

# FACTFILE: GCE BIOLOGY

## CANCER



## Cancer

### Learning outcomes

Students should be able to demonstrate knowledge and understanding of the cell cycle:

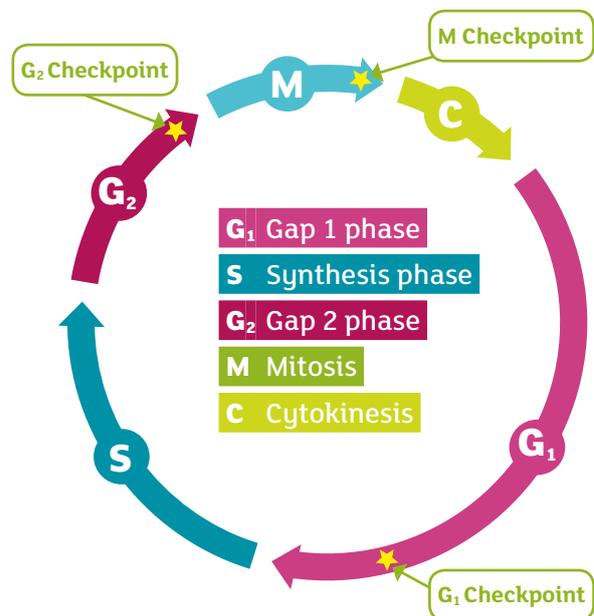
- the main events during  $G_1$ , S and  $G_2$  of interphase;
- that the two gap phases are more than time delays as they give time for the cell to monitor the internal and external environment to ensure all is ready for the S and M phases (in many cases, including unfavourable conditions, cells can delay progress through  $G_1$  and go into  $G_0$  [resting state], which they can remain in for days, weeks or years);
- nuclear division (mitosis) following the replication of DNA during the S phase;
- the link between loss of control points in the cell cycle and cancer.

Students should be able to demonstrate knowledge and understanding of the relationship of anticancer drugs to the cell cycle:

- mitotic poisons that inhibit microtubule formation, for example vincristine; and
- antimetabolites as S-phase inhibitors preventing DNA synthesis, for example 5'Fluorouracil.

### The Biology of Cancer

The cell cycle is the name given to the series of stages which a cell can go through from its own creation following cytokinesis, to the point where it divides into two new daughter cells itself.



#### The G1 checkpoint will check for:

- DNA damage
- Cell size
- Availability of nutrients
- Presence of growth factors (chemicals which stimulate cell division)

#### The G2 checkpoint will check for:

- DNA replication
- Cell size

The M checkpoint will check for number and alignment of chromosomes

The phases referred to as G1 and G2 are sometimes described as 'growth' or 'gap' phases. As well as carrying out normal cell functions, each of these phases also involves a 'checkpoint'. This is when various cell structures and molecules are involved in checking the integrity of the cell and its readiness for division, in order to ensure only healthy cells proceed to mitosis and cytokinesis. (A further checkpoint exists within mitosis, at the end of metaphase).

If a cell is identified as having low nutrient levels or if the correct growth factors are missing, then it will not proceed past the G1 checkpoint. Instead, it leaves the cell cycle and enters a phase referred to as G0, a resting phase. In some cases the cell will not enter the cycle again and will remain in G0 until it dies. In other cases, it will proceed onto S phase at a later stage if all the correct conditions are met for passing the G1 checkpoint. The period of time for which a cell remains in G0 is highly variable between cell types. For example cells such as neurones may remain there permanently, while epithelial cells rarely enter G0, but continuously divide. At any one time, most of the cells in the human body are in G0 and only return to G1 when stimulated to do so.

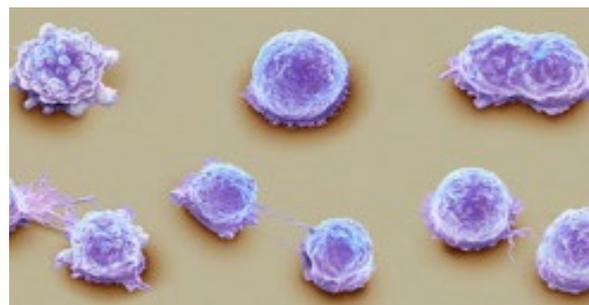
[NB. The reference to G0 as a resting phase is somewhat misleading because it is no longer in preparation for cell division but it does not mean it is no longer busy! In fact it will be carrying out all of its normal functions while in G0.]

## How uncontrolled cell division can arise

Cancer involves uncontrolled cell division and the production of a tumour. Hence it can be caused by problems with the checkpoints in the cell cycle, causing situations where cells repeatedly go through the cell cycle, despite there being no need.

There are many genes in humans which contribute to the regulation of the cell cycle, so that cells continue to divide in such a way as to meet the needs of the body. Many of these genes code for proteins which are involved in the checkpoints (described above) in some way. For example one of the genes codes for a growth factor receptor. This receptor is on the cell surface membrane and when the growth factor is present, the cell can detect it and is allowed to proceed past the G1 checkpoint (assuming all other conditions are favourable). Certain mutations in the gene can cause a faulty receptor to be produced, which is always in the 'on' state, whether the growth factor is present or not. The cell repeatedly goes through the whole cell cycle, dividing continuously, when really it should be entering G0.

Another gene is responsible for detecting DNA damage at either the G1 or G2 checkpoint. If significant DNA damage is discovered, the gene causes the cell to 'self-destruct'. If this gene is mutated, then cells with damaged DNA are allowed to divide, and this often results in a tumour. This gene is mutated in almost half of all cancers.



*Sequence showing colorectal cancer cells dividing*  
© Steve Gschmeissner/Science Photo Library

## The cell cycle and cancer treatments

With increased understanding of the causes of cancer, scientists continue to make progress in developing effective treatments, so that more and more cancers are being successfully treated.

### Vincristine

In order for cell division to be successfully completed, all of the events of mitosis must proceed in turn. An anti-cancer drug called vincristine interferes with the process of mitosis in rapidly dividing cells. Specifically, it binds to a protein called tubulin, which forms the microtubules of the spindle. When vincristine is bound to tubulin, the microtubules cannot be formed and hence anaphase cannot take place. Vincristine is referred to as a mitotic poison.

It not only affects cancerous cells; some of its side

effects are due to its impact on the rapidly dividing epithelium in the intestine and in the bone marrow. Vincristine is derived from the Madagascar periwinkle plant, as is another anticancer drug, vinblastine. The plant has been a staple of both Indian and Chinese traditional medicine for a long time. This has caused some conflict now that several substances isolated from the plant have been patented by western pharmaceutical companies.

### 5' fluorouracil

This chemical is an inhibitor of one of the enzymes necessary for DNA replication. It interferes with the production of nucleotides carrying the nitrogenous base thymine and so very few of these nucleotides are available. DNA replication cannot be completed when 5' fluorouracil is present and so it is referred to as an 'antimetabolite'.

#### Further information

[Animation on the cell cycle and mitosis](#)

[Interactive exercise on cancer and the cell cycle](#)

[Information on cancer drugs, including vincristine and 5' fluorouracil](#)

[Information on loss of control of the cell cycle](#)

