The instructions for constructing a living organism are encoded in long molecules called deoxyribonucleic acid (DNA). DNA is contained within the chromosomes in the nucleus of every cell in all organisms larger than bacteria.

DNA and genes

The DNA molecules look like tiny twisted ladders; each rung on the ladder is formed by a pair of chemicals called bases (Figure 1). There are four different bases, symbolised by the letters A, C, T and G, that can pair up (A with T and C with G) to make the rungs. The order in which the bases are stacked up in the DNA molecule determines what the DNA does.

The function of much of the DNA in an organism is rather mysterious; some may have no function at all while some is involved in controlling the cell. Only small fragments of the total DNA have a clear function and these parts are called genes. The DNA in a gene tells each cell how to make a particular protein.

What do proteins do?

Proteins have a wide range of roles in cells, but we can think of them either as tools or as building blocks for the organism:

- They can be thought of as tools when they perform an action such as digesting food (digestive enzymes), releasing energy from sugar (enzymes in respiration), carrying oxygen in blood (haemoglobin) or acting as hormones (insulin).
- They can be thought of as building blocks when they make up bones, tendons (collagen), nails and skin (keratin).

To remain healthy the genes in the body must produce the correct amount of the right proteins. Small differences in genes cause the characteristics in people that we recognise as running in families, such as eye colour, hair colour, baldness and height. In animals and plants these genetic differences cause the characteristics that we can alter by selective breeding, such as milk production in cows or stalk length in wheat.

In this article we look at some basic aspects of GCSE genetics and then at how fruit flies are being used in novel ways to study genetic diseases.
How do genes cause disease?

Random changes to a gene (mutations) may drastically disturb the activity of a gene. This can result in a marked imbalance in protein activity, which shows itself as a disease.

Alcaptonuria

The first genetic disease to be described, called alcaptonuria, was discovered by Archibald Garrod in 1908. Patients with this disease suffer with arthritis (pain and damage to joints) and Garrod noticed that their urine turned black when exposed to the air. The arthritis and the coloured urine are now known to be caused by the build-up of a chemical called homogentisic acid. Normally this chemical is removed by an enzyme (a specialised protein), but in sufferers the gene is mutated so that the enzyme is no longer active. If an individual inherits two copies of the mutant gene then he or she cannot remove homogentisic acid from the blood and develops the disease. Alcaptonuria is a rare disease.

Cystic fibrosis

One of the commonest genetic diseases in the UK is cystic fibrosis. This is caused by mutation in a gene involved in mucus production. Individuals with two copies of the mutant gene produce mucus that is too thick and sticks in the lungs, resulting in repeated lung infections. This thick mucus is also produced in the gut and from other internal surfaces of the body.

Haemochromatosis

Some genetic diseases are caused by mutations in genes that make their proteins overactive. Haemochromatosis, the most common genetic disease in the UK, is an example of this; in this case the mutant protein causes the body to absorb too much iron from the diet. Normally iron is required as part of haemoglobin, the protein that carries oxygen in red blood cells, but too much causes damage to many organs including the liver, heart and kidneys.

Alzheimer’s disease

Alzheimer’s disease is a common cause of memory loss in elderly people. About 5% of cases are caused by mutations that result in faulty forms of the enzymes that would normally remove a potentially toxic protein from the brain. Mutant forms of these enzymes allow the accumulation of toxic peptide fragments (called Aβ peptides). As these Aβ peptide fragments build up in the brain the nerve cells that are required for memory stop working and the patient becomes ill.

How do fruit flies get Alzheimer’s disease?

Genetic diseases are the subject of much research as scientists try to work out better treatments for them. One line of research is to utilise fruit flies with the human gene involved in Alzheimer’s disease.

The fruit fly (Drosophila melanogaster) has been used in genetic experiments for 100 years (see ‘A life in science’, pages 20–21). Scientists are now able to make a lot of different transgenic flies by placing new DNA into their chromosomes (see Box 2 and Figure 3). If the DNA is a human gene then the flies can be made...
to produce the corresponding human protein. If the human protein is involved in human disease we may find that the fly will suffer a similar disease. We can then use these flies to test new treatments that could be useful for human patients.

We want to find treatments for Alzheimer’s disease, so we gave the fruit flies the human gene for the toxic Aβ peptides so that they produced the peptides in their brains. Using a microscope we looked carefully at the brains of the transgenic flies (Figure 2); we also measured their life-span and their walking abilities. We found that the Aβ peptides cause damage in the fly that is similar to the disease in the human brain.

Testing drugs for Alzheimer’s disease
Because the fly develops the disease within a few days, rather than after 50–60 years as in human patients, we can do experiments much more rapidly. Importantly, we can test new drugs on the flies by putting the drugs in their food and testing whether the flies live longer or walk better. Since the genes in flies and humans are very similar we can start to think about new drugs for human patients by using the genetic information that we get from the flies.

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