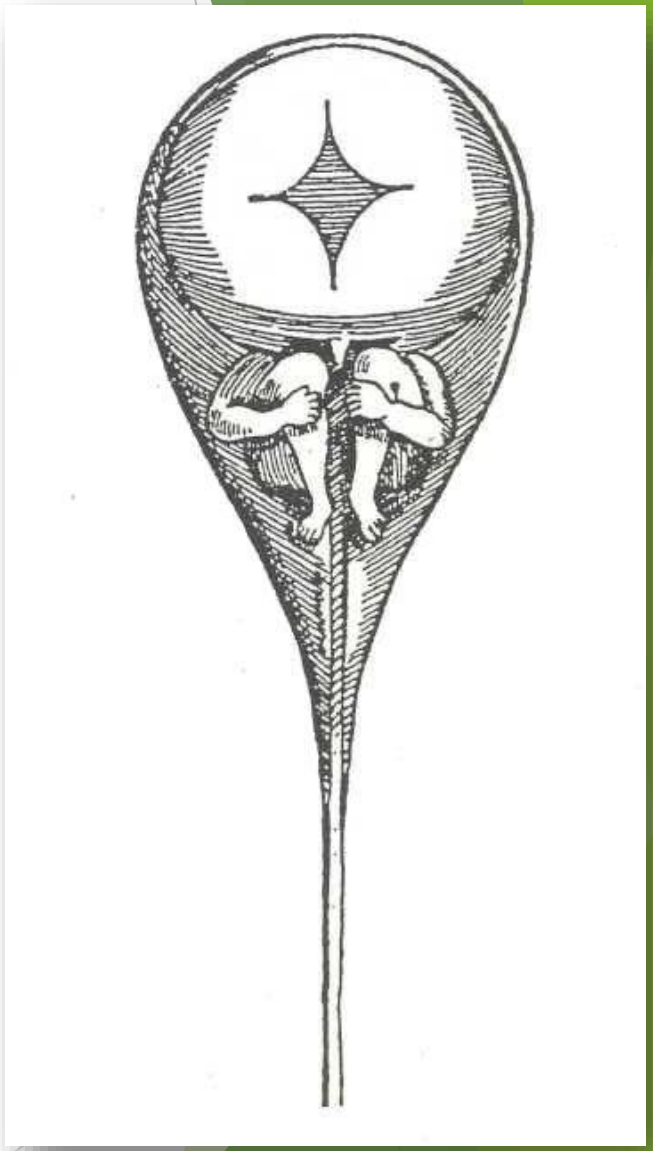
- Around 530 BC, Pythagoras proposed an early theory
- **Spermism**
- In 458 BC Aeschylys, playwright, used Spermism as a defence against matricide in a play where Orestes, the prince of Argos, murdered his mother
- Pythagoras also saw a connection between a triangle and the association between a father, mother and their offspring
- Plato later used Pythagoras's triangular metaphor in his work “The Republic” to define children as arithmetic derivatives
- **Perfect children from perfect parents**
- Numerological Eugenics

Hang on a minute!

- Aristotle rubbished both Pythagoras's and Plato’s conjectures, taking apart the ideas behind spermism in his treatise “Generation of Animals”

Alternative ideas

- Aristotle conjectured that males provided the information while females contributed the physical material in the production of a foetus
- Though his theory was flawed he did capture the essential truth about the nature of heredity
- **That Heredity was basically the transmission of information**
- But if Heredity was transmitted how then was that information encoded?
- Another contemporary theory envisaged a “Mini-me” contained in the sperm. This was termed **“Preformation”**
- This was like ever recursive nested Russian dolls

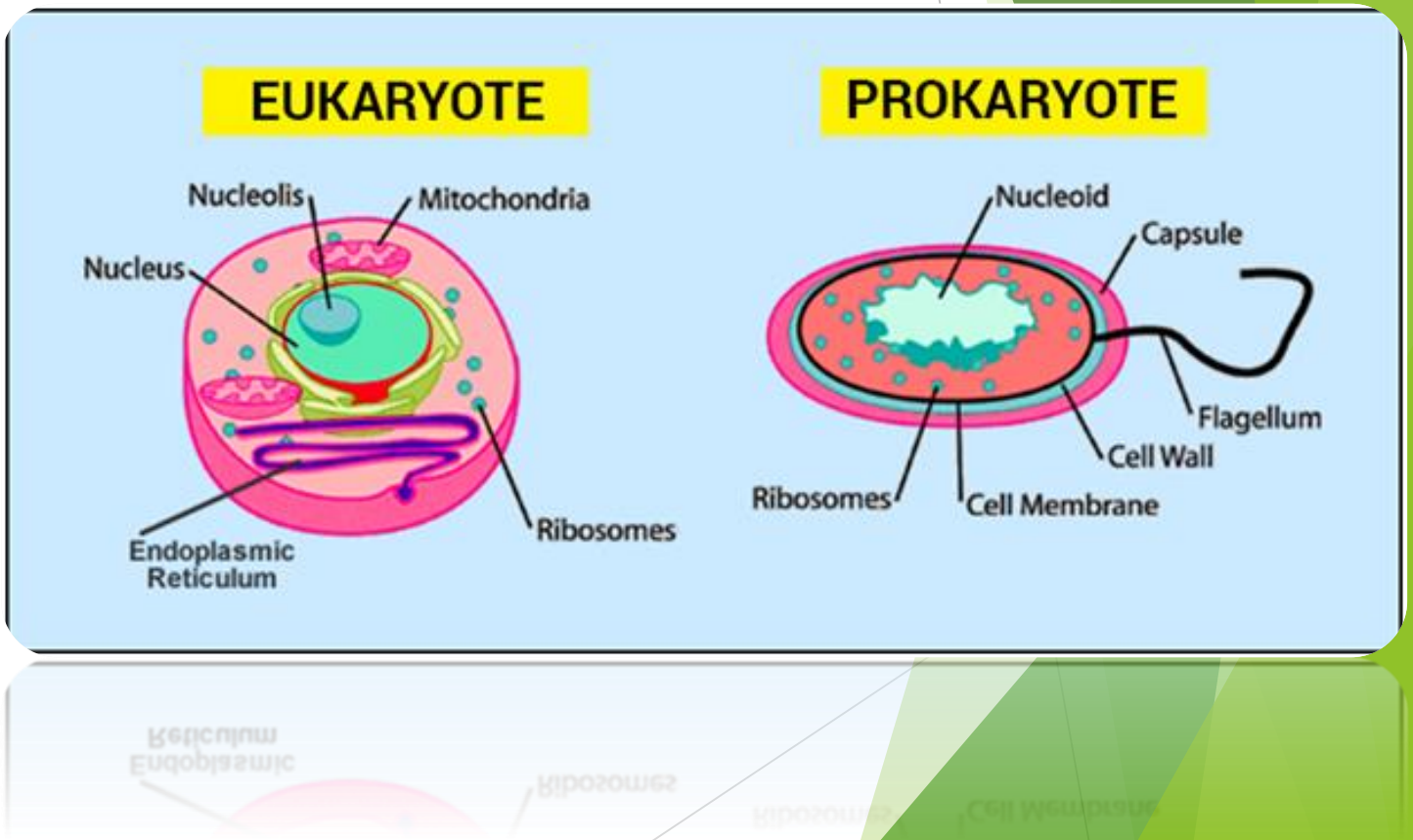


Gregor Mendel

- Though Mendel's work in understanding how heredity worked was crucial, unfortunately because he published his experimental results in an obscure journal in 1865, and written in German, he missed out on the recognition he deserved.
- It was not until 1901, 35 years later that his worked was rediscovered by three botanists and his conclusions were confirmed and made public
- As he was put in charge of the garden at the Abbey in Brno he was able to indulge his interest in heredity
- By crossing breeding strains of true/pure bred pea plants he was able to work out some basic laws governing heredity
- Before we go into these laws, let's take a look at some crucial concepts

Crucial Concepts 1

- All life is made of cells
- There are two cell types - **Eukaryotic cells** contain membrane-bound organelles, including a nucleus. **Eukaryotes** can be single-celled or multi-celled, such as you, me, plants, fungi, and insects. Bacteria are an example of **prokaryotes**. **Prokaryotic cells** do not contain a nucleus or any other membrane-bound organelle.

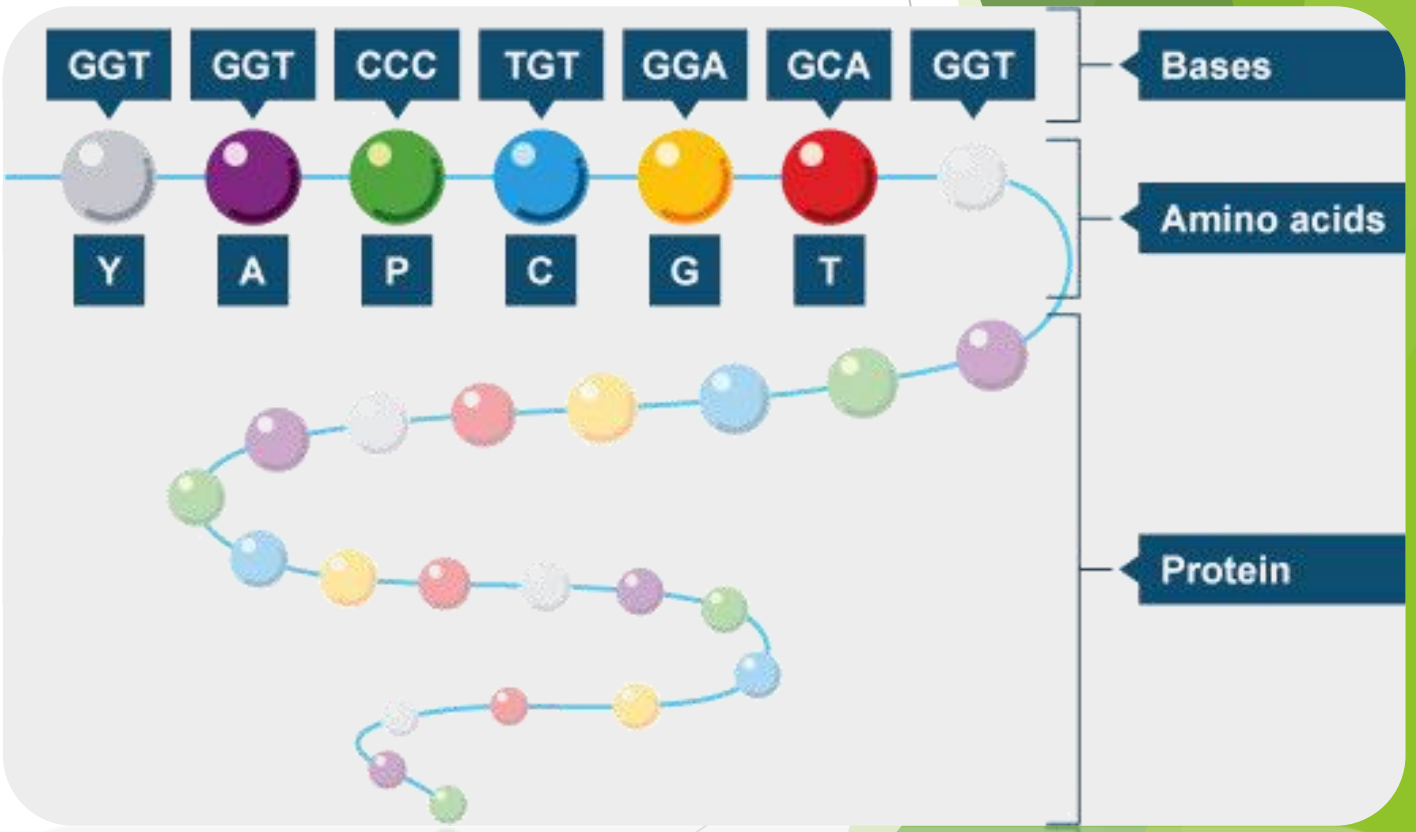


Crucial Concepts 2

- All living cells contain Deoxyribonucleic Acid or DNA which contains the information necessary to build a living organism.
- DNA is itself composed, in part, of four chemical bases – Adenine (A),Thymine (T), Cytosine (C) and Guanine (G) which can be imagined as the connecting rungs in a double helical ladder.
- The bases only pair up as follows A to T and C to G
- The double helical ladder along with a protein spindle is a called a chromosome
- There are 23 pairs of chromosomes present in human cells. One set from the mother the other from the father. However the sex cells only posses one set of chromosomes

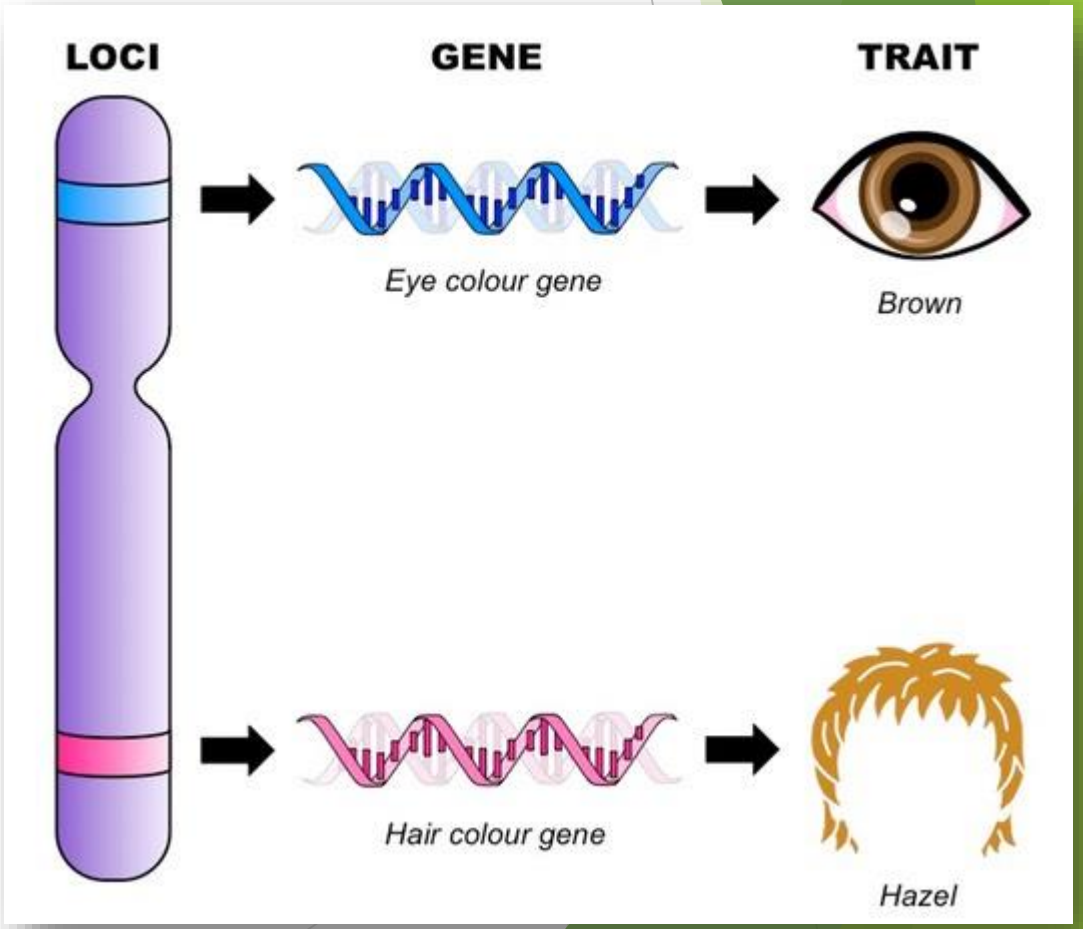
Crucial Concepts 3

- Genes are composed of triplets of base pairs along a chromosome and are essential for the production of amino acids and proteins in a cell
- Each **protein** is **made** up of large numbers of amino acid molecules. Each triplet of bases codes for one particular amino acid. Amino acids are **made** in the number and order dictated by the number and order of base triplets. Finally, the amino acid molecules join together in a long chain to make a **protein** molecule.



Crucial Concepts 4

- Genes code for many traits such as eye colour and hair colour
- Some genes work in tandem with others to create and modify a particular trait
- A **Genotype** is your complete heritable genetic identity but can also refer to a particular gene or set of genes carried by an individual.
- The physical manifestation of the Genotype is called the **Phenotype**
- Genes defining a particular trait can exist in different forms called **Alleles** for example brown eyes have one type of allele while blue eyes have a variant and some alleles are dominant to others



Crucial Concepts 5

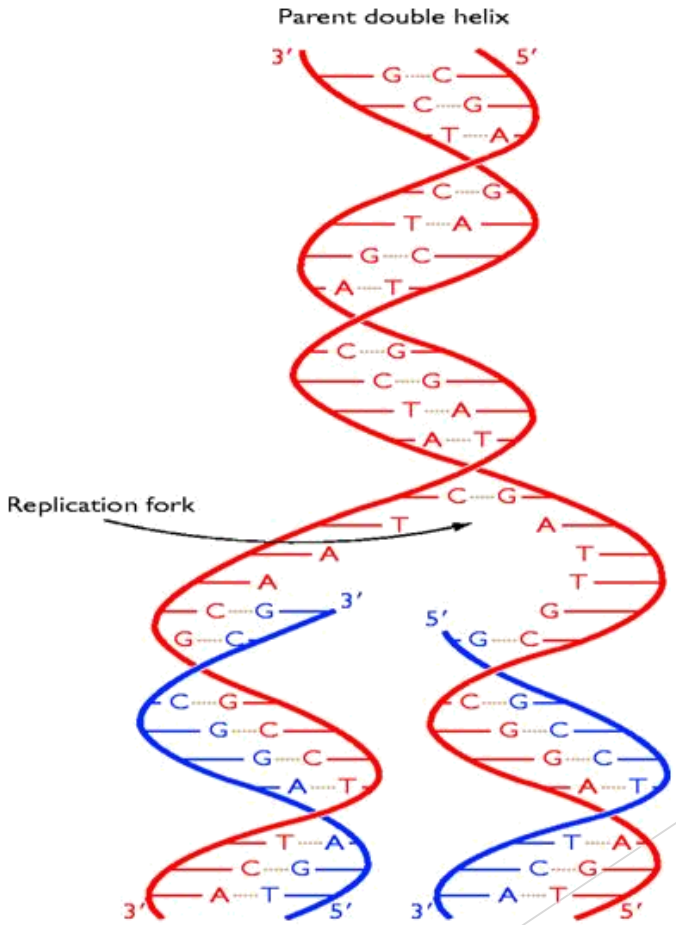
- There are around 21,000 genes in the human genome
- A mouse has 23,000
  A wheat plant has 26,000
  A worm has 20,500
  A water flea has 31,000
- Of the **20 amino acids** in your body's proteins, nine are essential to your diet because your cells cannot manufacture them.
- Genes are passed on to new cells through the process of **Mitosis**.
- Mitosis is a process of cell division that results in two genetically identical daughter cells developing from a single parent cell

Crucial Concept 6

- DNA Replication
- It is possible for mutations to occur during this process giving rise to abnormalities within the gene. It is also possible for advantageous mutations to occur. These are called **transcription** errors
- Click on the right hand illustration to play video

National Genetics Education and Development Centre

How are genes copied?



now have two strands from one

Crucial Concept 7

- We think of DNA as if it was a template cast in stone, but it isn't really like that. It can be thought of as more like a script for a play or film with differing productions.
- ***Epigenetics*** - is the study of changes in organisms caused by modification of gene expression rather than alteration of the genetic code itself. "**epigenetics has transformed the way we think about genomes**"
- In other words genes can be turned on or off dependent on both internal and external factors. This is governed by a process called **methylation**
- In Holland during WW2 throughout the winter of 1944 to spring 1945 Germany blockaded essential food supplies. This caused mass starvation in the population. The dreadful privations of the time also created a remarkable opportunity to study the effects of famine on both the current and future generations of the Dutch population.

Mendel's Laws

- As mentioned earlier Mendel used pure bred peas to experiment with
- Because peas had both male and female organs, by cutting off the male parts he was able to control the pollination process between plants
- Because of this he was able to breed well defined genetically different phenotypes i.e. tall or short stems, smooth or wrinkled seeds, green or yellow peas
- By crossing two pure bred strains one with smooth the other with wrinkled peas he found the offspring always showed one of the two characteristics. In this case smooth proved dominant and the wrinkled peas were recessive
- He postulated that the smooth offspring had both characteristics. However the wisdom of the time believed that characteristics blend. So how could this be?

Punnet Squares

- A good way of explaining his findings is to use what's called a punnet square. This is a way of showing the relationship and outcomes in a graphical format of such crosses
- In this example there is a 3:1 ratio of smooth peas to wrinkled peas as offspring
- If someone inherits two identical alleles they are said to be **"Homozygous"**
- If they inherit two different alleles, they are **"Heterozygous"**

Sp=smooth pea **wp=wrinkled pea**	**Sp**	**wp**
Sp	SpSp	Spwp
wp	wpSp	wpwp

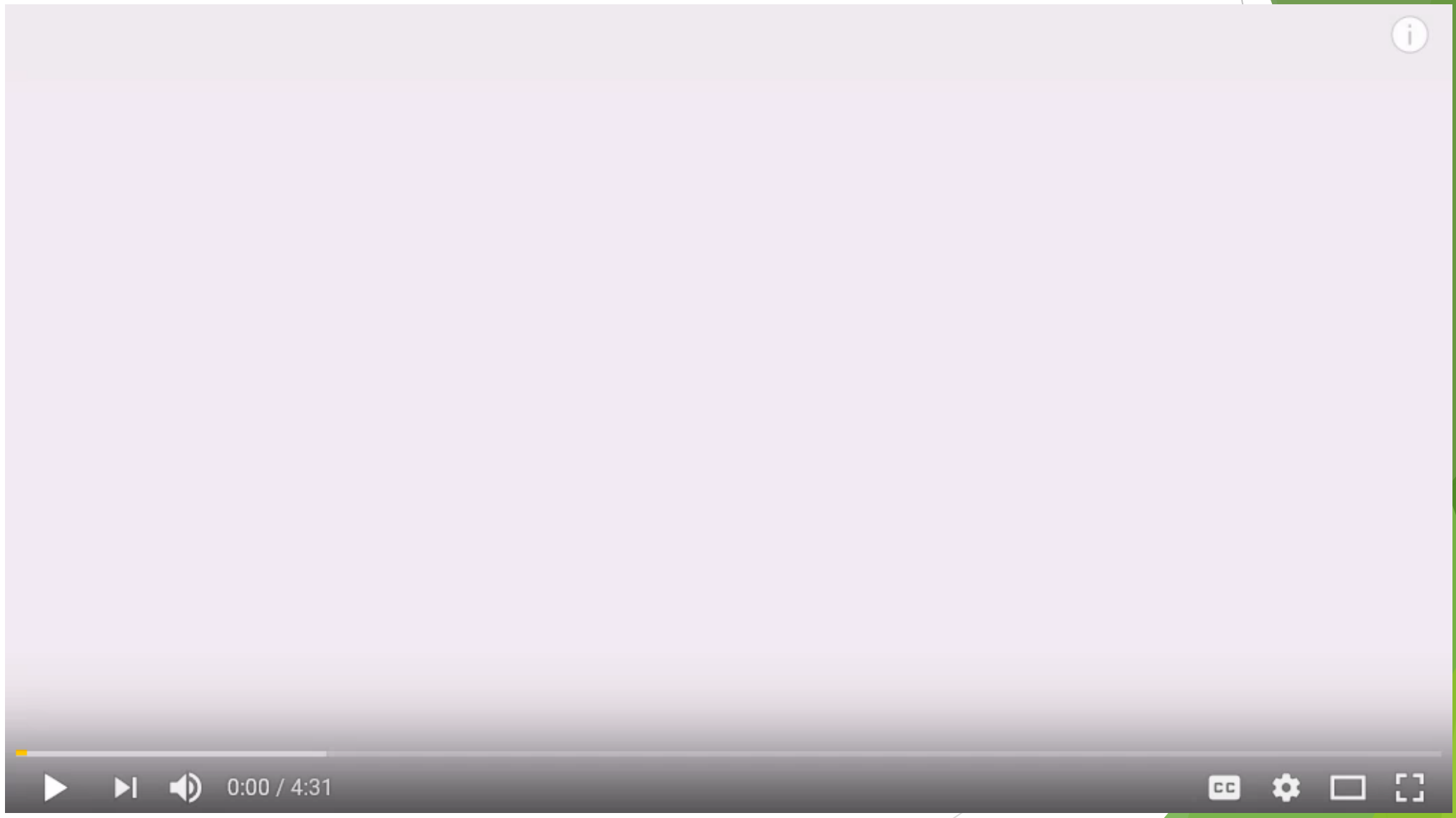
Mendel's Laws cont.

- He tried this out with other phenotypes and found:-
  1) Genetic determinants are particulate; not lost after fertilisation, no blending
  2) Each plant had two determinants which he called "**Elementen**", we call them Genes
  3) The genes for a particular characteristic can exist in different forms or "Alleles" i.e. one for smooth, one for wrinkled
  4) Only one allele is passed on to the next generation in the sperm or the egg. This is the law of "**Segregation**". The gametes only carry one or the other allele, either smooth or wrinkled
  5) Alleles for different characteristics are not linked. This is law of "**Independent Assortment**"

The Future

- Since the days of Darwin and Mendel the science of genetics has advanced, especially recently, in leaps and bounds
- With the recent discovery of the means by which genes can be edited namely CRISPR/Cas9, whole new areas of research are opening up
- Gene therapy is already being used to correct some of the more difficult to cure illnesses
- The moral, ethical, legal and personal aspects of this technology are as yet not fully understood. Though a moratorium was called a few years ago against using these techniques, to stop scientists going too far, recently in 2016 world governments rejected calls to globally ban the use of “gene drive” techniques that could spread modified genes throughout a population and which could be used to engineer entire new species

CRISPR/Cas9



So what do you think?

Any Questions?