D2.1 Cell and nuclear division

Continuity and change—Cells

Standard level and higher level: 3 hours

Additional higher level: 1 hours

Guiding questions

• How can large numbers of genetically identical cells be produced?

• How do eukaryotes produce genetically varied cells that can develop into gametes?

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D2.1.1—Generation of new cells in living organisms by cell division
In all living organisms, a parent cell—often referred to as a mother cell—divides to produce two daughter cells.
• All living organisms generate new cells by division of pre-existing **parent (mother) cells** to produce **two daughter cells**

D2.1.2—Cytokinesis as splitting of cytoplasm in a parent cell between daughter cells
Students should appreciate that in an animal cell a ring of contractile actin and myosin proteins pinches a cell membrane together to split the cytoplasm, whereas in a plant cell vesicles assemble sections of membrane and cell wall to achieve splitting.

• **Cytokinesis** is the division/splitting of cytoplasm where a parent cell splits into 2 daughter cells
• In animal cells:
  • **Actin** + **myosin (actomyosin) filaments** assemble at the **equator** (center) of the cell to form a **contractile ring** that is anchored by the cell membrane
  • Actomyosin filament **contraction** causes the contractile ring to shrink in size, which leads the cell membrane to **pinch/ingress inwards** to **bisect** (split) the mother cell
  • The **cleavage furrow** is the visible **indentation** in the middle of the cell that can be seen under a microscope when the contractile ring shrinks in animal cytokinesis
• In plant cells:
  • **Microtubules** align **vesicles** containing **cell wall material** (like polysaccharides) at the equator, which **fuse** together to form a **cell plate**
  • More vesicles are recruited at the cell plate to form a cell wall to divide the mother cell into 2 halves
  • The existing plasma membrane surrounds the cell wall to complete the formation of two daughter cells
• Cytokinesis overlaps with the later stages of nuclear division but it is a **distinct** process

D2.1.3—Equal and unequal cytokinesis

Include the idea that division of cytoplasm is usually, but not in all cases, equal and that both daughter cells must receive at least one mitochondrion and any other organelle that can only be made by dividing a pre-existing structure. Include oogenesis in humans and budding in yeast as examples of unequal cytokinesis.

- Cytokinesis usually but not always leads to equal division of the cytoplasm
  - **Equal division** is useful for growth and repair
  - **Unequal division** is useful for gamete production and stem cell differentiation
    - In human oogenesis, meiosis results in the production of 4 daughter cells, but only 1 cell receives most of the cytoplasm to become a mature egg (the remaining 3 become **polar bodies** and eventually disintegrate)
    - In yeast, mother cells reproduce **asexually** by **budding**; the daughter cell inherits a nucleus and a small amount of cytoplasm before splitting
- Organelles that can only come from pre-existing organelles (like mitochondria & chloroplasts) must be inherited by both daughter cells regardless of whether cytokinesis is equal or not

D2.1.4—Roles of mitosis and meiosis in eukaryotes

Emphasize that nuclear division is needed before cell division to avoid production of anucleate cells. Mitosis maintains the chromosome number and genome of cells, whereas meiosis halves the chromosome number and generates genetic diversity.

- Cell division requires **nuclear division** to occur before **cytoplasmic division** in eukaryotic cells to prevent the generation of **anucleate cells** (those without a nucleus)
- **Mitosis** is **nuclear** division that results in **two** genetically **identical** **diploid** daughter cells
- **Meiosis** is **nuclear** division that results in **four** genetically **different** **haploid** daughter cells
  - It **halves** the chromosome number of daughter cells and generates genetic diversity

D2.1.5—DNA replication as a prerequisite for both mitosis and meiosis

Students should understand that, after replication, each chromosome consists of two elongated DNA molecules (chromatids) held together until anaphase.

- DNA replication is a prerequisite for (occurs before) both mitosis and meiosis
- Before DNA replication, each DNA molecule (**46** in humans) is a **chromosome**
- After DNA replication, each DNA molecule is attached to its replica
  - The 2 elongated & identical DNA molecules are each called **chromatids**
  - Chromatids are attached to each other at the **centromere** (a region in each DNA molecule, usually the center, that enables chromatids to bind to each other)
  - In humans, there are **92 chromatids** (46 × 2) and **46 chromosomes** after DNA replication
    - Even though the number of DNA molecules has doubled from 46 to 92, the total number of chromosomes is still considered 46 (DNA replication does **NOT** double chromosome number)

Meiotic Stages	Number of chromosomes per cell	Number of DNA molecules (or chromatids) per cell
Meiosis I (reduction division)		
Prophase I	46	92
Metaphase I	46	92
Anaphase I	46	92
Telophase I	46	92
Post-cytokinesis	23	46
Meiosis II (equational division; similar to mitosis)		
Prophase II	23	46
Metaphase II	23	46
Anaphase II	46	46
Telophase II	46	46
Post-cytokinesis	23	23

D2.1.6—Condensation and movement of chromosomes as shared features of mitosis and meiosis

Include the role of histones in the condensation of DNA by supercoiling and the use of microtubules and microtubule motors to move chromosomes.

- DNA must be condensed before mitosis & meiosis for easier movement during division
- **Histones** are proteins that DNA wraps around to become more condensed
  - **Chromatin** (uncondensed DNA) undergoes further **supercoiling** by other proteins to condense into chromosomes (which are visible under a light microscope, unlike chromatin)
- **Microtubules** are the third main component of the cytoskeleton & are involved in the movement of chromosomes during mitosis and meiosis
  - **Kinetochore** proteins assemble at the centromere of each chromosome & function as attachment points for microtubules during cell division
  - **Centrioles** are a pair of protein structures that position themselves at opposite poles of the mother cell during division
  - During cell division, microtubules form at the centrioles and extend throughout the mother cell to form **spindle fibers** (a network of microtubules)
    - Microtubules attach to kinetochores to align the chromosomes in metaphase and pull them apart during anaphase

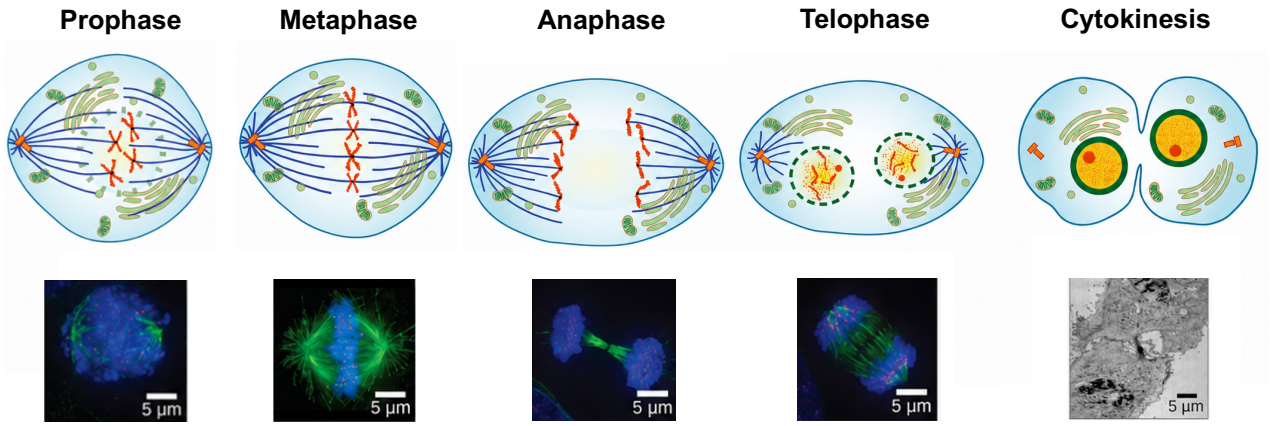
D2.1.7—Phases of mitosis

Students should know the names of the phases and how the process as a whole produces two genetically identical daughter cells.

- **Prophase**
  - Chromatin condenses into chromosomes
  - Centrioles migrate to opposite ends of the mother cell & spindle fibers begin to form
  - Nuclear envelope disintegrates to allow attachment of microtubules to kinetochores
- **Metaphase**:
  - Chromosomes align at the **metaphase plate/equator** (an imaginary line between the 2 cell poles)
- **Anaphase**:
  - **Sister chromatids** are pulled apart & the chromosomes migrate to opposite poles
- **Telophase**:
  - Nuclear envelope forms at each pole
  - Mitotic spindle depolymerizes
  - Chromosomes decondense into chromatin
- Cytokinesis occurs in late anaphase / early telophase to divide the mother cell into two genetically identical daughter cells

D2.1.8—Identification of phases of mitosis

Application of skills: Students should do this using diagrams as well as with cells viewed with a microscope or in a micrograph.



D2.1.9—Meiosis as a reduction division

Students should understand the terms “diploid” and “haploid” and how the two divisions of meiosis produce four haploid nuclei from one diploid nucleus. They should also understand the need for meiosis in a sexual life cycle. Students should be able to outline the two rounds of segregation in meiosis.

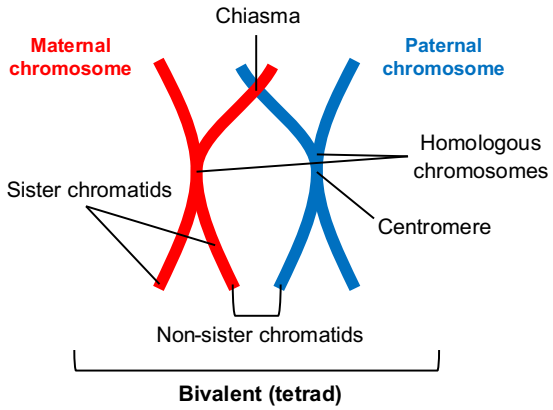
- Human cells are **diploid**; they contain **two sets of 23 chromosomes** from each parent (total 46)
  - 46 chromosomes can be grouped into **23 homologous pairs**; each chromosome in the pair is of different parental origin
  - Within a homologous pair, both paternal and maternal chromosomes carry the same genes at the same locus (DNA position) but often contain different alleles
- Meiosis is a reduction division because it produces 4 haploid daughter cells (gametes) from 1 diploid mother cell
  - **Haploid** cells only contain **one set of 23 chromosomes**
  - The 23 chromosomes are a random mix of parental & maternal origin due to random bivalent orientation
  - Meiosis is required in a sexual life cycle because it prevents the doubling of chromosome number after fertilization
- Meiosis occurs in two phases; meiosis I & meiosis II:
  - **Prophase I**:
    - Chromatin condenses into chromosomes
    - **Crossing over** occurs to increase genetic diversity;
      - **Non-sister chromatids** (chromatids that belong to the same homologous pair but are not connected by a centromere) form physical links called **chiasmata**
      - **DNA exchange** (segments of each chromatid break off and attach to the other chromatid) occurs between non-sister chromatids at chiasmata
      - A **bivalent/tetrad** is the association of a pair of homologous chromosomes physically held together by at least one chiasma
    - Centrioles migrate to opposite ends of the mother cell & spindle fibers begin to form
    - Nuclear envelope disintegrates to allow attachment of microtubules to kinetochores
  - **Metaphase I**:
    - Bivalents randomly align at the metaphase plate/equator
  - **Anaphase I**:
    - **Homologous chromosomes** are pulled apart & migrate to opposite poles
  - **Telophase I**:
    - Nuclear envelope forms at each pole
    - Mitotic spindles depolymerize
    - Chromosomes decondense into chromatin
- **Meiosis II** proceeds similarly to mitosis because sister chromatids are pulled apart in anaphase II, but it starts with haploid cells and produces haploid cells
- Cells may undergo a brief phase of growth after meiosis I before starting meiosis II

D2.1.10—Down syndrome and non-disjunction
Use Down syndrome as an example of an error in meiosis.

- **Non-disjunction** occurs when chromosomes or chromatids fail to separate during anaphase
  - In meiosis I, **homologous chromosomes** fail to separate
  - In meiosis II or mitosis, **sister chromatids** fail to separate
- Non-disjunction in mitosis is not passed onto offspring but can lead to diseases like cancer
- Non-disjunction in meiosis is passed to offspring and can lead to zygotes with extra chromosomes
  - For example, **Down syndrome (trisomy 21)** is a genetic disorder caused by non-disjunction of chromosome 21 during anaphase I or II
  - Non-disjunction can occur in both autosomal and sex chromosomes

D2.1.11—Meiosis as a source of variation
Students should understand how meiosis generates genetic diversity by random orientation of bivalents and by crossing over.

- Meiosis generates genetic diversity in several ways:
  - **Crossing over** produces new allelic combinations on chromosomes
  - **Random orientation of bivalents** along the metaphase plate means that for each homologous pair, either the maternal or paternal chromosomes can face either cell poles
    - This generates new combinations of paternal and maternal chromosomes in gametes



Additional higher level

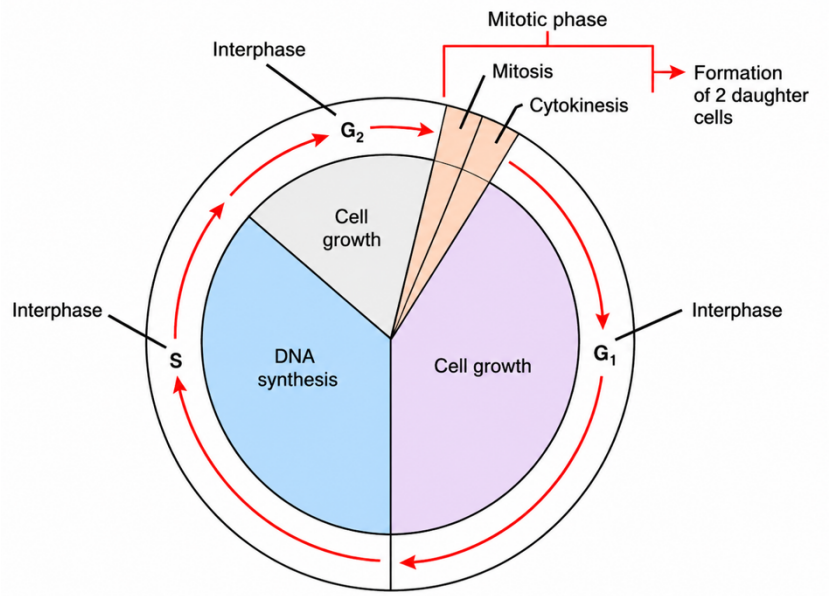
D2.1.12—Cell proliferation for growth, cell replacement and tissue repair
Include proliferation for growth within plant meristems and early-stage animal embryos as examples. Include skin as an example of cell proliferation during routine cell replacement and during wound healing. Students are not required to know details of the structure of skin.

- **Cell proliferation** is the increase in cell number through multiple rounds of division
  - In early-stage animal embryos, cell proliferation enables a rapid increase in cell numbers to establish future tissues and organs
  - In plants, **apical meristem** at the tips of shoots and roots enables plants to grow in length
  - Skin cells are constantly replaced in the human body to maintain a strong protective layer
    - During wound healing, tissue repair depends on rapid cell proliferation to replace damaged cells

D2.1.13—Phases of the cell cycle

Students should understand that cell proliferation is achieved using the cell cycle. Students should understand the sequence of events including G1, S and G2 as the stages of interphase, followed by mitosis and then cytokinesis.

- The **cell cycle** is a regulated process of cell growth and division, which occurs in 2 phases:
  - **Interphase**: the period between mitoses, which is composed of 3 stages:
    - **Gap 1 (G1)**: the period after mitosis where the cell grows to prepare for DNA replication
    - **Synthesis (S)**: a short period where DNA replication occurs
    - **Gap 2 (G2)**: the period after DNA replication where the cell grows to prepare for mitosis
  - **Mitosis (M phase)**: a period of nuclear division followed by cytokinesis to produce 2 daughter cells
- The duration of the cell cycle varies between different kinds of human cells
  - Some cells that never divide (like cardiomyocytes) permanently enter the **G0 phase** where they remain metabolically active (for specialized functions) but do not proliferate (i.e. no cell division)
  - Some cells temporarily enter G0 for different periods of time before resuming proliferation



D2.1.14—Cell growth during interphase

Students should appreciate that interphase is a metabolically active period and that growth involves biosynthesis of cell components including proteins and DNA. Numbers of mitochondria and chloroplasts are increased by growth and division of these organelles.

- **Interphase** (longest phase of the cell cycle) is a metabolically active period where cell size doubles:
  - Membrane-bound organelles (like the Golgi apparatus) bud off from existing ones
  - Non-membrane bound organelles like ribosomes are synthesized **de novo** (from scratch)
  - Mitochondria and chloroplasts grow in number (by division) & replicate their own circular DNA
  - Cell membranes increase in surface area (cell deposits phospholipids by exocytosis)
  - Cytoplasm increases in volume due to the biosynthesis of cell components

D2.1.15—Control of the cell cycle using cyclins

Limit to the concentration of different cyclins increasing and decreasing during the cell cycle and a threshold level of a specific cyclin required to pass each checkpoint in the cycle. Students are not required to know details of the roles of specific cyclins.

- The cell cycle is heavily regulated to ensure heredity occurs with little/no errors
- **Checkpoints** exist throughout the cell cycle to ensure that the cell has correctly carried out the functions of a specific phase before moving onto the next
  - **G1 to S**: determines whether the cell commits to division (by DNA replication) or enters G0
  - **G2 to M**: ensures correct DNA replication (no errors or damage) before entering mitosis
  - **Metaphase to Anaphase**: ensures chromosomes are correctly & firmly attached to spindle fibers
- **Cyclins** are a family of proteins that regulate the progression of cells throughout the cell cycle
  - Each phase of the cell cycle is controlled by a specific cyclin during which its concentration must pass a certain **threshold level** to help the cell progress past a particular checkpoint
    - Cyclin levels increase and decrease according to many **internal** (DNA damage, cellular stress) and **external signals** (nutrient availability, endocrine signalling)
    - The combined input from all signals determines whether the levels of a specific cyclin reach the threshold needed for a cell to pass through the checkpoint
      - This ensures that cyclins reach threshold levels only when progressing through the cell cycle is safe and supported by the environment
  - Cyclins are inactive on their own so they bind to **cyclin-dependent kinases (CDKs)** in order to phosphorylate and activate **target proteins** necessary for that specific cell cycle phase

D2.1.16—Consequences of mutations in genes that control the cell cycle

Include mutations in proto-oncogenes that convert them to oncogenes and mutations in tumour suppressor genes, resulting in uncontrolled cell division.

- Mutations in genes that control the cell cycle lead to uncontrolled cell division
  - **Proto-oncogenes** are genes that promote cell proliferation & progression through the cell cycle
    - **Gain-of-function mutations** convert these genes into **oncogenes**, which cause them to become overactivated & thus promote uncontrolled cell division
  - **Tumour suppressor genes** slow down cell division & promote cell death if needed
    - **Loss-of-function mutations** in these genes prevent them from carrying out their inhibitory role on cell proliferation, resulting in uncontrolled cell division

D2.1.17—Differences between tumours in rates of cell division and growth and in the capacity for metastasis and invasion of neighbouring tissue
Include the terms “benign”, “malignant”, “primary tumour” and “secondary tumour”, and distinguish between tumours that do and do not cause cancer. **Application of skills**: Students should observe populations of cells to determine the mitotic index.

• **Tumours** are groups of cells that divide uncontrollably due to dysregulation of the cell cycle
  • **Benign (non-cancerous) tumours** do not invade other unrelated tissues or organs of the body but can continue to grow in size abnormally
  • **Malignant (cancerous) tumours** invade other tissues of the body
  • **Primary tumours** are groups of cancer cells at the original site where cancer first developed
  • **Secondary tumours** are groups of cancer cells that have **metastasized**; spread to other body parts (by blood or lymph)
• There are differences between tumours in rates of cell division and growth and in the capacity for metastasis and invasion of neighbouring tissue
  • Influenced by the acquired mutations, epigenetic changes, and the tumour microenvironment
• **Mitotic index** is the ratio between the number of cells in a population undergoing mitosis to the total number of cells in a population
  • It is a useful measure of cell proliferation that can be used to determine the rate of tumor growth & efficacy of cancer drugs

Linking questions

• What processes support the growth of organisms?

• How does the variation produced by sexual reproduction contribute to evolution?

Review questions

SL and HL

- Define chiasmata. [1]
- Explain why cytokinesis occurs after nuclear division. [1]
- Explain how Down syndrome occurs. [2]
- Describe the changes in chromosome number during meiosis. [3]
- Distinguish between a chromosome, a chromatid, and a homologous pair. [3]
- Explain how crossing over generates genetic diversity. [3]
- Explain how errors in meiosis can change the karyotype of an individual. [3]
- Explain how meiosis generates genetic diversity. [4]
- Discuss the importance of cell proliferation in living organisms. [4]
- Distinguish between equal and unequal cytokinesis using **one** example of each. [4]
- Compare and contrast animal and plant cytokinesis. [5]
- Describe the phases of mitosis. [8]
- Compare and contrast mitosis and meiosis. [8]
- Describe the phases of meiosis. [8]

Additional Higher Level

- Distinguish between primary and secondary tumors. [1]
- State **two** ways primary tumors can metastasize to other body tissues. [1]
- Distinguish between benign and malignant tumors. [1]
- Explain how cyclin-dependent kinases regulate the cell cycle. [2]
- Explain why the increase and decrease in cyclin levels throughout the cell cycle is an important feature of their regulatory function. [2]
- Describe the role of checkpoints in regulating the cell cycle. [4]
- Explain how mutations in genes that control cell cycle increase the risk of developing cancer. [4]
- Vincristine is a cancer drug that inhibits the formation of spindle fibers in cells. Explain why vincristine is an effective drug for eliminating malignant tumors. [4]
- Explain how cyclins regulate the cell cycle. [4]
- Explain why interphase is a metabolically active period in the cell cycle. [4]

References

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