**Cell Cycle Notes Guide:**

**Concept: Most cell division results in genetically identical daughter cells**

Function of cell division

-making new cells

-continuity of life

-asexual reproduction

-unicellular organisms

-growth

-repair & renew

Cell Cycle: life of a cell from origin to division into 2 new daughter cells

Cell Division in Prokaryotes

-Prokaryotes are single celled organisms without a nucleus. Their genetic material is arranged in a single circular chromosome of DNA, which is anchored to the cell membrane.

-As in eukaryotes, the genetic material of prokaryotes is duplicated before division. However, instead of entering into a complex cycle for cell division, prokaryotes simply elongate until they are double their original size.

-At this point, the cell pinches in and separates into two identical daughter cells in a process known as \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ fission.

Making new cells (eukaryotic cells)

Nucleus with chromosomes and DNA

Cytoskeleton using centrioles (in animals) and microtubule spindle fibers

Function of Nucleus:

-protects \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (genetic information)

-All the cell’s DNA is its genome

Structure of Nucleus:

-nuclear \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

-double membrane

-membrane fused in spots to create \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

-allows large macromolecules to pass through

Function of Cytoskeleton

-Provide structural support that maintains shape of cell and provides anchorage for organelles with protein fibers such as microfilaments, intermediate filaments, \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

-motility for cell locomotion, using cilia and flagella etc

-regulation of organizes structures & activities of cell

Centrioles aid in cell division in animal cells, using a \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ of centrioles, organize microtubules called spindle fibers. Also, centrioles also aid to guide chromosomes in mitosis

What is passed on to daughter cells? An exact copy of genetic material = DNA through mitosis

division of organelles & cytoplasm through cytokinesis

-Eukaryotic cells have chromosomes in their nuclei. Example: Humans have 46 chromosomes in \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ cells (body cells). These cells are diploid meaning there are 2 sets of similar chromosomes in each cell. They divide through a process called \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

Mitosis is the division of the cell’s nucleus. It may be followed by cytokinesis, the division of the cell’s organelles and cytoplasm.

Gametes -sperm and \_\_\_\_\_\_\_\_\_\_\_ cells- are haploid and have half the number of chromosomes of the diploid cells. Example: Humans have 23 chromosomes in each gamete. They divide through a process called \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

**Concept: The mitotic phase alternates with interphase in the cell cycle**

**Interphase**: 90% of cell life cycle in which the cell doing its “everyday job”. Cells produce RNA, synthesize proteins/enzymes and prepares for duplication if triggered

-Divided into 3 phases:

--G1 = 1st Gap includes the cell doing its “everyday job” and cell grows in size

--S = DNA Synthesis in which it copies chromosomes

--G2 = 2nd Gap includes preparing for division and the cell grows (more). Also it produces organelles, proteins, membranes

Nucleus well-defined where DNA loosely packed in long chromatin fibers and prepares for mitosis by replicating chromosome (DNA & proteins). Also produces proteins & organelles

Copying / Replicating DNA occurs in the synthesis phase of Interphase where dividing cell replicates \_\_\_\_\_\_\_

It must separate DNA copies correctly to 2 daughter cells. In human cell duplicates ~3 meters DNA. Each daughter cell gets complete identical copy

error rate = ~1 per 100 million bases

There are 3 billion base pairs in mammalian \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

There are ~30 errors per cell cycle. These mutations (to somatic cells) don’t get passed down to offspring.

DNA is organized in \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. Double helix DNA molecule is wrapped around histone proteins (like thread on spools). This DNA-protein complex =\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (organized into long thin fiber). It is further condensed further during mitosis into chromosomes.

Mitosis is the Dividing cell’s DNA between 2 daughter nuclei called the “dance of the chromosomes”

Includes 4 phases: prophase, metaphase, anaphase, telophase

**Prophase:**

-Chromatin condenses into visible chromosomes made of chromatids

-\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ move to opposite poles of cell (in animal cell)

-Protein fibers cross cell to form mitotic spindle made of microtubules

-actin, myosin

-coordinates movement of chromosomes

-Nucleolus disappears

-Nuclear membrane breaks down

Transition to Metaphase

**Prometaphase**

-spindle fibers attach to centromeres creating kinetochores

microtubules attach at \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ and connect centromeres to centrioles

chromosomes begin moving

**Metaphase**: Chromosomes align along middle of cell and form “metaphase \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_”

meta = middle

-spindle fibers coordinate movement

-helps to ensure chromosomes separate properly

-Each new nucleus receives only 1 copy of each chromosome

**Anaphase**

-Sister chromatids separate at kinetochores and move to opposite poles. They are pulled at centromeres. Each is pulled by motor proteins “walking” along microtubules by actin, myosin protein filaments. There is an increased production of ATP by mitochondria

-Poles move farther apart as the polar microtubules lengthen

Separation of chromatids

In anaphase, proteins holding together sister chromatids are inactivated. They separate to become individual chromosomes

Chromosome movement: Kinetochores use motor proteins that “walk” chromosome along attached microtubule. The microtubule shortens by dismantling at kinetochore (chromosome) end

**Telophase**

Chromosomes arrive at opposite poles where daughter nuclei form. Nucleoli form and the chromosomes disperse into DNA strands. The spindle fibers disperse and \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ begins cell division

**Cytokinesis**

In animals, constriction belt of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ microfilaments around equator of cell. A cleavage furrow forms and splits cell in two. Just like tightening a draw string

Cytokinesis in Plants: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ forms where vesicles line up at equator (derived from Golgi). Vesicles fuse to form 2 cell membranes and new cell wall laid down between membranes. New cell wall fuses with existing cell wall

Evolution of mitosis

Mitosis in eukaryotes likely evolved from binary fission in bacteria. Bacteria have single circular chromosome and no membrane-bound organelles

Evolution of mitosis: A possible progression of mechanisms intermediate between binary fission & mitosis seen in modern organisms

**Concept: The eukaryotic cell cycle is regulated by a molecular control system**

**Regulation of Cell Division**

A multicellular organism needs to coordinate cell division across different tissues & organs. It is critical for normal growth, development & maintenance. Coordination of timing of cell division, coordination of rates of   
cell division, and understanding that not all cells can have the same cell \_\_\_\_\_\_\_\_\_\_\_\_ frequency of cell division.

-Frequency of cell division varies by cell type

-An embryo goes through the cell cycle < 20 minute

-skin cells: divide frequently throughout life in 12-24 hours cycle

-liver cells: retain ability to divide, but keep it in reserve. They divide once every year or two

-mature nerve cells & muscle cells: do not divide at all after maturity. Permanently in G0

Overview of Cell Cycle Control

-Two **irreversible** points in cell cycle

-replication of genetic material

-separation of sister chromatids

-\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

-process is assessed & possibly halted

Checkpoint control system

-Checkpoints

-cell cycle controlled by STOP & GO chemical signals at critical points

-signals indicate if key cellular processes have been completed correctly

3 major checkpoints:

-G1/S: can DNA synthesis begin?

-G2/M: -has DNA synthesis been completed correctly?

-commitment to mitosis

-­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ checkpoint

-are all chromosomes attached to spindle?

-can sister chromatids separate correctly?

G1/S checkpoint: Is most critical

-primary decision point

-“\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ point”

-if cell receives “GO” signal, it divides

-internal signals: cell growth (size), cell nutrition

-external signals: “growth factors”

-if cell does not receive signal, it exits cycle & switches to G0 phase

-non-dividing, working state

**G0 phase:** non-dividing, differentiated state and most human cells in G0 phase eg. Liver cells; in G0 but can be called back to cell cycle by external cues. Nerve and Muscle cells are highly specialized and arrested in G0 and can never divide.

**Activation of cell division**

-How do cells know when to divide?

-cell communication signals

-chemical signals in cytoplasm give cue

-signals usually mean \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

-activators

-inhibitors

“Go-ahead” signals

-Protein signals that promote cell growth & division

-internal signals eg. “promoting factors”

-external signals eg. “growth factors”

Primary mechanism of control

-phosphorylation

-kinase enzymes

-either activates or inactivates cell signals

**Cell cycle signals**

Cell cycle controls

-cyclins

-regulatory proteins

-levels cycle in the cell

Cdk’s: cyclin-dependent kinases

-phosphorylates cellular proteins

-activates or inactivates proteins

Cdk-cyclin complex: triggers passage through different stages of cell cycle

-Interaction of Cdk’s & different cyclins triggers the stages of the cell cycle

**-Cyclin & Cyclin-dependent kinases**

-CDKs & cyclin drive cell from one phase to next in cell cycle

-Proper regulation of cell cycle is so key to life the \_\_\_\_\_\_\_\_\_\_\_\_ for these regulatory proteins have been highly conserved through evolution.

-The genes are basically the same in yeast, insects, plants, and animals (including humans).

**External signals**

-Growth factors allow coordination between cell and allow protein signals released by body cells that stimulate other cells to divide

-density-dependent inhibition

-crowded cells stop dividing

-each cell binds a bit of growth factor

-not enough activator left to trigger division in any one cell

-\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ dependence

-to divide cells must be attached to a substrate

-“touch sensor” receptors

Example of a Growth Factor signal

-Platelet Derived Growth Factor (PDGF)

-made by platelets in blood clots

-binding of PDGF to cell receptors stimulates cell division in fibroblast (connective tissue)

-heal wounds

Growth Factors and Cancer

-Growth factors can create cancers

-proto-oncogenes

-normal growth factor genes that become oncogenes (cancer-causing) when mutated

-stimulates cell growth

-if switched “ON” can cause cancer

-example: RAS (activates cyclins)

-tumor-suppressor genes

-inhibits cell division

-if switched “OFF” can cause cancer

-example: p53

-Cancer is essentially a failure of cell division control

-unrestrained, uncontrolled cell growth

What control is lost? lose checkpoint \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

-gene p53 plays a key role in G1/S restriction point

-p53 protein halts cell division if it detects damaged DNA

-options:

-stimulates repair enzymes to fix DNA

-forces cell into G0 resting stage

-keeps cell in G1 arrest

-causes apoptosis of damaged cell

-ALL cancers have to shut down p53 activity

**Development of Cancer**

Cancer develops only after a cell experiences ~6 key mutations (“hits”)

-unlimited growth

-turn on growth promoter genes

-ignore checkpoints

-turn off tumor suppressor genes (p53)

-escape apoptosis

-turn off suicide genes

-immortality = unlimited divisions

-turn on chromosome maintenance genes

-promotes blood vessel growth

-turn on blood vessel growth genes

-overcome anchor & density dependence

-turn off touch-sensor gene

What causes these “hits”?

Mutations in cells can be triggered by UV radiation, chemical exposure, radiation exposure, heat, cigarette smoke, pollution, age, genetics.

**Tumors**

Mass of abnormal cells

-Benign tumor

-abnormal cells remain at original site as a lump

-p53 has halted cell divisions

-most do not cause serious problems & can be removed by surgery

-Malignant tumors: cells leave original site

-lose attachment to nearby cells

-carried by blood & lymph system to other tissues

-start more tumors = \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

-impair functions of organs throughout body

**Traditional treatments for cancers**

Treatments target rapidly dividing cells

-high-energy radiation: kills rapidly dividing cells

-chemotherapy

-stop DNA replication

-stop mitosis & cytokinesis

stop blood vessel growth

**New “miracle drugs”**

Drugs targeting proteins (enzymes) found only in cancer cells. Example : Gleevec: treatment for adult leukemia (CML) & stomach cancer (GIST. Became 1st successful drug targeting only cancer cells