لجنة الصيدلة

رايةٌ للخير وفارسٌ لن يترجّل

ALQUSOUR ACADEMY

أكاديمية القصور

لجنة الصدلة

BIOLOGY

103

Subject

Second Exam - Chapter Twelve

تحذير: محاضراتنا (الملخصات) متوفرة فقط لدى:
1) أكاديمية القصور بفروعها. 2) جمعية التصوير الطبية (مفرج التمريض).

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The Cell Cycle

-The cell division process is an integral part of the cell cycle and results in genetically identical daughter cells

-Roles of Cell Division

1. Reproduction (formation of gametes): the continuity of life

2. Repair: replace dead cells (renewal)

3. Growth: increase in size from single cell to fully grown organism.

-Unicellular organism depends on cell division for Reproduction (Asexual reproduction)

-Multicellular organisms (plant, animals) depend on cell division for development, growth, and repair

-Cells duplicate their genetic material before they divide, to make sure that each daughter cell receives exact copy [identical] of the genetic material (DNA), so DNA is passed from generation to generation without dilution

مستمرون بالعطاء

Cellular Organization of the Genetic Material

-**Genome:** the total DNA content in cells

-**Prokaryotic genome** is a single long DNA molecule, while **eukaryotic genome** is a many DNA molecules (Human cell: 2m DNA, 250,000x cell diameter).

-The DNA is packaged into chromosomes (**chroma:** color; **soma:** body), so named as it takes up certain dyes used in microscopy.

-Each chromosome is a long linear DNA molecule, consisting of hundreds and thousands of genes.

-Eukaryotic chromosomes consist of chromatin, which is a complex of DNA and protein that condenses during cell division.

-In animals there are 2 types of cells:

1. **Somatic cells:** have two sets of chromosomes; (human cells have 46 chromosomes).
2. **Reproductive cells (gametes):** have one set of chromosomes; (human gametes, sperm and egg, have 23 chromosomes).

Distribution of Chromosomes during Cell Division

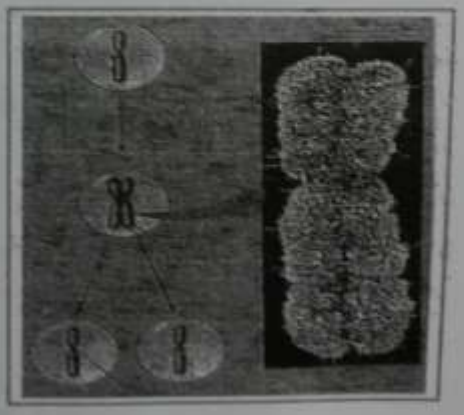
In Preparation for Cell Division:

-DNA is duplicated and the chromosomes condense.

-Each chromatin becomes densely coiled & folded, making chromosome much shorter and so thick, and can be seen with light microscope.

-Each duplicated chromosome has two sister chromatides, each containing identical copies of DNA.

-The chromosome has a narrow "waist" region called centromere (where the two chromatids attached)



Eukaryotic Cell Division

1. **Mitosis:** the division of the nucleus.
2. **Cytokinesis:** the division of the cytoplasm.

So we end with two daughter cells, each one contains identical genetic material to the parent cell.

-**Meiosis** is a division of cells in gonads (ovary\testis) to produce sex (eggs or sperm)to produce non identical daughter cells that have only one set of chromosomes(half the number of parent cell, in human, from 46 to 23).

-**Fertilization:** joining of the two gametes together & return the chromosome number to 46.

The Human Life Cycle

Sperm, egg (gametes, 23 chromosomes) → fertilization → fertilized egg (zygote, 46 chromosome) → mitosis → multicelluar organism → meiosis in gonads → gametes

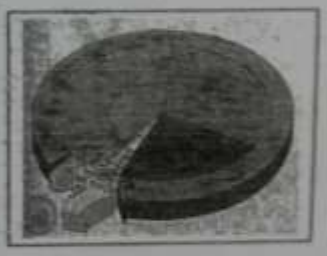
Phases of the Cell Cycle

-The mitosis is just one part of the cell cycle, the cell cycle consists of:

1. **Interphase:** longest part of cell cycle (90% of the cell cycle) in which cell grows, copies its chromosomes and preparing for division.

2. **Mitotic phase (M phase):** mitosis & cytokinesis, the shortest part of the cell cycle.

1. Interphase:



-During interphase, cell grows, produces proteins, organelles.

-Consists of:

a. **G1 phase (first gap):** growth of the cell.

b. **S phase** (DNA synthesis): duplication of chromosomes.

c. **G2 phase (second gap):** complete preparation for cell division (more growth).

2. The Mitotic Phase (mitosis and cytokinesis):

-Mitosis is divided into 5 sub-phases:

1. Prophase **2. Prometaphase** **3. Metaphase** **4. Anaphase** **5. Telophase**

Late Interphase (G2 of interphase):

-Nucleus is surrounded by the nuclear envelope with one or more Nucleoli.

-Two centrosomes (formed by duplication of single centrosome).

-Microtubules extended from the centrosomes in radial arrays called asters.

-Chromosomes are duplicated but can't be distinguished individually.

1. Prophase: changes in cytoplasm and in the nucleus

-Condensation of chromatin; into chromosomes seen by light Microscope (2 sister chromatids), and nucleoli disappears.

-Spindle begin to form, they are made from microtubules extending from the two centrosomes move away from each other by lengthening microtubules between them.

-Spindle: made of microtubules (MT) & proteins, when it assembles, MT of cytoskeleton partially disassemble into tubulin, to provide the material to construct the spindle.

2. Prometaphase:

-Nuclear envelope fragments

-Spindles can now invade the nuclear area and interact with Chromosomes.

-More condensed chromosomes.

-Kinetochores: specilized structure made of proteins & sections of chromosomal DNA at the centromere, and each chromatid has one kinetochore.

-Kinetochore MT: the microtubules that attach to the kinetochores.

-Nonkinetochore MTS interact from opposite poles.

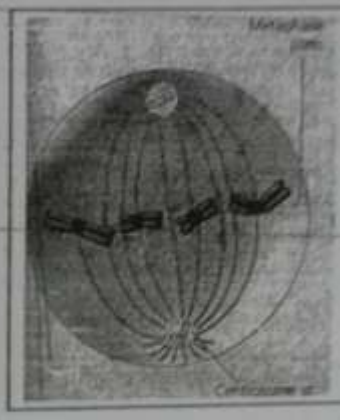
3. Metaphase: Longest stage, 20min

-Centrosome at opposite poles.

-Kinetochores are attached to microtubules coming from opposite Poles.

-Metaphase plate: an imaginary plane that is equidistant between the spindle's two poles.

-The centromeres of the chromosomes are all on the metaphse plate.



4. Anaphase: Shortest stage, few min

-Paired kinetchores of each chromosomes separate.

-The two sister chromatids separate, and each chromatid becomes a full fledged chromsome

-Kinetochore MT shorten by depolymerising at their kinetochores ends, so the two librated chromosomes moved toward opposite poles.

-The non kinetochore lengthen and the cell elongates

- Now each chromatid is condsidered full chromosome, so at each pole of the cell there is a complete collection of chromosomes

5. Telophase: Reversal of prophase and prometaphase

- 2 daughter nuclei form
- Spindles disaapeare
- Nuclear envelope reformation from fragments of parents cell's nuclear envelope and the endomembranous system
- The chromatin becomes less tightly coiled
- Nucleolus starts to appear

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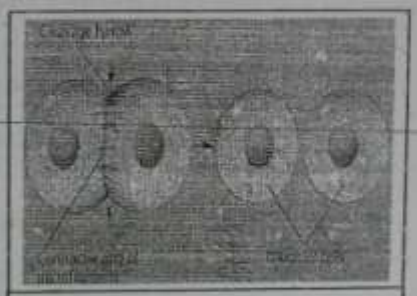
Cytokinesis

The division of the cytoplasm is usually well underway by late telophase, so the two daughter cells appear shortly after the end of mitosis

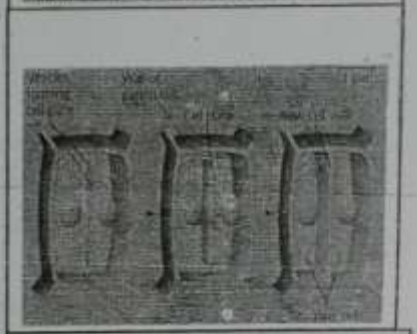


1. In animal cells cytokinesis occurs by cleavage:

-First sign is the cleavage furrow beginning as a groove in cell surface near old metaphase plate.

-On cytoplasmic side of furrow: contractile ring of actin microfilament associated with myosin (muscle contraction).

-Microfilament ring contracts & groove deepens until The parent cell is pinched in two



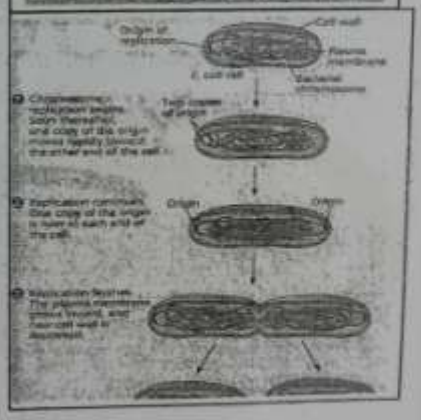
2. In plant cells cytokinesis occurs by cell plate:

-During telophase, vesicles from golgi apparatus move along MT to the middle of the cell.

-The vesicles coalesce to form cell plate (Cell wall materials collect in cell plate).

-Cell plate enlarges until it fuses with the cell membrane.

-New cell wall forms between the 2 daughter cells



Prokaryotic Cell Division (Bacteria)

- Reproduce by a type of cell division called **binary fission** (dividing in half), asexual reproduction

-Most genes are carried on single chromosome, which consists of circular DNA associated with proteins.

-E. coli chromosome is 500 x longer than cell (highly folded), and it's attached to plasma membrane.

-In binary fission:

1. The bacterial chromosome replicates
2. The two daughter chromosomes actively move apart

-There is a hypothesis proposed that mitosis in eukaryotes have been evolved from binary fission in bacteria with an intermediate stages as in algae.

Bacteria (prokaryotes) → dinoflagellate (unicellular algae) → diatoms (unicellular algae) → eukaryotes

-In bacteria, elongation of cell separates the chromosome.

-In dinoflagellates, nuclear envelope remains intact, and microtubules from cytoplasm passed through the nuclear envelope.

-In diatoms, nuclear envelope remains intact, microtubules within nucleus.

-In eukaryotes, the spindle from outside the nucleus, the nuclear envelope breaks down during mitosis.

Control System of Cell Cycle

-The timing and rate of cell division is crucial to normal growth, development, and Maintenance.

-The sequential events of the cell cycle are directed by a distinct cell cycle control system, which is similar to a clock.

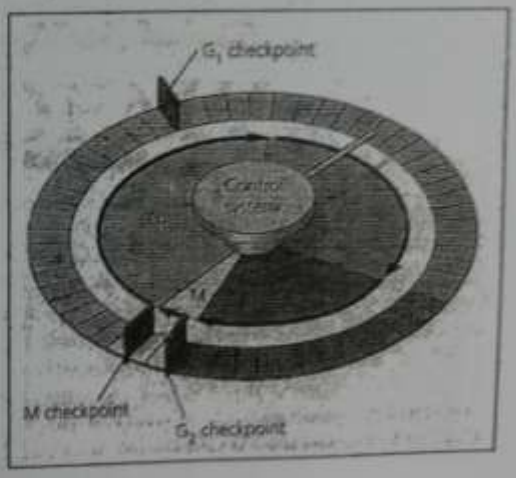
-The clock has specific checkpoints, where the cell cycle stops until a go ahead signal is received.

Cell Cycle Checkpoints

-There is a critical control points where stop and go ahead signals regulate the cell cycle

-In animal cell signals stop cycle at checkpoints until overridden by go-ahead signal

-Signals come from cell surveillance mechanisms check to see if all processes up to that point is completed correctly: **if yes, cell cycle proceeds, but if no, cell cycle stops**



-3 Major checkpoints:

a. G1 checkpoint: restriction point (most important)

-If go ahead at G1, cell completes cycle & divides.

-If no go-ahead signal, cell exits cycle to the **non-dividing state (Go phase)**

-Nerve & muscle cells never divide so they are always in Go (permanently arrested)

-Liver return to cycle by growth factors during injury.

b. G2 checkpoint: mitosis checkpoint

c. M checkpoint: spindle assembly checkpoint, immediately before anaphase

The Cell Cycle Clock:

1. Cyclin-Cyclin Dependent Kinases (cdk)

-2 types of regulatory proteins involved in cell cycle control, **Cyclins and cyclin-dependent kinases (Cdks)**

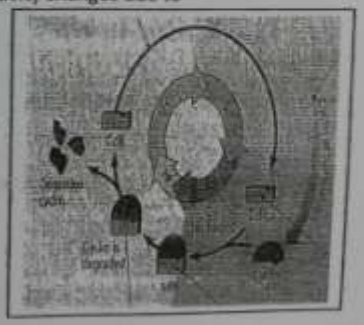
-Called cyclin dependent kinases (cdks) because they will remain inactive until they associated with cyclins.

-**Protein kinase:** activate/inactivate other proteins by phsphorylating them, and particular protein kinases gives go-ahead signal at G1 & G2 checkpoints

-Kinases that drive cell cycle:

1. Present at constant concentration in growing cell but its activity changes due to change in cyclin concentrations.

2. Must be linked to cyclin to become active.



-**Cyclins** changes in concentration cyclically, and the activity of cyclines and cdks fluctuates during cell cycle.

Maturation Promoting Factor (MPF)

-1st cyclin-cdk complex discovered

-Triggers passage past **G2 checkpoint to M phase**

-Cyclins accumulate during G2 and associate with cdk and falls down during M phase
-As MPF complex has been formed, it **initiates mitosis by phosphorylation** of different proteins taking part in mitosis

-MPF acts:

a. Directly: causes phosphorylation of various proteins of nuclear lamina (NL) causing nuclear envelope to fragment

b. Indirectly: activating other kinases, and contributes to events needed for chromosome condensation and spindle formation during prophase

-Later in M phase (during anaphase), MPF helps switch itself off by initiating a process leading to destruction of its cyclin by special enzymes

-Kinase activity restored by association with new cyclin synthesized during S and G2 phases of next round of cycle

-At **G1 checkpoint** there are at least 3 cdk proteins and several cyclins.

2. Internal and External Signals at the Checkpoints

-Both internal and external signals control the all cycle checkpoints

Internal Signals (kinetochores)

-At anaphase chromatid separation begins when all chromosomes are attached to spindle at metaphase

-**M-phase checkpoint** ensures that daughter cells don't end up with missing or extra chromosomes

-Kinetochores not yet attached to spindle MT send molecular signal that causes sister chromatids to remain together, delaying anaphase, by keeping the **anaphase-promoting complex (APC) inactive**

-When all kinetocheres are attached to spindles, the APC become active, so the sister chromatids separate by inactivation of proteins hooking them together.

External Signals

a. Chemical Signals (Growth Factors)

-Cells don't divide if growth factor (GF) is not present

-GF: proteins released by certain body cells which stimulates other to divide

Platelet-derived GF (PDGF) from platelets

-Necessary for division of fibroblasts (type of connective tissue cells)

-Fibroblasts have PDGF receptors on their plasma membrane

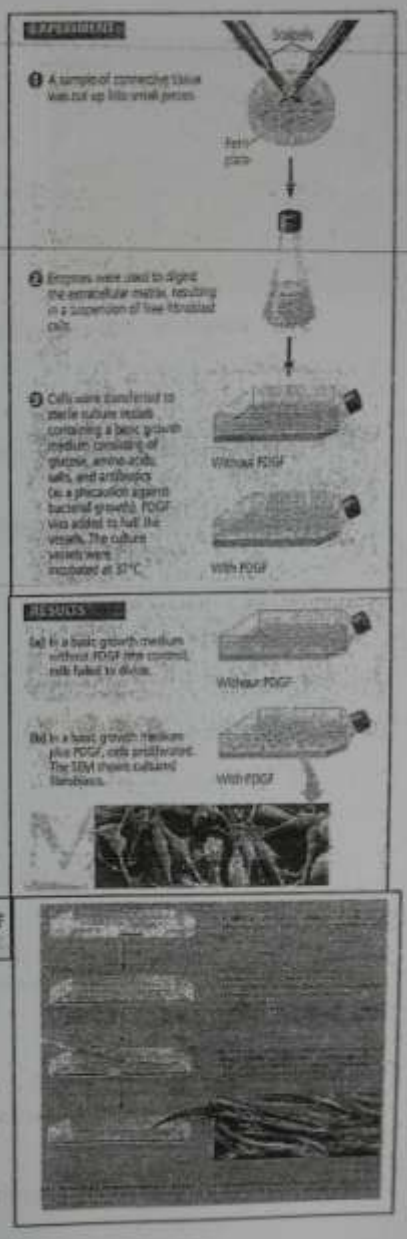
-Binding of PDGF to receptors triggers signal-transduction pathway that allow cell to pass G1 checkpoint and divide.

-PDGF stimulates fibroblast division in animals' body as well as cell culture.

-On injury platelets release PDGF, fibroblasts grow and heal the wound.

-Different GF discovered, each cell type respond to GF or combination of different GFs.

-At least 50 different growth factors have been discovered.



CONCLUSION This experiment confirmed that PDGF stimulates the division of human fibroblast cells in culture.

b. Physical Signals:

1. Density Dependent Inhibition of Cell Division

-Cells grown in vitro stop dividing if they contact another cell, high cell numbers = low amounts of Growth factors & nutrients

-In density-depentent inhibition, crowded cells stop dividing

2. Anchorage Dependence

-Seen in most animal cells

-Cells to divide must be attached to a substratum (Culture dish/ECM of tissue.

-Anchorage: signaled to cell cycle control system via pathways involving membrane proteins & elements of cytoskeleton linked to them.

-Cancer cells exhibit neither density-dependent inhibition nor anchorage dependence.

Cancer Cells

-Have escaped from cell cycle controls as they don't respond normally to control mechanisms.

-Divide excessively, and don't show density dependent inhibition.

-They don't stop dividing when GF are depleted.

Hypothesis: Cancer Cells

a. May make a required GF themselves.

b. May have an abnormality in signaling pathway that conveys GFs signal to cell' cycle control system even in the absence of that factor.

C. Cell cycle control system is abnormal.

-Cancer cells may stop dividing but do so at random points, not the normal Checkpoints.

-In culture they are immortal (if nutrients are present), while nearly all normal mammalian cells growing in culture divide 20-50 time, stop dividing, increase in age, and die.

Loss of Cell Cycle Controls in Cancer Cells

-The problem begin when a single cell in tissue undergoes transformation (converted to cancer cell).

-Body's immune system destroys cancer cell but if it escapes, it will form tumor (mass of abnormal cells).

a. **Benign Tumor:** remains at original site.

b. **Malignant Tumor:** moves, invades other sites, and impairs function of one or more organs.

-Cell of malignant tumor undergo excessive proliferation, may have unusual number of chromosomes and metabolism is deranged, so cells stop function in constructive way.

-**Metastasis:** malignant tumors invade surrounding tissues and form more tumors

-**How does it happen?**

1. Cancerous cells will have abnormal changes in cell surface.
2. Lose attachment to neighboring cell & ECM.
3. Go to blood and lymph vessels.
4. Spread into nearby tissue, invade other parts of body, and form more tumors (Secondary tumors).

Cancer Treatment

1. **Ionizing Radiation:** high energy radiation damages DNA in cancer cells more than in normal, because cancer cells cannot repair damage while normal can.

2. **Chemotherapy:** using drugs toxic to actively dividing cells(Drugs interfere with steps in cell cycle).

-**Taxol** freezes mitotic spindle by stopping MT depolymerization ; cannot go past Metaphase.

-**Side Effects:**

1. **Nausea:** effect of drugs on intestinal cells
2. **Hair loss:** effect on hair follicle cells
3. **Susceptibility to infection:** effect on immune system cells
4. **Infertility:** effect on sperms

Sample Questions

1. The function of the cell cycle is to produce daughter cells that _____.

a) are genetically identical to the parent cell.

b) have the same number of chromosomes as the parent cell but not the same genetic content.

c) have a random assortment of maternal and paternal chromosomes.

d) have the same number of chromatids as the parent cell had chromosomes.

e) none of the above.

2. Sister chromatids _____.

a) are created when DNA is replicated

b) are attached at the centromere prior to division

c) are separated during mitosis

d) have matching copies of the chromosome's DNA

e) all of the above

3. The complex of DNA and protein that makes up a eukaryotic chromosome is properly called _____.

a) a chromatid

b) a chloroplast

c) chromatin

d) a chromoplast

e) a centrosome

4. The region of a chromosome holding the two double strands of replicated DNA together is called _____.

a) chromatin

b) a centriole

c) a centromere

d) a chromatid

e) an aster

5. If an intestinal cell in a grasshopper contains 24 chromosomes, a grasshopper sperm cell would contain _____ chromosomes.

a) 3

b) 6

c) 12

d) 24

e) 48

Question Answers

Question	Answer
1	a) Are genetically identical to the parent cell.
2	e) All of the above
3	c) Chromatin
4	c) A centromere
5	c) 12