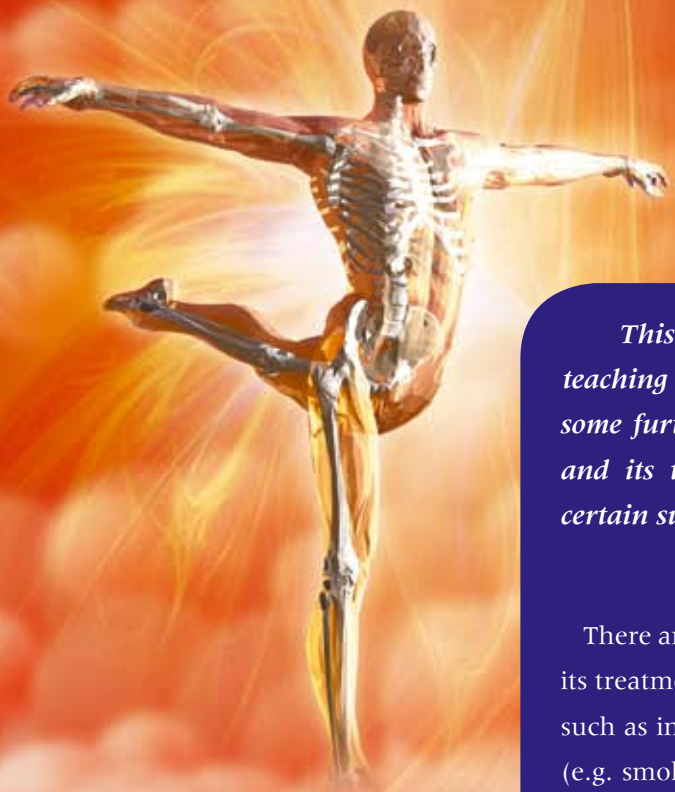
APPLYING YOUR SCIENCE

CELLS, CELL DIVISION, CANCER and CANCER TREATMENT

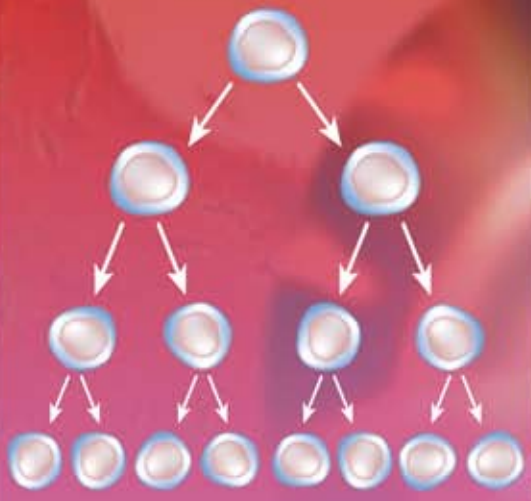


This resource has been developed to support the teaching of Cell Biology and at the same time to develop some further understanding of certain aspects of cancer and its treatment. In particular, the potential role of certain substances derived from plants is emphasised.

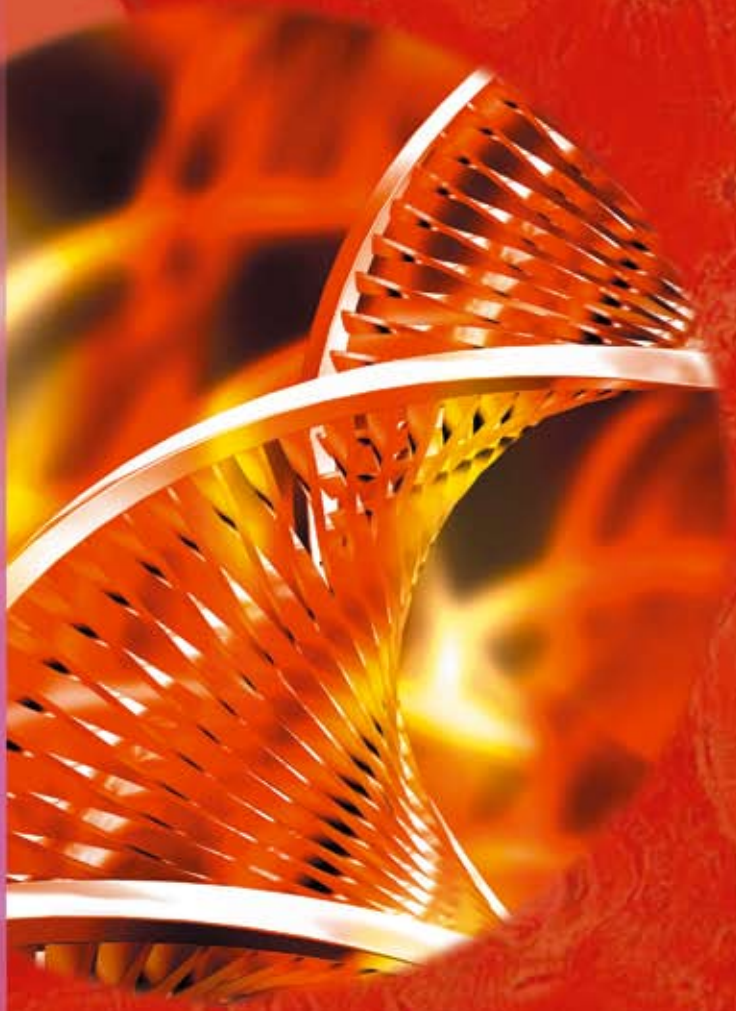
There are, of course, many other dimensions to cancer and its treatment. There is a wide range of other relevant factors such as inherited traits, environmental and lifestyle factors (e.g. smoking as well as diet). Other related matters would include occupational exposures to certain chemicals and the possibility of certain viral infections triggering some types of cancer. Plants, and substances derived from them, certainly have a key role in both the prevention and treatment of cancer. It should be emphasised, however, that simply eating certain plants will not in itself prevent or cure cancer without other lifestyle changes being adopted.

This resource has been produced by the SAPS Biotechnology Scotland Project in partnership with AstraZeneca and Cancer Research UK.
AstraZeneca provided funding towards the development and publication costs of this booklet.
Additional contributions from the Scottish Institute for Biotechnology are gratefully acknowledged.

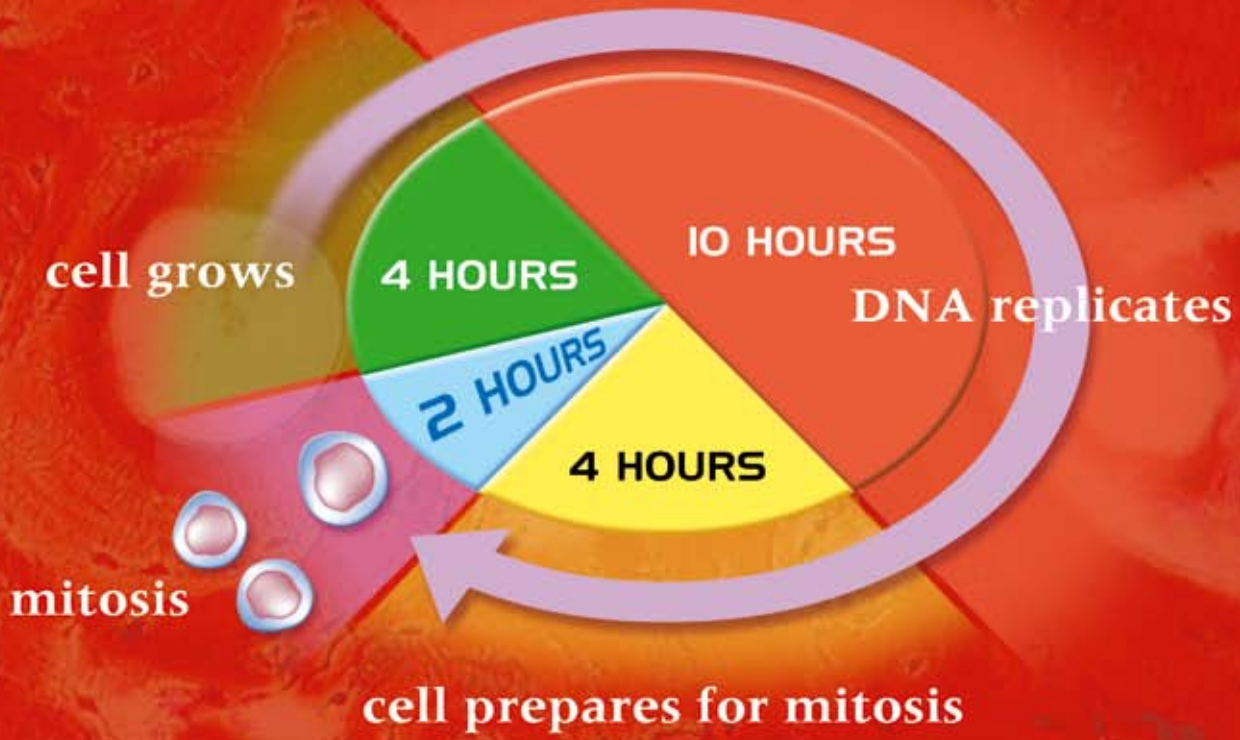
MITOSIS



CELL DIVISION

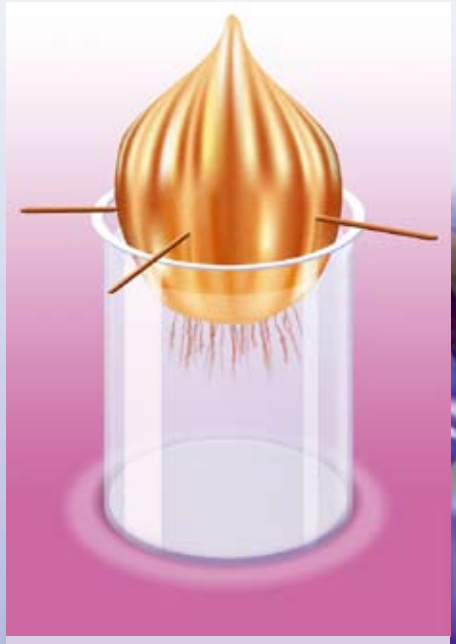


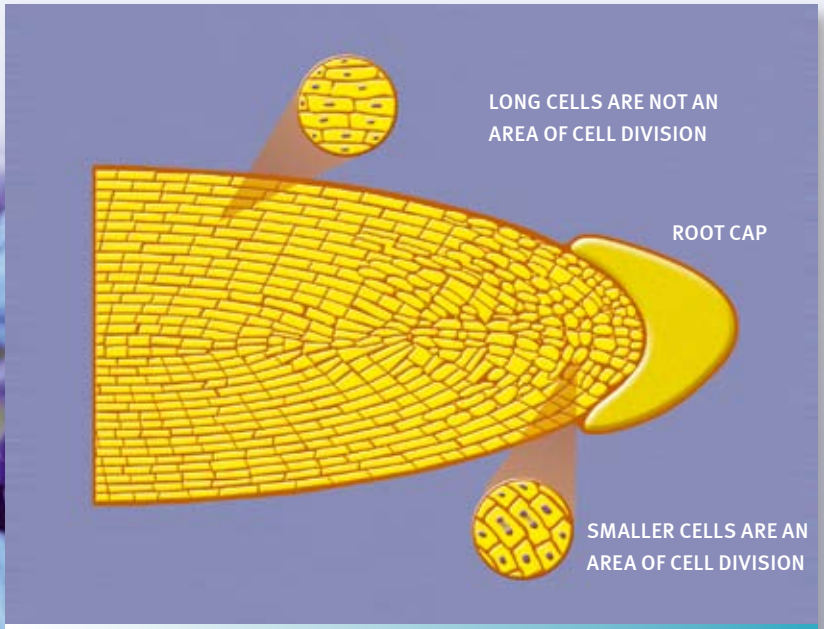
All cells are formed from other cells, so cells must be able to make copies of themselves and divide into two. The genetic material (DNA) inside a cell, in the form of chromosomes, is duplicated and then passed on to the new cells called daughter cells. So every cell has a cycle from its own beginning until its own division into two – we call this the Cell Cycle.



Mitosis is one part of this process and accounts for about 10% of the cell cycle. In the next practical you are going to investigate mitosis – the division of the nucleus. When you look at cells through a microscope they will not usually be dividing, but in this practical you are going to look at a special growing area of a plant where a larger number of the cells are dividing. This area is known as a meristem.

MITOSIS IN ROOT TIPS





MITOSIS IN THE GROWING ROOT TIP

Method

A garlic or hyacinth plant has been grown to produce long roots. At the tip of these roots many of the cells are growing and dividing so it is a good place to look for cells undergoing mitosis.

Collect: a microscope and slide, a large cover slip, forceps and blue stain.

Cut off 2 root tips of about 2 cm.

Wash your root tips in cold water and dry them carefully on filter paper.

Give your teacher your root tips – they will be placed into 1M hydrochloric acid which has been heated to 60°C for 5 minutes.

Your teacher will now return your root tips to you – be very careful with them as they are now very fragile – do not touch them with your fingers.

Using forceps very carefully rinse your root tip in water again and then put it onto a microscope slide – mark your slide with a X to show which is the cut end of the root.

Add a tiny drop of toluidine blue stain to your root tips and cover with a cover slip.

Carefully squash your root tip by gently pressing the slide and cover slip together until the coverslip lies flat on the slide.

Observe and draw what you see under medium and high power.

SAFETY NOTE The hydrochloric acid is an irritant. Take care not to touch the roots with your hands once they have been in the acid. Keep the blue stain off your skin. If you spill any on your skin wash it off at once with water.

Questions

In which part of your root do you find cells with highly stained nuclei?

In which part of your root do you find the smallest cells?

In which part of your root do you find the largest cells?

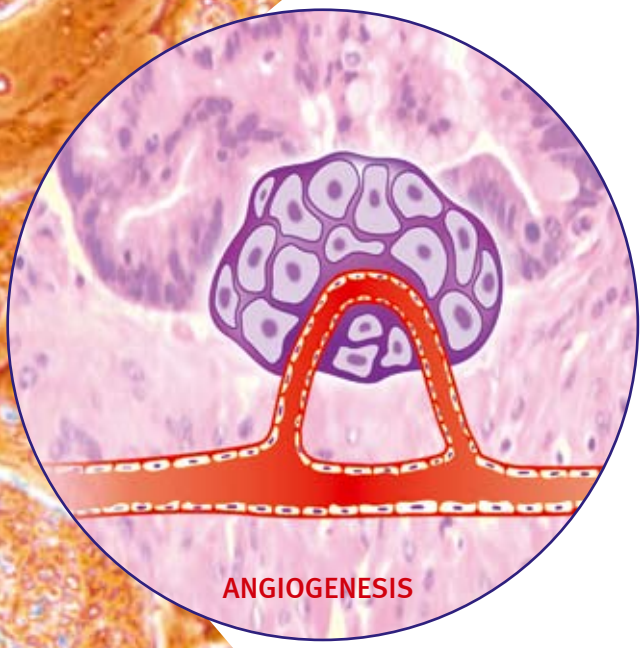
Nearest the cut end you might see some structures which look like long corkscrews – what are these structures?

Name 2 other areas within a plant or an animal where you might find cells dividing.

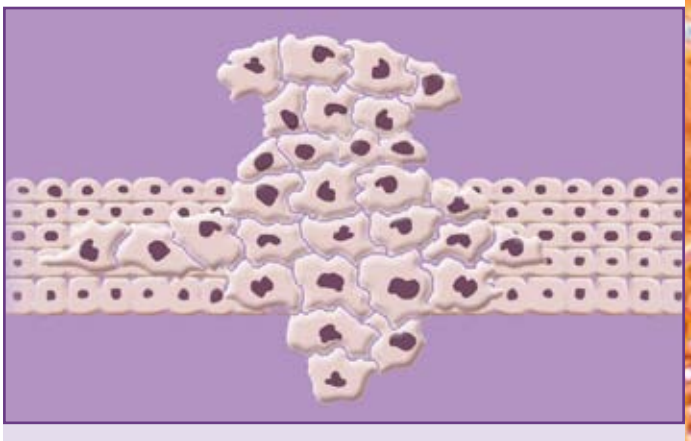
You will probably all have heard of cancer and might have some idea that cancer cells divide too many times. Many of the scientists working on cancer research are trying to understand how cancer cells manage to escape the normal control of the cell.

Cancer

Cancer cells divide in an uncontrolled way and have the ability to invade other tissues. If they are left unchecked, this growth and spread can result in death. In a cell culture, a normal cell will divide around 20-50 times and then stop dividing and die. Cancer cells appear to be immortal: growing and dividing, on and on, for as long as they have all the nutrients they need. These nutrients are supplied to the cancer cells by newly formed blood vessels, a process called *angiogenesis*.



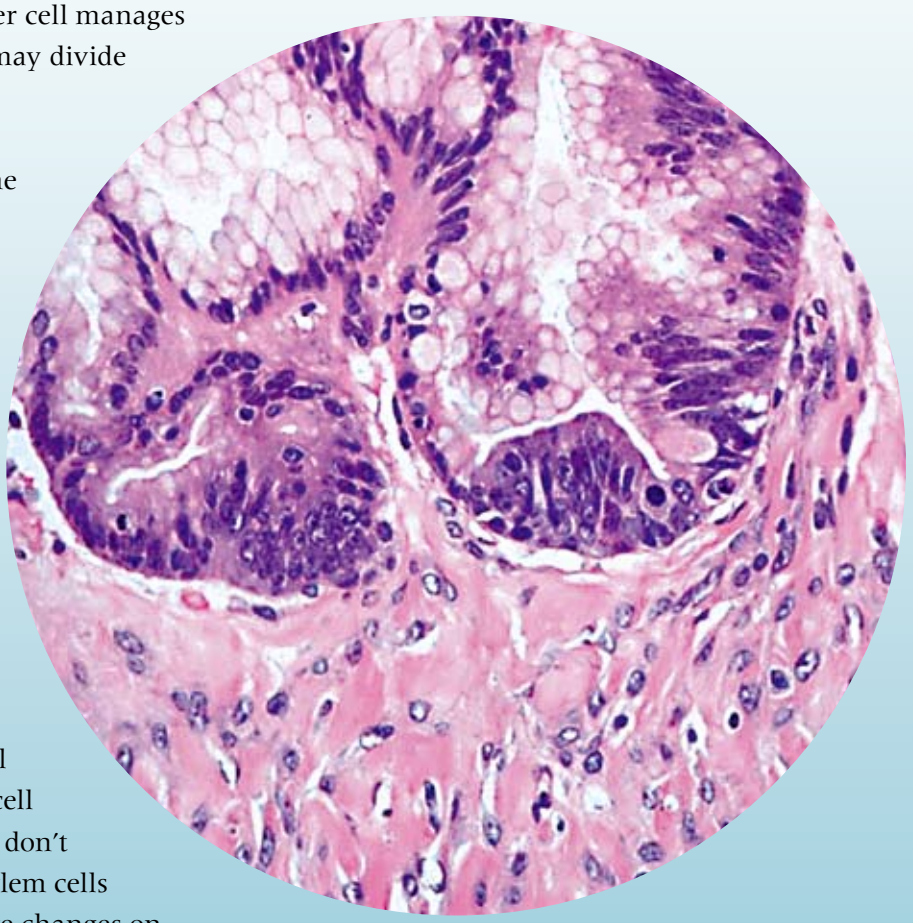
ANGIOGENESIS



What goes wrong?

The rate of cell division in different parts of a plant or animal is crucial to normal growth. In some areas, such as these root tips or in human skin, cells divide often, but in other areas such as mature nerve cells there is little or no division. Clearly something regulates or 'controls' this cycle in the cell.

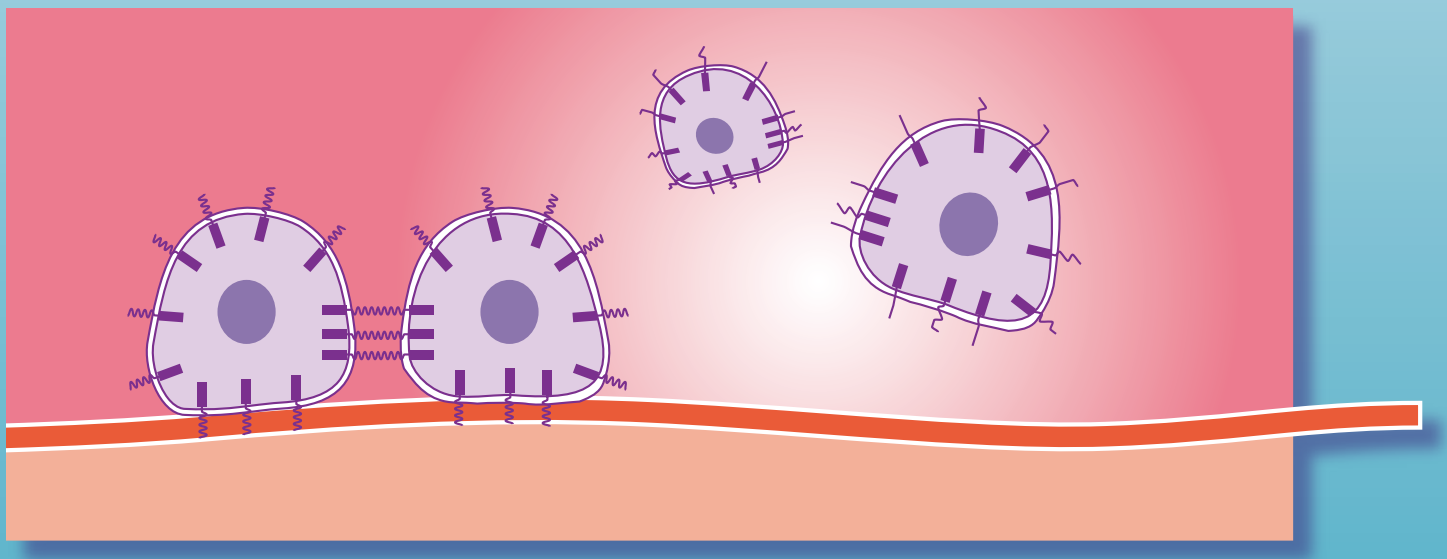
This abnormal behaviour of cancer cells can be disastrous when it occurs in the body. If the cancer cell manages to avoid the body's immune system it may divide to form a tumour.



Benign tumours usually remain in the place where they formed. By contrast, malignant tumours can move around the body and invade other organs: they *metastasise.*

Benign tumours are growths like warts or cysts which are usually fairly harmless. It is only malignant tumours which become cancers.

Malignant cells may have other properties, as well as dividing out of control. They may have unusual numbers of chromosomes; their cell processes may be abnormal (they don't mature into specialised cells like the xylem cells you saw in the root); and they may have changes on their surface which mean that they lose their attachments to other cells.



CANCER CELLS THAT HAVE CHANGED SURFACE ATTACHMENTS

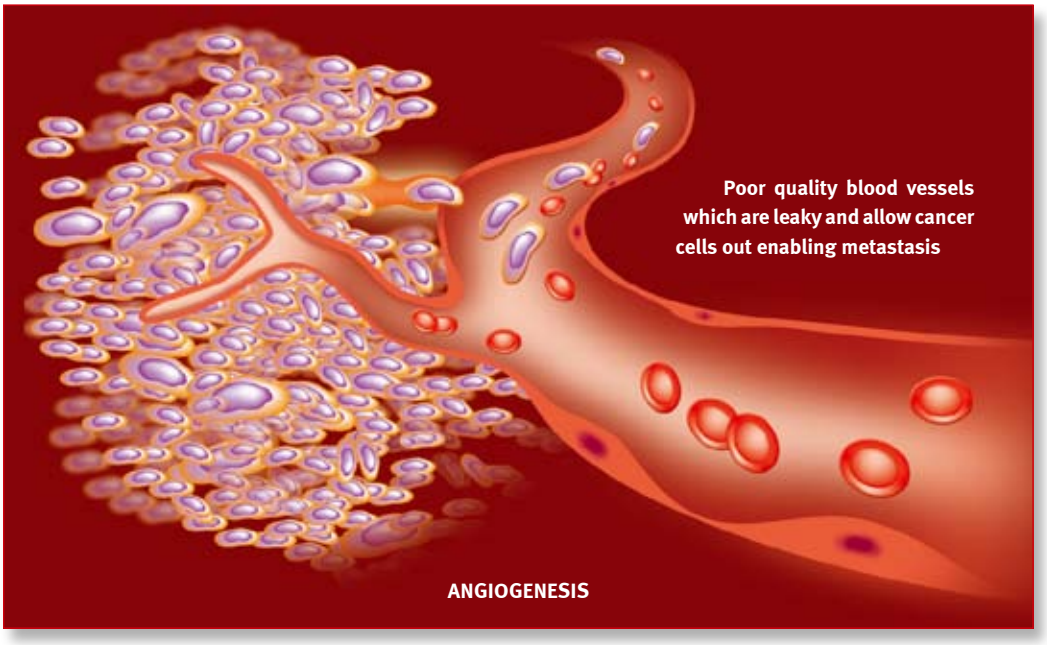
These cancer cells may now separate from the tumour and enter the blood and lymph vessels and invade other parts of the body forming new tumours.

Cancer Treatment		
Cancer can be treated in a variety of ways:	**SURGERY** removal of the tumour – almost all patients go through a surgical procedure	**RADIOTHERAPY** destroying the cancerous cells using radiation, e.g. X-rays
CHEMOTHERAPY using drugs which damage the cancer cells more than they harm the normal cells	**HORMONAL THERAPY** using drugs which alter the body's hormones as some hormones encourage the cancer cells to grow	**NOVEL TARGETED THERAPIES**

Chemotherapy and radiotherapy both work by affecting how the cancer cells divide.

Radiation will affect the cells which are undergoing mitosis, causing them to die. The radiotherapy will be directed at the cancerous cells to try to minimise damage to normal healthy cells.

Chemotherapy drugs work by destroying cells when they are dividing. They damage the nucleus which controls cell division. Because cancer cells divide much more often than normal cells, many of them are killed by chemotherapy. However, although chemotherapy drugs are targeted to act on cancer cells, they will also kill normal cells which are dividing. This explains why chemotherapy causes side effects. It affects tissues which grow all the time, like hair and skin and the digestive system, so these cells are killed, too, and people have side effects such as hair loss, liver damage and nausea. Different cancers have different growth rates and are sensitive to different drugs; often doctors have to use a combination of different drugs to try to treat the cancer. In many cases the cancer cells become resistant to the effects of one particular form of chemotherapy and then another is used. Many of the drugs used in chemotherapy originate from plants – one widely used drug, paclitaxel, originally came from the bark of yew trees.



Finding the right drugs

Recent research has focussed on finding the differences between normal cells and cancer cells. Drugs are then developed which target these differences.

Several new drugs to fight cancer are now available – many of these drugs are targeted carefully to the processes within a cell which control cell growth. This might be a specific hormone or an enzyme within a cell – these drugs are known as novel (new) targeted therapies[1]. Another exciting type of novel therapy, which will be available soon, targets one of the signals which tumours give out. These signals coming from the tumour make sure that the tumour has the blood supply which it needs if it is going to grow. The new drugs stop the blood vessels forming so the tumours cannot grow bigger than a few millimetres[2]. These new drugs do not have the type of side effects associated with chemotherapy.

The Balancing Act

When developing new medicines, including those used to combat cancer, researchers must first determine the main properties of the drug over a range of dose levels. These properties include the ability of the drug to cause the effect desired, as well as the toxicity level and any undesirable side effects. Only in this way can scientists determine which dose will maximise the desired effect while causing the lowest side effects. There are often four main phases in clinical trials:

PHASE 1
The drug is tested on humans for the first time, usually on between 20 to 80 people. Researchers begin to evaluate the drug's overall safety, its safe dosage range, and any side effects it produces.

PHASE 2
In this phase, the drug is further evaluated with testing on a larger group of people (100-300).

PHASE 3
The drug is administered to large groups of people (1000 to 3000) to confirm its effectiveness, monitor its side effects, and compare it to commonly used treatments.

PHASE 4
After the drug has been marketed, testing is continued to monitor how the drug reacts in various populations and to determine the consequences of long term use.

In this activity, you will look at some features of a dose response curve, investigating the effect of salt on a vital intracellular process in liver cells. The salt is to simulate a drug undergoing trials. You may know that salt is harmful to cells. Can you suggest why this is so? Your objective is to find the lowest concentration of salt that will still allow the liver cells to function relatively normally.

MATERIALS for each group

- ❑ dropper bottle 5 ml liver cell homogenate
- ❑ dropper bottle 5 ml 2% salt solution ❑ test tubes
- ❑ test tube rack ❑ spotting tiles ❑ small long balloons
- ❑ stop watch ❑ plastic pipettes
- ❑ graduated cylinder 10-25 ml
- ❑ 30-40 ml 3% hydrogen peroxide ❑ eye protection

SAFETY NOTE Take care when using hydrogen peroxide. Wear eye protection and do not touch the solution with your hands.

Method

Copy down the data table shown here:

Trial number	Drops of liver cell homogenate	Dosage of salt (number of drops)	Response time (number of seconds)
1	10 drops		
2	10 drops		
3	10 drops		

Add 10 drops of liver cell homogenate to three different wells in the spotting tile. You will be carrying out three dosage trials and determining their average.

Add the prescribed dose (number of drops) of salt solution, that has been assigned by your teacher, to each well.

Wait four minutes for the salt to "act" on the liver cells. While waiting, prepare a test tube with 10 ml 3% hydrogen peroxide. Prepare your balloon and decide who will be the time-keeper.

Begin trial #1: Use a pipette to add 5 drops of liver cell/ salt mixture directly to the hydrogen peroxide. Immediately place the balloon on the test tube and start recording the time.

Avoid shaking or tapping the test tube because this will release too many oxygen gas bubbles too quickly and bias the readings.

When the balloon is filled with enough oxygen gas, it will stand upright. Stop the watch and record the time.

Repeat the above procedure for trials # 2 and # 3. Make sure you use 10 ml of fresh hydrogen peroxide each time and that you squeeze any gas out of the balloon.

Average your results for the three trials and provide this figure for the class data table.

Using the class results, graph the response of the liver cells/salt mixture to hydrogen peroxide.

Discussion and Questions:

According to the graph, what does salt do to the intracellular processes in liver cells? Explain your reasoning.

What might happen to cells and tissues of the body if the liver is unable to eliminate hydrogen peroxide?

Based on the class data table, what do you think are acceptable doses of salt? What doses do you think might be too toxic? Why?

Epidemiology – Can Trinovin help prostate cancer?

Prostate cancer is a common cancer in men but like many cancers it is not evenly distributed throughout the world. For example Japanese men who have prostate cancer find that the disease progresses much more slowly than it does in men living in the western world. This observation led to some studies taking place on differences in the diet of men living in these different areas.

Trinovin has been identified as a dietary substance which might have an effect on dividing cancer cells. It comes from the red clover plant, a legume belonging to the same family of plants as peas and beans. A small study of 38 men measured the effect of Trinovin on the size of prostate tumours between diagnosis and surgery. Half of the men were given Trinovin; their tumours were significantly smaller at surgery than the tumours of men who did not receive Trinovin, suggesting Trinovin slowed the growth of prostate tumours in these Asian men. These compounds might therefore be good targets for new prostate cancer therapies[3]. However, we need much larger trials before we will know how important Trinovin or any other isoflavones are in preventing prostate and other cancers.

In an area of Northern Kenya local people use the sap of a closely related plant to treat moles and warts which they get on their skin and they find that the sap reduces the growths. It could be that this clover plant sap is having a similar effect as Trinovin has on the prostate cancers.

There are probably many other plants and plant products which have similar anti-cancer type effects.

Cells, cell division, cancer and cancer treatment

14–16 Resource References:

1 Early Breast Cancer Trialists' Collaborative Group (2001). Tamoxifen for early breast cancer. *Cochrane Database of Systematic Reviews* 2001, Issue 1. Art No CD000486. http://dx.doi.org/10.1002/14651858.CD000486.

2 Mayo Clinic (2007). Angiogenesis inhibitors: New cancer drugs stop tumor growth. www.mayoclinic.com/health/angiogenesis/CA00079

3 Jarred RA *et al.* (2002). Induction of apoptosis in low to moderate-grade human prostate carcinoma by Red Clover-derived dietary isoflavones. *Cancer Epidem Biomarkers & Prev* **11**:1689–96. http://cebp.aacrjournals.org