

- Ability to reproduce = one characteristic of living things
- Continuity of life based on the reproduction of cells
- Cell division functions in reproduction, growth, and repair

UNICELLULAR ORGANISMS use cell division for reproduction

MULTICELLULAR ORGANISMS use cell division to:

- repair/renew cells that die from normal wear and tear
- grow and develop from a single fertilized egg (zygote)
- reproduce asexually (EX: plants grow by cuttings)
- Results in genetically identical daughter cells

- DNA molecules packaged into chromosomes

- **GENOME**= cell's genetic information

Prokaryotes genome - single circular loop of DNA

Eukaryotes - several DNA molecules in multiple chromosome bundles

- Every eukaryotic species has characteristic number of chromosomes in each cell nucleus

~Human **SOMATIC** cells (body cells) have 46 chromosomes (two sets of 23; one from each parent).

~Human **GAMETES** (sperm or eggs) have one set (23 chromosomes); $\frac{1}{2}$ number in somatic cells

- Eukaryotic chromosome

- made of **CHROMATIN** (DNA + associated proteins)

PROTEINS maintain shape and control gene activity

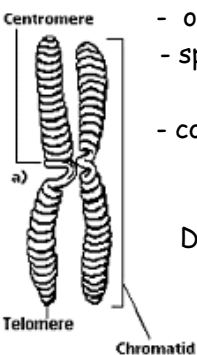
- one long, linear DNA made up of 100's-1000's of genes

- spread out as **CHROMATIN** in **NONDIVIDING** cells;

allows access to info

- condensed as **CHROMOSOMES** in **DIVIDING** cells;

allows easier transport



Duplicated chromosomes made up of:

- TWO IDENTICAL SISTER **CHROMATID** ARMS

- **TELOMERES**-region at ends of arms; prevent degradation

- Region where chromatids are most closely attached = **CENTROMERE**

- **KINETOCHORES**-proteins in centromere region where microtubules attach

- Once chromatids separate in anaphase ~ considered individual chromosomes

CELL CYCLE:

INTERPHASE = 90% of cell cycle

NON dividing phase

nuclear envelope/nucleoli are visible;

DNA spread out as **CHROMATIN**

Cell is "doing its job"

G₁ phase ("first gap")

grow by producing proteins and organelles;

S phase ("synthesis") - grow; copy DNA

G₂ phase ("second gap") grow;

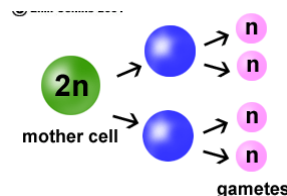
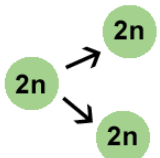
make molecules/organelles needed for cell

division

MITOSIS (in all body cells)

produces

TWO IDENTICAL
daughter nuclei (clones)



MEIOSIS in gonads

(ovaries or testes)

produces

FOUR

NONIDENTICAL
daughter cells with

$\frac{1}{2}$ the number of chromosomes

as parent cell

TYPICAL hours M and G_0 - cell stops dividing	EX: CENTROSOMES copied (Contains CENTRIOLES in ANIMAL cells) G_0 phase-cell leaves cycle; stops dividing Some cells can rejoin cycle with external cues (Liver divides when injured) Some cells never divide once mature (nerve,muscle)	HUMAN CELL might divide once every 24 phase < 1 hour S = 10-12 hours G_1 G_2 = rest of time G_1 most variable
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MITOTIC PHASE (M)- dividing phase includes

- MITOSIS-division of nucleus & CYTOKINESIS-division of cytoplasm

MITOSIS = continuum broken into 5 subphases;

PROPHASE

- chromatin becomes tightly coiled into chromosomes
- nucleoli disappear
- mitotic spindle begins to form
 - microtubules that extend from the centrosomes = ASTERS
- centrosomes move toward poles

PROMETAPHASE

- nuclear envelope fragments
- microtubules attach to centrosome at kinetochore proteins
- nonkinetochore fibers don't attach to chromosomes

METAPHASE

- longest dividing phase
- spindle fibers push chromosomes to line up along imaginary plane at equator =METAPHASE PLATE

ANAPHASE

- shortest dividing phase
- sister chromatids separate and move to opposite poles

TELOPHASE

- also called "reverse prophase"
- two daughter nuclei begin to reform
- nuclear envelope reforms
- chromosomes spread out as chromatin
- spindle/centrosomes disappear

CYTOKINESIS = cytoplasm splits

- usually underway in late telophase
- CLEAVAGE FURROW splits animal cells
 - ACTIN and MYOSIN proteins interact to contract ring
- CELL PLATE deposited by vesicles from Golgi divides plant cells; cell wall prevents "pinching"

HOW SPINDLE WORKS:

Assembled from elements of cytoskeleton

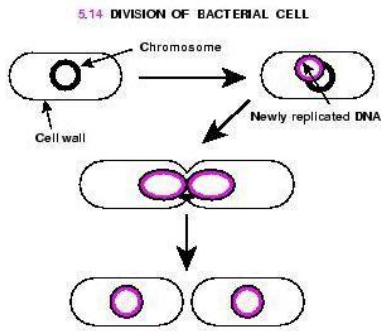
Fibers elongate by adding TUBULIN subunits

Assembly starts in CENTROsome= "microtubule organizing center"

Possible mechanisms:

- chromosomes are "reeled in" by the shortening of microtubules at the poles
- evidence suggests microtubules shorten at chromosome end as MOTOR PROTEINS on kinetochore "walk" chromosomes along microtubules toward poles
- MOTOR PROTEINS walk along nonkinetochore microtubules to lengthen/move them apart and elongate cell

BINARY FISSION- used by BACTERIA reproduce



- Chromosome = single, circular coiled loop
- Replication begins at one point = **ORIGIN OF REPLICATION** moves in both directions
- Cell elongates
- Plasma membrane grows inward
- Divides cell into 2 daughter cells with a complete genome
- No spindle or microtubules; several proteins play role

MITOSIS HAD ORIGINS IN BINARY FISSION:

- some proteins similar to eukaryotic proteins
- two of these related to tubulin and actin

Possible intermediate evolutionary steps:

Dinoflagellates-replicated chromosomes are attached to the nuclear envelope

Diatoms- the spindle develops within the nucleus

REGULATION OF CELL CYCLE

Timing crucial for normal growth, development, maintenance

Frequency varies with cell type

- some divide frequently (skin cells, blood cells)
- some can be induced to divide (liver cells)
- some don't divide after maturity (nerve, muscle cells)

Understanding mechanisms of regulation may explain cancer

Chemical signals in cytoplasm drive cycle

Cyclical molecules trigger and coordinate key events in the cell cycle

Cycle has a built-in clock, but also regulated by external/internal controls

Critical control point where stop and go signals regulate cycle = **CHECKPOINT**

Cell stops at checkpoint until surveillance mechanisms indicate key processes have been completed then stop signal is overridden

THREE MAJOR CHECK POINTS in the G_1 , G_2 , and M phases

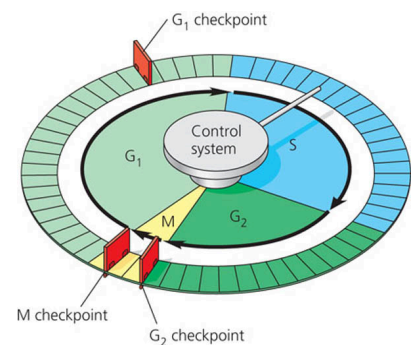
G_1 = "restriction point" is most important in mammalian cells

If gets go-ahead signal cell → cell copies its DNA & divides

If no signal-cell exits cycle → nondividing state = **G_0 phase**

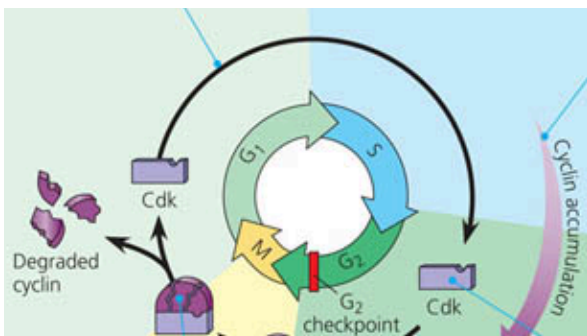
- Most human body cells in G_0

-Some can return to cycle with external cues



EX: growth factors released by injury stimulate liver cells to divide again

-Some never divide once mature EX: nerve and muscle cells



CYCLIN-DEPENDENT KINASES (Cdk's)

- Inactive form of Cdk present all the time
- Activated by attachment of **CYCLIN** proteins
- Levels of cyclin rise throughout interphase; fall abruptly during mitosis

- **MPF** = Cyclin-Cdk complex
 "maturation-promoting factor"/"M-phase-promoting-factor"
 -triggers passage past G_2 checkpoint into M phase
 -At least 3 Cdk proteins/several cyclins regulate G_1 checkpoint
- Most mechanisms unknown;
 but KINASES (Cdk's) work by phosphorylating other proteins

INTERNAL SIGNALS

M phase checkpoint makes sure all chromosomes are attached to spindle at metaphase before anaphase

EXTERNAL SIGNALS

Particularly important for mammalian cells

1) **GROWTH FACTOR** = protein released by one group of cells that stimulate other cells to divide

EX: PDGF (platelet-derived growth factors) produced by platelet blood cells

Needed by fibroblasts in culture to divide

Released in body in vicinity of injury; proliferation of fibroblasts heals wound

2) **DENSITY DEPENDENT INHIBITION** of cell division

Crowded cells stop dividing

Cultured cells divide until form a single layer on surface of container

If a gap is created, the cells will grow to fill the gap; then stop dividing

At high densities, insufficient growth factors/nutrients stop growth

3) **ANCHORAGE DEPENDENCE**

Cells must be anchored to substrate/extracellular matrix to divide

CANCER CELLS

- Causes are diverse but always involve the alteration of genes that control cell cycle
- may have unusual numbers of chromosomes
- may secrete signal molecules that cause blood vessels to grow toward tumor
- have lost both: density-dependent inhibition /anchorage dependence
- Continue to divide excessively and invade other tissues
- Don't stop when growth factors are depleted
- Don't stop at normal cell cycle checkpoints
- Most cells divide 20-50 times in culture conditions; then stop, age, die; cancer cells are "immortal"
 -HeLa cells from a tumor removed from a woman (Henrietta Lacks) in 1951 are still reproducing in culture

SO: making its own growth factors? Abnormality in cell cycle control system? Signaling abnormality?

Change from normal cell → cancer cell = **TRANSFORMATION**

Normally immune system recognizes & destroys transformed cells;

if not found can proliferate → **TUMOR** = mass of abnormal cells

MALIGNANT tumors invade and impair functions of other organs

METASTASIS - cancer cells are carried in blood & lymph system to start tumors in new places

TREATMENT: (target actively dividing cells)

High energy radiation

Many chemotherapeutic drugs interfere with specific steps in the cell cycle

EX: Taxol interferes with breakdown of microtubules; cells get stuck in metaphase

Side effects of treatment due to effects on normal cells