CANCER

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D2.1.12 Cell proliferation for growth, cell replacement and tissue repair

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D2.1.14 Cell growth during interphase

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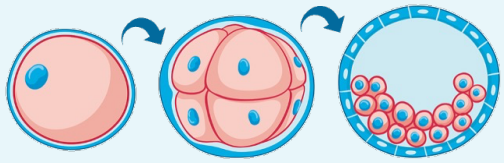
D2.1.17 Differences between tumours in rates of cell division and growth and in the capacity for metastasis and invasion of neighbouring tissue

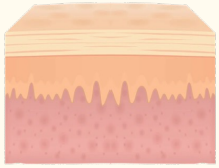
CELL PROLIFERATION

Multicellular organisms require cell proliferation to allow for growth, the replacement of dead cells and the repair of damaged tissues. In plants, meristem tissue allows for continuous growth and development, while animals only retain pluripotency in early-stage embryos. Adult animals may retain multipotency in stem cell niches, which can be used to regenerate tissues during wound healing (such as the repair of damaged skin).



Animal Growth: Early-stage embryos

Plant Growth: Meristematic tissue



Repair: Skin cells

CELL CYCLE

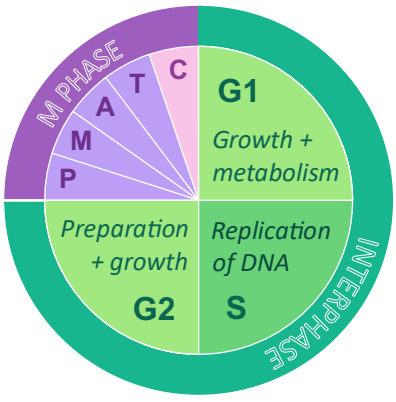
The cell cycle is an ordered set of events which results in the division of eukaryotic cells into identical daughter cells. It involves two key phases:

Interphase is an active phase of the cycle with many processes occurring in the nucleus and cytoplasm. It is a continuum of three distinct stages:

- **G1:** Cell grows and prepares for division (organelles are duplicated)
- **S:** A synthesis stage in which DNA replication occurs in the nucleus
- **G2:** Acts as a final growth and preparation stage prior to cell division

The **M phase** is the period of the cycle in which the cell and its contents are divided into two separate daughter cells. It involves two key stages:

- **Mitosis or Meiosis:** A process of nuclear division (DNA is separated)
- **Cytokinesis:** A process of cytoplasmic division (the cell splits in two)



The cell cycle moves in a clockwise direction as per the diagram shown above

Mitosis produces genetically identical daughter cells (diploid) for growth and repair, while meiosis produces genetically distinct daughter cells (haploid) for sexual reproduction. Division of the cytoplasm in cytokinesis can be either even (all daughter cells equally sized) or uneven (one daughter cell retains more cell content).

INTERPHASE

Interphase is the stage of the cell cycle that acts to prepare the cell for division.

- **DNA replication** – DNA molecules are copied during the S phase of interphase
- **Organelle duplication** – Cell content will be duplicated for both daughter cells
- **Cell growth** – Cytoplasmic volume must typically increase prior to cell division

Synthesis of the cellular materials needed for division involves enzymes and thus requires active **gene expression** (transcription and translation). Additionally, ATP is needed to drive division processes, so high levels of **cell respiration** are needed.

Hint: DOC!

CYCLINS

The cell cycle contains multiple checkpoints to ensure the fidelity and viability of continued proliferation.

- G_1 checkpoints confirm appropriate growth conditions and assess the overall level of DNA damage
- G_2 checkpoints ensure the cell is suitably sized and identify any copying errors during DNA replication
- Metaphase checkpoints test the attachment of spindle fibres to centromeres (prevent non-disjunction)

Progression through cell cycle checkpoints is controlled by a family of regulatory proteins called **cyclins**. A cyclin will bind to a **cyclin dependent kinase** (CDK) and form an activated complex which controls cell cycle processes through phosphorylation. The complex targets proteins that trigger specific events within the cell cycle when in a phosphorylated state. After the event has occurred, the target protein is dephosphorylated and the cyclin is degraded in order to render the cyclin dependent kinase inactive. Concentrations of cyclins must be tightly regulated within a dividing cell to ensure the cell cycle progresses in the proper sequence.

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Tumours are abnormal cell growths resulting from **uncontrolled cell division** and can occur in any tissue or organ. Diseases caused by the growth of tumours are collectively known as *cancers*. Tumours are caused by mutations to the genes that control the cell cycle. Proto-oncogenes code for proteins that stimulate the cell cycle and promote growth, while tumour suppressor genes (anti-oncogenes) code for proteins that repress the cell cycle and cause apoptosis. Mutations to either group of genes creates a cancer-causing **oncogene**.

METASTASIS

Tumour cells may either remain in their original location (**benign**) or spread and invade neighbouring tissue (**malignant**). Benign tumours do not cause cancer as they grow slowly and have distinct borders that do not encroach on surrounding tissue). **Metastasis** is the spread of cancer from one location (primary tumour) to another (forming a secondary tumour). Cancer diagnoses can be made by determining the **mitotic index** of a particular tissue. A higher mitotic index than standard may indicate that a given tissue may be cancerous.

Worked Example:

MI = (cells in mitosis ÷ total cell number)

Total cells = 22 Cells in mitosis = 10

Mitotic Index = 10 ÷ 22 = **0.45** (45%)