Chapter 12  The Cell Cycle
Rudolf Virchow-1855

“Omnis cellula e cellula”
Every cell from a cell.
In this chapter we will learn how cells reproduce to form genetically equivalent daughter cells.
Chapter Note

• Most of this chapter’s content should have been in your Biology class and will be review.

• Result – we will move rapidly through this material.
Roles of Cell Division

- Reproduction
- Growth
- Repair
- In all cases, cell division must distribute identical genetic material to two daughter cells.
Genome

- The cell's hereditary endowment of DNA.
- Usually packaged into chromosomes for manageability.
Chromosomes

• Made of a DNA and protein complex called **Chromatin**.

• During cell division, the chromatin becomes highly condensed into the chromosomes.
Chromosomes
Chromosomes - Structure

- At cell division, each chromosome has been duplicated.
- The duplicated chromosome consists of two sister chromatids.
Centromere

- The point where two sister chromatids are connected.

Comment - other chromosome structures will be discussed in future chapters.
Goal of cell division

• To split the sister chromatids and give one to each new cell.
Cell Cycle - parts

1. Interphase - (90% of cycle) - when the cell grows and duplicates the chromosomes.
2. Mitotic Phase (M) - when the chromosomes are split into separate cells.
Interphase
Interphase - parts

- G1 - first gap
- S - synthesis
- G2 - second gap
G1

- Cell grows and carries out regular biochemical functions.
When the DNA is replicated or synthesized. Chromosomes are replicated.
G2

- Cell completes preparations for division.
- Note - a cell can complete S, but fail to enter G2.
Mitotic Phase - parts

1. Mitosis - division of replicated chromosomes and nucleus.
2. Cytokinesis - division of the cell’s cytoplasm.
Mitosis - Purpose

• To divide the 2 copies of the DNA equally.
• To separate the sister chromatids into separate cells.
Mitosis Steps

• Prophase
• Prometaphase
• Metaphase
• Anaphase
• Telophase
Prophase
Prophase

- Nucleoli disappear.
- Chromatin condenses into the chromosomes.
- Centrioles separate to opposite ends of the cell.
- Mitotic spindle begins to form.
Prometaphase
Prometaphase

• Nuclear envelope dissolves.
• Spindle fibers join with the kinetochore of the centromeres.
Metaphase
Metaphase

• Centrioles now at opposite ends of the cell.
• Chromosomes line up on the metaphase plate.
• Spindle apparatus fully developed.
Anaphase
Anaphase

- Centromeres break and the duplicate chromosomes are pulled away from each other toward opposite ends of the cell.
- Cell elongates; poles move slightly further apart.
Kinetochores

• Specialized regions of the centromeres where spindle microtubules attach.
Kinetochores

- Structure on the chromosome
- Appear to “ratchet” the chromosome down the spindle fiber microtubule with a motor protein.
- Microtubules dissolve behind the kinetochore.
(a) Hypothesis

(b) Experiment
Telophase
Telophase

- Chromosomes uncoil back to chromatin.
- Nuclear envelope reforms.
- Nucleoli reappear.
- Spindle fibers disappear.
- Cytokinesis usually starts.
Cytokinesis

(a) Cleavage of an animal cell

- Cleavage furrow
- Contracting ring of microfilaments
- Daughter cells

(b) Cell plate formation in a plant cell

- Nucleus of daughter cell
- Wall of parent cell
- Vesicles forming cell plate
- New cell wall
- Daughter cells
Cytokinesis - Animal

- Cleavage furrow forms.
- Microfilaments contracts and divides the cytoplasm into two parts.
Cytokinesis - Plants

- Cell plate develops from Golgi vesicles.
- New cell wall developed around the cell plate.
Plant Cell - Mitosis
Evolution of Mitosis

<table>
<thead>
<tr>
<th>Hypothetical sequence</th>
<th>Evidence from modern organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(a) Prokaryotes</td>
</tr>
<tr>
<td>Bacterial chromosome</td>
<td></td>
</tr>
</tbody>
</table>

|                       | (b) Dinoflagellates            |
| Chromosomes           |                               |
| Microtubules          |                               |
| Intact nuclear envelope |                            |

|                       | (c) Diatoms                    |
| Kinetochore microtubules |                           |
| Intact nuclear envelope |                            |

|                       | (d) Most eukaryotes            |
| Kinetochore microtubules |                     |
| Centrosome              |                                |
| Fragments of nuclear envelope |                 |
Regulation of Cell Division

• Must be controlled.
• Rate of cell division depends on the cell type.
  – Ex - skin: frequently
  – liver - as needed
  – brain - rarely or never
Checkpoints

• A critical control point in the cell cycle.
• Several are known.
• Cells must receive a “go-ahead” signal before proceeding to the next phase.
G1 Checkpoint

- Also called the “restriction point” in mammalian cells.
- Places cells in a non-dividing phase called the $G_0$ phase.
- Most important checkpoint according to some.
(a) Cell receives a go-ahead signal

(b) Cell does not receive a go-ahead signal
\( G_0 \) Phase

- Non-dividing state.
- Most cells are in this state.
- Some cells can be reactivated back into M phase from the \( G_0 \) phase.
Protein Kinase Checkpoint - G2

- Uses protein kinases to signal “go-ahead” for the G2 phase.
- Activated by a protein complex whose concentration changes over the cell cycle.
MPF

• **M-phase Promoting Factor.**
• Protein complex required for a cell to progress from G2 to Mitosis.
• Role of MPF - to trigger a chain of protein kinase activations.
Active MPF has:

1. Cdk
2. Cyclin
CDK

- Protein Kinase.
- Amount remains constant during cycle.
- Inactive unless bound with cyclin.
(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle
Cyclin

- Protein whose concentration builds up over G1, S and G2.
- When enough cyclin is present, active MPF is formed.
(b) Molecular mechanisms that help regulate the cell cycle
Active MPF

• Triggers Mitosis.
• Activates a cyclin-degrading enzyme, which lowers the amount of cyclin in the cell.
• Result - no active MPF to trigger another mitosis until the cycle is repeated.
(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle

(b) Molecular mechanisms that help regulate the cell cycle

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Growth Factors

• External signals that affect mitosis.
• Examples:
  – PDGF
  – Density-dependent inhibition
  – Anchorage dependence
PDGF

• Platelet-Derived Growth Factor.
• Stimulates cell division to heal injuries.
1. Cut up a sample of connective tissue into small pieces.
2. Obtain suspension of free fibroblast cells by using enzymes to digest extracellular matrix.
3. Transfer cells to sterile culture vessels. The cells adhere to the glass. Incubate at 37°C.

Using cell culture to demonstrate the effect of a growth factor.

SEM of cultured fibroblasts

In basic growth medium plus PDGF, cells proliferate.

In basic growth medium, cells fail to divide.
Density-Dependent Inhibition

• The number of cells in an area force competition for nutrients, space, and growth factors.
Density-Dependent Inhibition

- When density is high - no cell division.
- When density is low - cells divide.
Cells anchor to dish surface and divide (anchorage dependence).

When cells have formed a complete single layer, they stop dividing (density-dependent inhibition).

If some cells are scraped away, the remaining cells divide to fill the gap and then stop (density-dependent inhibition).

(a) Normal mammalian cells

Cancer cells do not exhibit anchorage dependence or density-dependent inhibition.

(b) Cancer cells
Anchorage Dependence

- Inhibition of cell division unless the cell is attached to a substratum.
- Prevents cells from dividing and floating off in the body.
Cancer Cells

• Do not stop dividing. The control mechanisms for cell division have failed.
1. A tumor grows from a single cancer cell.
2. Cancer cells invade neighboring tissue.
3. Cancer cells spread through lymph and blood vessels to other parts of the body.
Comment

• Regulation of cell division is a balance between:
  Mitosis - making new cells.
  Apoptosis - cell suicide or death
• Cancer can result if either process doesn’t work.
Summary

• Know the phases and steps of the cell cycle.
• Be able to discuss the “regulation” of the cell cycle.