Fig. 4 The Mutation of a Proto-Oncogene

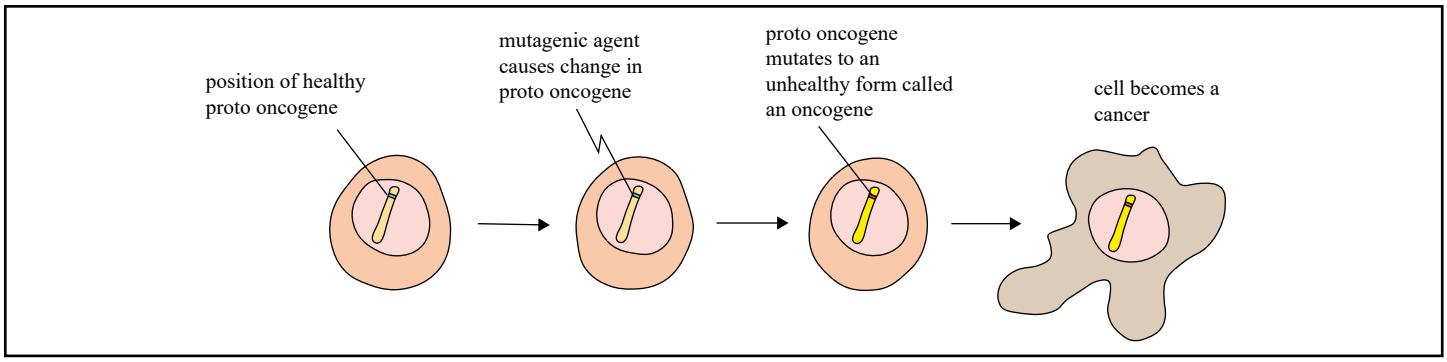
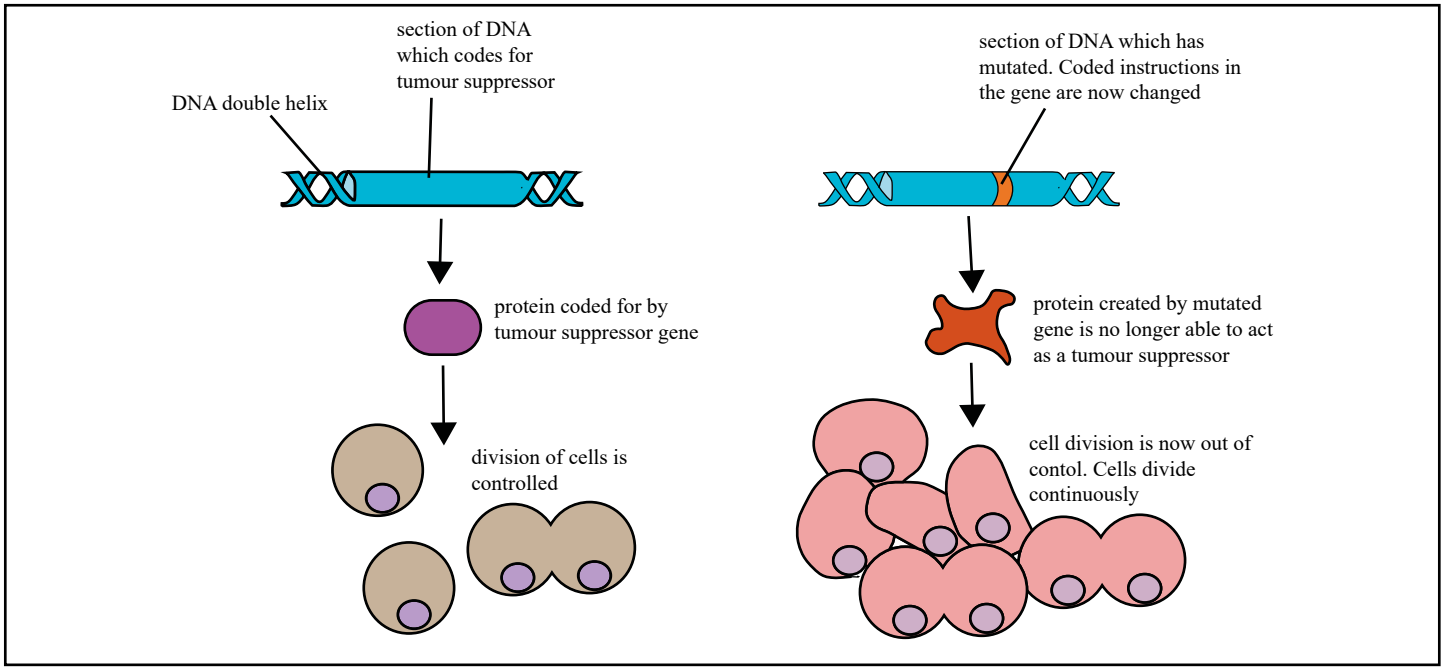


Fig. 5 The Effect of a Mutation in a Tumour Suppressing Gene



Cells can often repair faults in their DNA. This is done during cell division when the DNA is checked. If a mutation is too great, the cell may die or be destroyed by the immune system.

Some genes are essential for cell division. If such genes mutate, a cell may start to multiply out of control. Rapid division of such an abnormal cell will result in a cancerous tumour.

There are multiple causes of these mutations:

- **Proto-oncogenes.** The genes essential to cell division are called **oncogenes**. These are mutated forms of healthy **proto-oncogenes**. Oncogenes cause cells to grow and divide out of control.
- **Tumour suppressing genes**. These genes slow down cell division and repair DNA. They also control apoptosis so that a cell dies at the correct time. Mutated tumour suppressor genes also cause cells to divide out of control.
- **Inheritance of genes**. A person who inherits an abnormal copy of a gene starts life with a mutation. This gene may increase the likelihood of developing cancer. The person is said to have inherited a **genetic predisposition** to the disease. Cancers inherited in this way show up earlier in the life of the individual and affect younger people.
- **DNA methylation.** Methylation is the process of adding a methyl group to part of the DNA molecule. When the methyl group is added, the DNA structure is changed. The methylated gene can no longer create a protein. This means that the gene is turned off. If this happens to a tumour suppressor gene, cell division becomes uncontrolled.
- **Viral infections.** Viruses that cause cancer tend to be those carrying DNA. The viral DNA mixes with the cell's DNA. The viral DNA causes the cell to grown and divide. For example, cancer of the cervix is due to the **human papilloma virus** (HPV). Children in the UK are now offered a vaccine against HPV.
- **Exposure to carcinogenic substances**. Mutations happen by chance. However, certain chemicals and forms of radiation increase the chances of a mutation occurring. These are called **carcinogens**. Carcinogens include the chemicals in cigarette smoke, asbestos, lead, benzene, and vinyl chloride, as well as forms of radiation such as X-rays and UV light.
- **Diet.** There are some foods that will increase the risk of developing cancer. For example, barbecued food, if blackened with carbon, is high in cancer-causing chemicals called **free radicals**. Other foods can help reduce the risk of cancer, such as fruit and vegetables. Many contain protective chemicals called **antioxidants**. Antioxidants can neutralise harmful free radicals. A diet high in unsaturated fats and rich in fibre can protect against cancer of the colon.

Detecting Cancer

Cancerous cells can develop anywhere in or on the body. Most cannot be seen, so the disease may develop to a late stage before any symptoms are noticed. The more common cancers can be **screened**. Screening picks up early stage cancers before they have a chance to develop and spread. The screening programmes are very successful in reducing the number of patients who develop cancer. People in high risk groups are offered free screening by the NHS:

- **Cancer of the cervix.** Women aged between 25 and 50 are screened every 3 years for cervical cancer. The test involves taking a small sample of cells from the **cervix** (the neck of the womb) and examining them under a microscope. Abnormal cells can be identified by an experienced technician. HPV is a common cause of cervical cancer.
- **Bowel cancer.** A test for bowel cancer is offered to men and women over the age of 60. The test is repeated every 2 years. This test involves taking a small sample of faecal material and examining it for blood. If the test is positive, **a colonoscopy** is carried out. During a colonoscopy, a camera on a tube is pushed into the colon. The picture of the colon lining is examined for abnormal growths.
- **Breast cancer.** Breast cancer screening is offered to all women between the ages of 50 – 70. The test involves taking an x-ray of the breast tissue. This is called a **mammogram**.

Other means of detecting non-routine cancers can be:

- **CT scanners**. These machines use X-rays to show internal body structures and soft tissue.
- **MRI scanners**. These use magnetic fields to produce a picture of internal body structures. Images on an MRI scan are clearer than on a CT scan. An experienced radiologist interprets the images. MRI scanners are very useful to detect cancers in soft body tissues.
- **PET scanners.** The images from PET scanners can detect small changes in the chemical reactions inside cells. Any abnormal metabolic reactions can often lead to organs or tissues becoming cancerous.
- **Blood tests.** These can identify marker chemicals in blood.
- **Genetic tests.** These tests identify genes that may increase the likelihood of a cancer developing.
- Taking a **biopsy**. This involves cutting out a section of a tumour. A **pathologist** will make a microscope slide of the cells collected. The cells are stained and examined for any abnormalities.

Exam Hint: *Details of how the different scanners work is not required. The basic methods of scanning internal soft body tissues should be understood.*

Fighting Cancer

If a person is diagnosed with cancer, the disease needs to be treated before it spreads.

Cancer treatments can include:

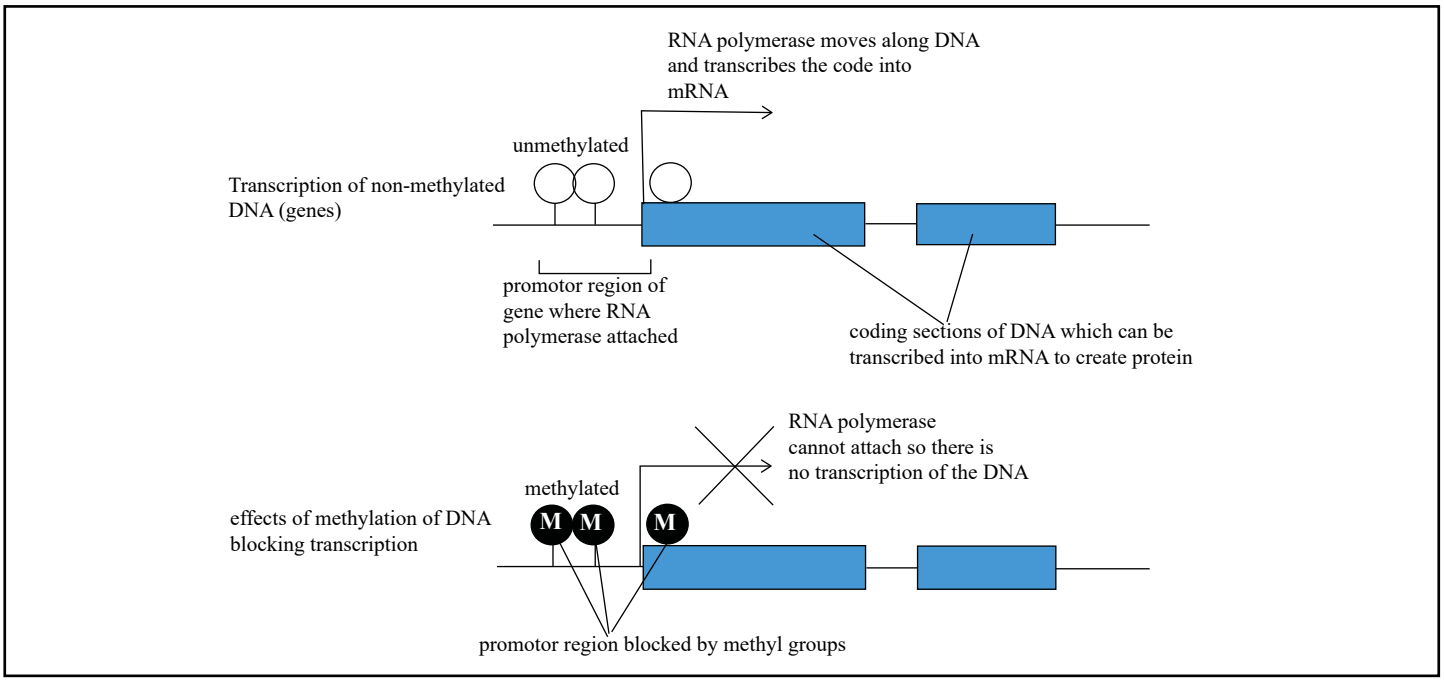
- **Surgery.** Surgery involves cutting cancerous growths out of the body. Surgery will only be used if the tumour can be located and has not spread. When a tumour is cut out, the surgeon will remove as much of the cancer as possible. This means some surrounding healthy cells are also removed. Surgery is usually combined with radiation and chemotherapy. If a tumour is removed, the patient may be completely cured.
- **External radiotherapy. Radiotherapy** is used to kill cancer cells and will shrink tumours. A beam of radiation is directed onto the cells. External radiotherapy uses high energy X-rays such as **photon beams**. These destroy cancer cells on the outside of the body. Other types of radiation used include particle beams, such as **protons** or **electrons**. Radiation will also kill healthy cells, but these usually survive when the treatment is over. Radiation treatment can cause damage to the genes of healthy cells. This means that the treatment is given in carefully controlled doses. It is also spread out over time.
- **Internal radiotherapy.** This treatment is used to target a cancer inside the body. Internal radiotherapy uses radioactive liquids that can either be drunk or are injected into the blood. The liquid contains a **radioactive isotope**. The isotope is often attached to another inert material. The material carries the radioactive isotope into the tumour. Different types of cancer require different forms of internal radiotherapy. The liquids include radioactive forms of radium and strontium, which are used to treat bone cancer, and phosphorus, which targets blood cancers.
- **Radioactive implants.** An implant uses a **radioactive metal.** The metal is put into the body on a wire or tube. It is placed in or next to the tumour. Depending on the type of tumour, the implant is left inside the body for different lengths of time.
- **Chemotherapy**. Many chemotherapy drugs target cells that are undergoing rapid cell division. Cells that are not dividing are less likely to be damaged during chemotherapy. Chemotherapy drugs affect all tissues (healthy and cancerous) that divide rapidly, particularly the hair follicles, skin, nails, and the lining of the gut. These healthy cells will suffer the side effects of chemotherapy.
- **Hormone therapy**. Some hormones stimulate cancers to grow. Breast cancer, prostate cancer, and ovarian cancers can be promoted by hormones. Hormone therapies work by:
  - Preventing hormones being made
  - Stopping hormones from stimulating cell division.

  For example, the hormone **oestrogen** stimulates cell division. The drug **tamoxifen** is used to prevent breast cancer. Tamoxifen will block oestrogen receptors on cancerous cells in breast tissue.
- **Transplants.** Bone marrow and stem cell transplants can be used to treat certain types of blood cancers. Initially, a patient has a very high dose of chemotherapy. This will kill off their own unhealthy bone marrow. The patient then receives a donation of healthy bone marrow. The donor must be closely matched to the patient so that these cells are not rejected. Alternatively, stem cells are transplanted into the patient.
- **Immunotherapy.** These are treatments which stimulate the body's own immune system to fight cancer. There are several types of immunotherapy:
  - **Monoclonal antibodies**. These are antibodies that can be made to work against foreign antigen. The antibodies are created by a **hybridoma**. A hybridoma is an artificially created cell. It is made by fusing a lymphocyte (which creates the antibodies) with a cancer cell (which divides rapidly). Specific antibodies can be created that will target proteins on the outside of cancer cells. The antibodies will mark the cancer cells so that the immune system can recognise and destroy them.
  - **Interferons and interleukins**. These are chemicals made in the body. They can help the immune system destroy cancer cells. Artificial versions of these chemicals can be made in the laboratory.
  - **Virus therapy. Genetically modified** (GM) viruses can be used to kill cancer cells. The GM virus is injected into a tumour. The virus copies itself and the tumour cells burst and die. The cell releases chemicals. These chemicals stimulate the patient's immune system, which then destroys the damaged cells. The viruses do not enter healthy cells.
  - **T-cell therapy.** T-cells are part of the human immune system. They are able to destroy cells. A patient's T-cells are removed from their blood. The cells are altered so that protein receptors are added to their cell surface membrane. The receptors help the T-cells to recognize cancer cells. This treatment is still being trialled and is not yet available.

- **Cancer vaccines.** Cancer vaccines boost the body's own immune system. The immune system can then recognise and destroy the antigens on cancer cells. There are only three cancer vaccines that are available:
  - i. A vaccine targeting cervical cancer, anal cancer, and genital warts.
  - ii. A vaccine protecting against human papilloma virus.
  - iii. A vaccine preventing hepatitis B infection. Infection with this virus can lead to liver cancer.

- **Drug treatment and methylation.** Some drugs work by methylating the genes that cause cancer. If a cancerous gene is methylated, it may be turned off. Other drugs can reverse methylation. These drugs can be used to treat cancers which are caused by genes which have been abnormally methylated.

Fig. 6 The Effects of Adding a Methyl Group to a Gene



Exam Hint: *Knowing the details of DNA methylation is not required by some exam boards.. However, the processes of switching genes on and off should be understood. The detailed theory is covered by the lac operon and genetic control of transcription factors.*

Reducing the Risk of Developing Cancer

There are lifestyle changes that people can make to reduce the risk of developing cancers. These are:

- **Diet**. As mentioned, a diet rich in fresh fruit, vegetables, wholegrains, and fibre has been shown to reduce the risk of bowel cancer. High intake of red meat, processed meats, salt and refined sugars increases the risk.
- **Exercise**. Regular aerobic exercise and reducing body weight both help lower the risk of developing cancer.
- **Smoking**. Smoking significantly increases the risk of all cancers, particularly of the mouth, throat, and lungs. Cigarette smoke contains a cocktail of carcinogenic chemicals. Even chewing tobacco is a risk.
- **Alcohol.** Moderate intake of alcoholic drinks may not damage health. However, increasing alcohol consumption can increase the chances of developing cancer.
- **Sunlight**. The ultra-violet light rays from the sun can cause the DNA in skin cells to mutate.
  To avoid skin cancer, a person should:
  - cover their skin with clothes or a sun block.
  - avoid being out in the sun at the hottest part of the day.
  - avoid tanning beds and sunlamps.
- **Safe sex.** Certain viruses like the HPV can be contracted through sexual intercourse. Using a condom will prevent any sexually transmitted diseases from being passed on.

Questions

1. Explain how the mutation of a tumour suppressor gene can result in the formation of a tumour.
2. Some cancer cells have a receptor protein in their cell-surface membrane. The receptor binds to a hormone called growth factor. When the hormone binds to the receptor, it stimulates the cancer cells to divide. How might scientists develop monoclonal antibodies that could stop the growth of a tumour?

Answers

1. A tumour suppressor gene could be inactivated by the mutation. The gene would not be able to control or slow down cell division. The rate of cell division by uncontrolled mitosis would be too fast.
2. The growth factor or hormone binds to the receptor protein in the cell surface membrane. Monoclonal antibodies are created by hybridomas. A hybridoma is a lymphocyte fused to a cancer cell. The lymphocyte produces a specific antibody. The cancer cell divides rapidly. The antibody created by this hybridoma has a specific tertiary structure (or binding site or variable region). This shape is complementary to the receptor protein. The antibody binds to the receptor and prevents GF binding. If the growth factor cannot bind, it will not stimulate excess growth in the cell.

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