DNA, genes and genomes - Detailed

Many genomes: variation

Am I unique?

Yes. Although, at the level of our DNA, researchers currently think that any two human beings are more than 99% alike, there are differences between us*. These differences can be small changes in a single DNA letter or duplicates and deletions of much larger chunks of DNA.

*At the DNA level, only identical twins are expected to be exactly alike, but even then, each individual twin is shaped by their environment and the lifestyle they lead.

Mutations

Genomes change - between generations or over a lifetime - these changes are called mutations. Mutations are happening in your cells all the time. Such changes can happen spontaneously and at random. You also inherit mutations from your parents. Environmental factors like smoking and sunlight can increase the rate of DNA mutation in your cells.

If a mutation happens in a part of the DNA that does not control activity or code for a protein, the chances are that the mutation will not even be noticed by the organism. Even mutations in the coding parts of a gene won't necessarily make a difference; for example, if the letter T is swapped for an A in the codon GCT then the protein will still be the same, since both the old and the new codon still code for the amino acid Alanine.

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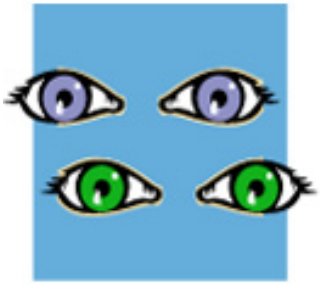
However, some mutations can be detected because they lead to a change in the structure or the amount of protein produced. These relatively few mutations directly affect the ability of the protein to carry out its job - often resulting in a genetic disorder - or change the way the protein does its job (e.g. changing eye colour from blue to green, or earwax texture from sticky to crumbly).



Using information from the Human Genome Project, researchers are learning more about mutations with small or indirect effects on the way our bodies work. We expect to find that a number of small mutations that switch genes on at the wrong times, or produce too much or too little protein will contribute to common diseases such as diabetes and coronary heart disease.

Mutations: large and small

Mutations come in many different shapes and sizes: a single base may be changed into a different base, a whole segment of DNA sequence may be flipped over and reverse itself, or huge sections of the genome could be duplicated or deleted. Some of these can be seen at the chromosomal level, under a high-powered microscope, but most require techniques that can compare the sequence or activity of specific DNA segments.

These mutations can be passed on from parent to child along with the rest of the gene. This is why diseases can run in families.

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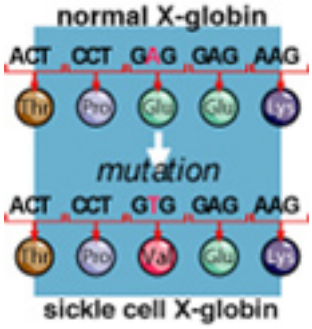
Copy number: Small or large sections of DNA can be duplicated or deleted in different individuals. These duplications or deletions can have a dramatic effect on the health of an individual. For example people with Down's syndrome have an additional copy of chromosome 21 causing a condition with significant physical differences and learning difficulties. People with Huntington's Disease have an excessive number of repeated sequences within the huntingtin gene that cause degeneration of their nervous system. However, people who have additional copies of a gene called CCL3L1 have a reduced risk of HIV infection.

Translocations/inversions: Small or large sections of DNA can be can reversed or swapped between different chromosomes. Some leukaemias, including chronic myeloid leukaemia (CML), are caused by chromosomes swapping material to make mutated genes. Some forms of haemophilia are caused by short segments of the Factor VIII gene being inverted, or reversed inside the gene.

Mutations: Small changes, big differences

Small changes can make big differences in our bodies. The most common mutation to cause cystic fibrosis - a disorder where a person's internal organs become clogged with thick mucus - is the loss of 3 base pairs in the CFTR gene. A single change to the dystrophin gene sequence can cause one of the muscle-weakening conditions known as muscular dystrophy.



Swapping an A for a T in a gene for haemoglobin - the protein in our blood that carries oxygen around the body - causes a serious disease called sickle cell anaemia. In people with sickle cell anaemia, the haemoglobin includes the amino acid valine where a glutamic acid would usually be. This causes the proteins to clump together and changes the shape and behaviour of the red blood cells. However, this mutation can be beneficial: people who carry this change on only one of their chromosomes are resistant to infection by the parasite that causes malaria.