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Science at the Edge Series

克隆技术

Cloning

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Introduction

On 5 July 1996, Dolly the sheep was born. Dolly became the most famous sheep in the world. The reason for her fame was that she was a clone – she was genetically **identical** to her mother, a sheep that was born six years earlier. This means that Dolly was born with exactly the same genes as her mother. This was a major achievment in the field of genetics, the biological equivalent to splitting the atom or breaking the sound barrier. Before Dolly's birth, many scientists thought it was impossible to clone an adult cell. Since her birth, the potential development of cloning technology has both excited and worried people – scientists and non-scientists alike.

Dolly is probably the best known sheep in the world. She was the first clone of an adult cell to be produced. She is a perfectly normal sheep and has led a relatively healthy life, although she has begun to suffer from **arthritis**.

What is cloning?

Cloning is the creating of a genetically identical copy of an individual. Cloning itself is not new. Identical human twins are natural clones. Just after **fertilization**, the newly formed cell splits into two identical halves and each half continues to develop normally. The result is two identical people or clones. Normally, children of the same parents have different appearances. They are similar in that half their genes come from their father and the other half from their mother, but the actual mix of genes in each case is different. Identical twins also have genes from each parent, but in their case the genes are the same. Gardeners have been producing clones of plants, too. They produce new plants by taking cuttings. The cuttings develop into plants that are identical to the parent plants. They call this vegetative **propagation**, but it is the same as cloning.

Cloning concerns

Cloning raises a wide range of issues. Scientists and many other people believe that, if carefully regulated, the scientific technique of cloning could be used to benefit people. For example, cloning offers hope to many people suffering from diseases such as **Parkinson's** and **leukaemia**. Many people who **contract** leukaemia need a **bone marrow transplant**. They may be lucky and have a close relative that has **compatible** cells. Otherwise they have to hope somebody on a bone marrow register (a list of potential donors) has suitable cells. But the chances of finding a match are fewer than one in 20,000. Cloning could change that. Doctors could use a cloning technique to produce bone marrow cells that would be identical to the patient's own.

However, the issue of human cloning is one that concerns many people, both scientists and non-scientists. Some fear the consequences if doctors or scientists are able to produce human clones, including the possibility of health defects, and there are many ethical and religious objections which you will read about.

In this book you will learn about DNA and **chromosomes** and the difference between cloning in plants and animals. You will discover how cloning may be used in transplant surgery, and read about some of the issues associated with the cloning of human cells. You will also find the answers to questions such as 'Is Dolly the only cloned animal?', 'Is it legal to clone humans?' and 'Could the dead be cloned?'

The path to Dolly

Dolly the sheep was born in July 1996. The research institute where she was born kept the news of her birth secret until February 1997. When the news was finally released, it made headlines around the world. In the months that followed, cloning was rarely out of the news. Although there was a great deal of excitement, the news also raised concerns about the potential implications of this major advance in our knowledge of genetics.

People have thought about cloning for thousands of years, long before there was knowledge of genetics or biochemistry. However, it wasn't until towards the end of the 19th century, when scientists began to study **embryology** using microscopes, that the relevant science began to develop. One of the most important embryologists of this time was Hans Spemann, a Nobel Prize winner, who published his book *Embryonic Development and Induction* in 1938. He took from a **salamander** (a type of amphibian) an **embryo** that consisted of just two cells and split it into two. Each of the embryos developed into a normal salamander. They were identical copies or clones of each other. In his book, he proposed doing a fantastical experiment which would involve removing a **nucleus** from an adult salamander cell and placing it in an egg which had had its nucleus removed. But it was not until 1952, years after his death, that this experiment was carried out successfully.

Eggs, tadpoles and toads

During the 1950s, scientists Robert Briggs, Tom King and later John Gurdon experimented on the eggs of frogs and toads. They cloned frogs and toads by removing the nucleus from an egg and replacing it with a nucleus taken from a cell of a **tadpole**. However, they were unable to successfully clone a cell taken from an adult frog or toad.

These experiments fired the public's imagination. If Dolly had been born at this time, the reaction would have been very different. During the 1950s and 1960s many people thought that tinkering with life would be a boon and something to be encouraged. Few people raised concerns

During the 1950s and 1960s many scientists studied frogs' **eggs**, including those of the leopard frog. Frogs' eggs are large and easy to **manipulate**, making them good for research.

over the risks and ethics of cloning. Today, there is much more public debate and there are numerous committees that debate ethical issues and advise governments. Such pressure can force governments to change laws, for example to prevent scientists experimenting with human cloning.

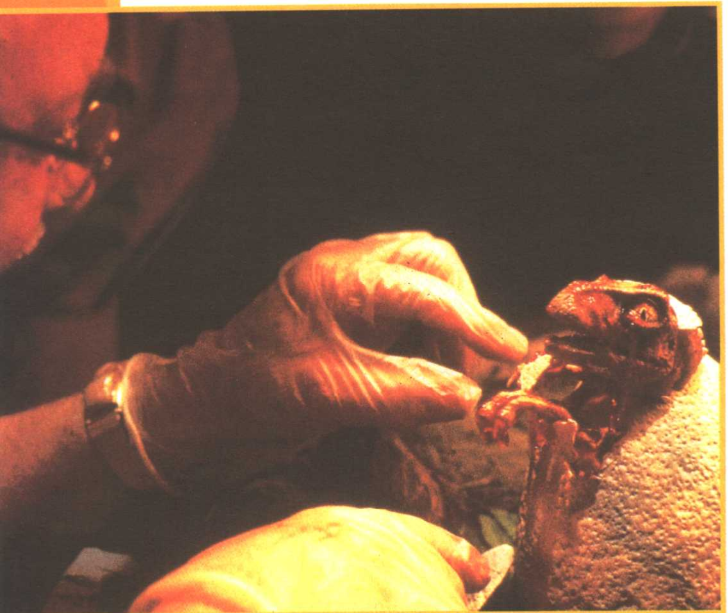
Although Hans Spemann was the first to describe the process of cloning, he called it nuclear transplantation. The term 'clone', the Greek word for 'twig', was first used by the British biologist J.B.S. Haldane in 1963. He was speaking at a convention about the future of science, speculating on how long people would live in the future, how they would fight disease and how cloning of humans would be possible. The brightest and the best of society, he suggested, could be cloned in order to further human achievement.

> *'We got a good deal of reaction, both from scientists and non-scientists. They thought it was phenomenal. We thought we could clone any cell.'*
>
> Tom King, talking about the work he carried out on cloning during the 1950s

A change in mood

By the 1970s the mood of the public had changed. The first steps in genetic engineering had been made and the world's first test-tube baby was born. This involved the technique of ***in vitro* fertilization**, in which an egg is taken from a woman, fertilized in the laboratory and then replaced in the woman's **uterus** to develop into a baby. However, many people were getting worried as geneticists were achieving more complex processes and science fiction writers were publishing books on cloning which predicted that cloning could have terrible consequences. In 1978 a science writer published a book claiming that a human had been cloned. The book was presented as the 'true' story of a secret project to produce a clone of a man who had paid one million dollars to a scientist. After much debate the story was finally revealed to be a hoax. But the book was a bestseller. The book concerned both scientists and non-scientists and they did not want similar things to happen in real life.

During the 1980s, hundreds of experiments into cloning mammals failed and many leading scientists thought that it would be impossible. The breakthrough came in 1986 when sheep and cows were successfully cloned from embryo cells. However, scientists still could not successfully clone an adult cell.



In the film *Jurassic Park*, scientists had managed to reconstruct the DNA of dinosaurs. This enabled them to produce living dinosaurs.

During the early 1990s, the concept of cloning was featured in many science fiction movies. The film *Blade Runner* featured human clones that were created to be drones, or workers, on other planets, but the clones revolted and returned to Earth to destroy their creators. *Jurassic Park* featured **dinosaurs** that were created by cloning.

But cloning was a real science. In 1995 a team at the Roslin Institute in Scotland, led by Ian Wilmut, had their first success when they successfully cloned two sheep called Morag and Megan. A year later Dolly was born. She was the first clone to be produced by taking a nucleus from an adult cell and placing it into an empty egg cell. The arrival of Dolly took many people, including scientists, by surprise. For years they had convinced themselves that it was impossible to make a clone of an adult cell.

'I am not a fool. I know what is bothering people about this. I understand why the world is suddenly at my door. But this is my work. It has always been my work and it doesn't have anything to do with creating copies of human beings. I am not ***haunted*** *by what I do, if that is what you want to know. I sleep very well at night.'*

Ian Wilmut, speaking about his work in the field of cloning and the future of human cloning

Dolly's creator

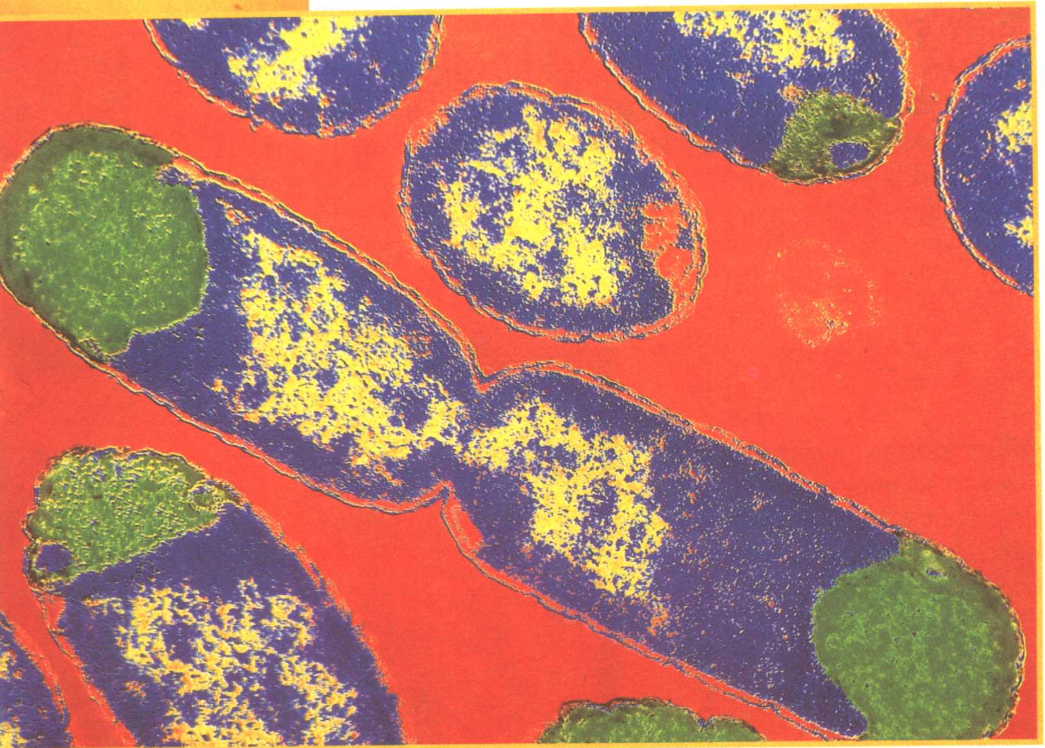
Ian Wilmut was the embryologist who produced Dolly. He had worked at Roslin Institute in Scotland for 23 years and had worked on the cloning project for ten years. The painstaking research he undertook required endless patience. He worked long hours over a microscope, studying embryonic cells. Knowing that many life-saving drugs were either difficult or expensive to produce, his aim was to create animals that could produce drugs for human use. He wanted to alter their DNA so that they had new genes to give them the ability to make a human drug. However, it was important to be able to produce many of these animals. So once an animal with new abilities had been created he needed a technique to clone it – and so his research led to the cloning of adult cells. The creation of Dolly was a huge scientific breakthrough (see pages 24–5).

Megan and Morag are identical twins. They were cloned from the same embryo that was just a few days old. The method by which they were produced was different to that which produced Dolly.

Natural cloning

This book is concerned with cloning that is carried out artificially in a laboratory. However, cloning is a process that occurs naturally, too. Cloning is used by many micro-organisms, single-celled animals and plants in order to reproduce and increase in number.

Many organisms reproduce **asexually**, for example bacteria, **amoebae** (single-celled organisms that live in water), **yeast** and **hydras** (related to the sea anemone). This means that one individual reproduces on its own without the involvement of another individual. These organisms reproduce asexually when conditions are ideal for an increase in population size, for example when there is plenty of food and space. All the new individuals are identical to the parent, so they are clones of each other. When conditions change, these organisms reproduce sexually, which involves two individuals.



A bacterium undergoes **binary fission**. The cell simply divides into two. The two new daughter cells are genetically identical to each other.

Binary fission and budding

A bacterium or an amoeba can divide into two by a process called binary fission. When an amoeba is ready to reproduce, it simply splits into two. First the nucleus divides and then the rest of the cell. This produces two small amoebae that feed and grow. Under ideal conditions, an amoeba may divide once a day. Bacteria divide in a similar way, but they do so at a faster rate than the amoeba. Under ideal conditions, bacteria can divide every 20 minutes, so one bacterium can become one million in 7 hours.

Hydra and yeast cells reproduce asexually by budding. A hydra reproduces by growing a new hydra out of its side. At first the new bud gets its food from the parent, but eventually it is large enough to break away and live independently. Yeast is a **fungus**, but unlike many other types of **fungi**, yeast consists of single cells. When a yeast cell is large enough it produces a small outgrowth or bud which gradually gets larger. Eventually the bud breaks off to form a new cell.

Spores

Many fungi produce **spores** asexually. Spores are tiny **spherical** structures that will grow into a new individual. One such fungus is the pin mould which grows on bread and other foods. The fungus consists of a mass of tiny threads called **hyphae**. The hyphae grow over the surface of the food source, absorbing food. A few hyphae grow **vertically** and their ends become **swollen**. Inside, thousands of tiny spores are produced. These are released into the air where they are carried away on air currents.

Plant reproduction

Asexual reproduction occurs in plants, too. Plants such as the strawberry produce side-shoots called runners. A runner grows along the surface of the ground. Roots appear at intervals and grow into the soil. Eventually the runner between the roots withers away leaving a row of daughter plants. Grasses produce similar shoots, called **tillers**, while blackberries produce **stolons**. All of these methods are ways by which the plant can increase in number very quickly.

Potato plants reproduce asexually by producing **tubers**. During the summer months, the potato plant makes lots of food using **photosynthesis**. The food is moved to underground stems, which swell up and form tubers. Within the tuber the food is stored as **starch**. At the end of autumn the potato shoots above the ground die back, but the tubers survive underground. In spring the food in the tuber is used to fuel new growth, and each tuber begins to grow into a new plant. Since all the new plants come from the same parent, they are clones.

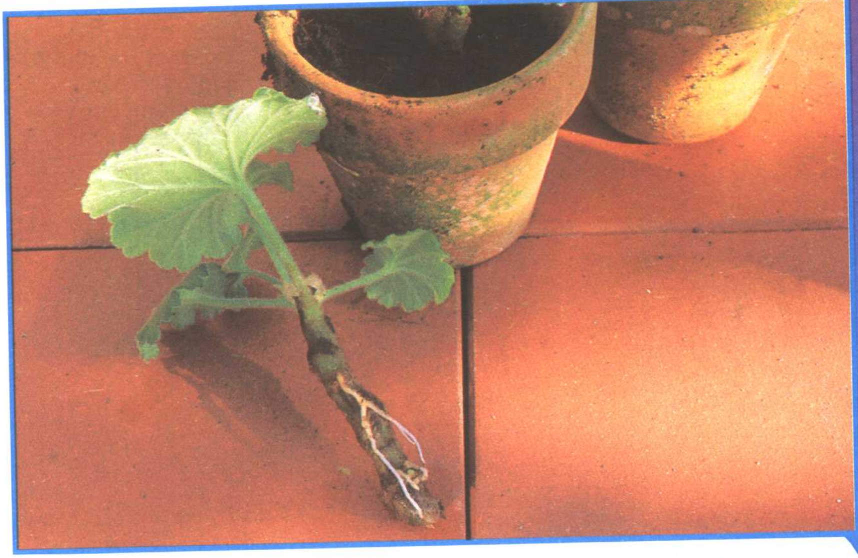
A strawberry plant produces a shoot called a runner, that grows along the ground. New plants form at intervals along this shoot.

Cloning plants

Plants have been cloned artificially for hundreds of years. However, the word 'cloning' is not normally used. Instead, gardeners refer to the process as 'vegetative propagation'. One example of this is when cuttings are taken. If you cut off a length of shoot from a plant and place it in a beaker of water, after a few weeks you will probably see roots appearing at the end of the shoot. Once the cutting has rooted, it can be potted into soil to grow into a new plant.

Gardeners can take cuttings of most plants in order to produce new and identical plants cheaply and quickly. Commercial companies also use vegetative propagation as it enables large numbers of identical plants to be produced in a short period of time.

New plants can be grown from seed, but seeds are produced by sexual reproduction. The **pollen** from one flower is transferred to another flower, where the male nucelus within the pollen fertilizes the female egg. The resulting seeds have new combinations of genes, so they are all different. When plants with new features are wanted, the process of sexual reproduction is useful. By crossing selected plants there is a chance that the new combination of genes will produce a plant with different features, for example a new colour of flower. But once the desired plant has been produced, the only way to produce more plants with the same features is to use vegetative propagation. This ensures that all the **offspring** are identical to the parent and the new feature is not lost.



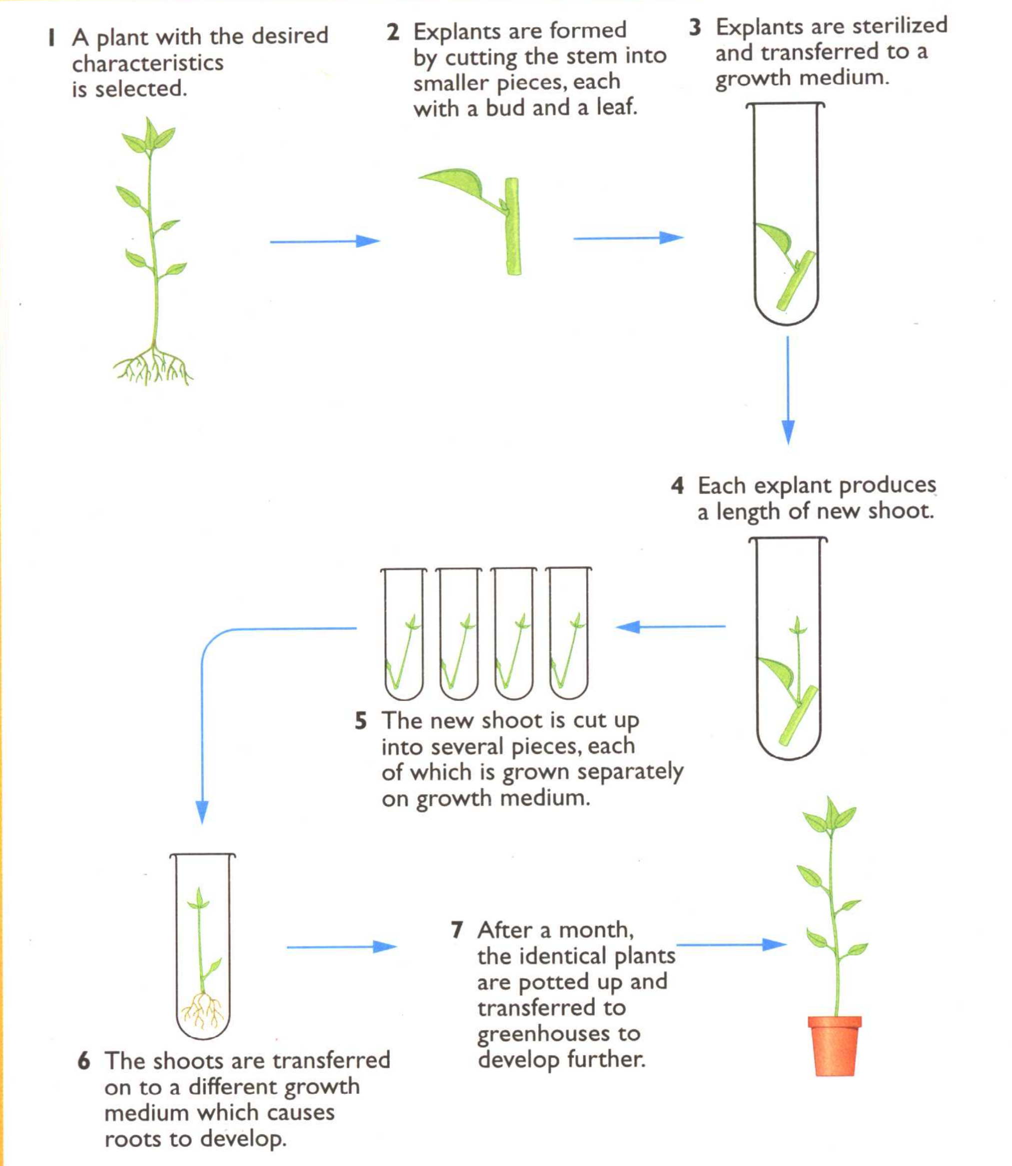
Gardeners produce new plants by taking cuttings. A cutting is a short length of shoot with some of its leaves removed. The cutting is dipped in a rooting powder which stimulates the formation of roots from the bottom of the cutting.

Micropropagation

The propagation methods used commercially are slightly different to those used by gardeners, as plant companies have to produce large numbers of quality plants. One of the methods is called micropropagation or plant-tissue culture. It uses a single plant to produce a large number of clones. A short length of shoot is taken from the parent plant. This is called an explant. It is sterilized and transferred onto a jelly-like growth medium, which encourages the growth of shoots. The shoot that grows is divided again into many smaller pieces, each of which is grown on fresh growth medium. Then the shoots are transferred to a different medium that encourages root growth. After about four weeks the plantlets (young plants) are large enough to be potted into sterile **compost**.

Micropropagation has a number of advantages:

- it is quick
- it produces a large number of identical plants from one or a few parent plants
- it retains all the good features of the parental material such as colour or shape of flower, disease-resistance or high yield
- it is cost-effective
- it is easy to transport large number of plants under sterile conditions
- only healthy stock are produced
- it eliminates problems with seasonal production, as it can be carried out all year round.



This diagram shows how it is possible to produce a large number of identical plants from a single plant.

Cloning plants is a relatively straightforward process. It is possible to clone a whole plant from a single cell because every plant cell, if given the right set of conditions and chemicals, has the ability to produce unspecialized plant cells that can then be cultured to produce a whole plant.

Protoplast cloning

Improved cloning techniques mean it is now possible to clone a plant from a single cell. A small sample of tissue is removed from a plant and treated with an **enzyme** to remove the **cellulose** cell wall around each plant cell. All that is left is the **protoplast** – a cell without its cell wall. The protoplasts are cultured individually under sterile conditions. First they grow into a mass of unspecialized cells called a callus. Then the callus is placed on a different growth medium, which causes some of the cells to turn into roots and others to become shoots to form a tiny but complete plant.

Micropropagation units

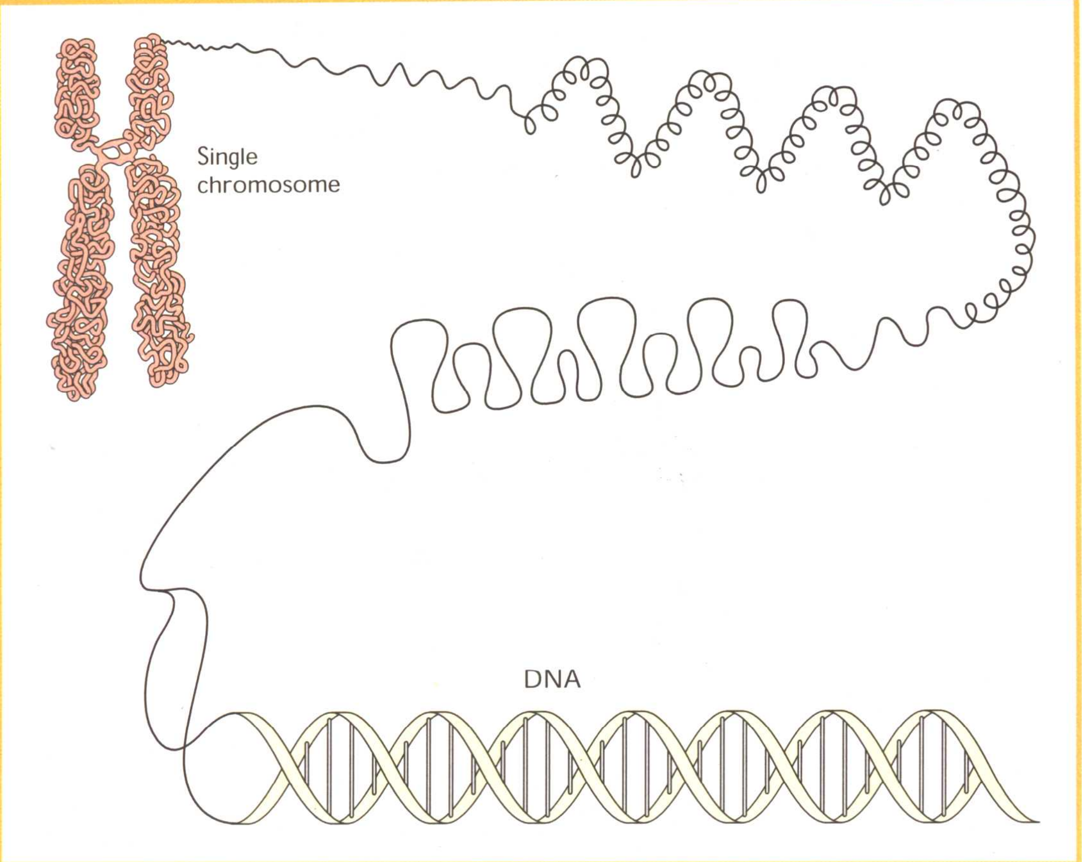
A few **botanic** gardens have set up micropropagation units in order to propagate plants that are rare, **endangered** or difficult to propagate conventionally. The unit at the Royal Botanic Gardens, Kew (in London) has propagated a wide range of plants, and expertise has been developed in the micropropagation of plants that are seldom, if ever, worked on elsewhere. At any one time, approximately 500 species from all over the world are being worked on. Many of these rare and endangered species are found on islands and are particularly at risk. Projects include the propagation of rare plants from St Helena, the Mascarene Islands, Hawaii and the Canary Islands. Successful micropropagation often produces more plantlets than are required by Kew. The **surplus** plants are distributed to other botanic gardens around the world. Where conditions allow, some of these plants will be used in reintroduction trials – that is, attempting to return them to their country of origin. Examples of species which have been sent back include rare orchids from Sabah, Borneo and a range of plants from the Canary Islands.

The young plants in these jars have been produced by tissue culture at a micropropagation unit. They are clones of the original plant.

Chromosomes and DNA

Scientists working in the field of cloning have to have a good understanding of the role of the genes in the cell before they can begin their research into cloning animals.

The body needs a set of instructions to work properly. These instructions are found in almost every cell. They tell a cell what substances to make, how to grow, when to divide, and how to repair itself. In fact, they control every process that takes place in a cell. Every organism inherits these instructions from its parents. The instructions take the form of a chemical code that is located on the chromosomes within the nucleus of a cell.



This diagram shows how the long length of DNA that makes up a chromosome is tightly wound up so that the chromosome does not occupy too much space.