Cell Cycle

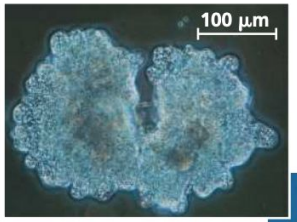
Presentation by Laurie, Slides by Slidesgo

01

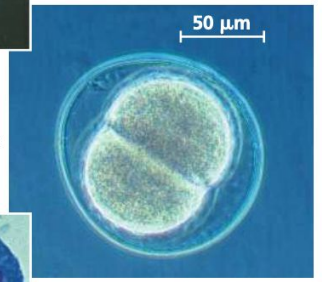
Cell Division

Key Roles

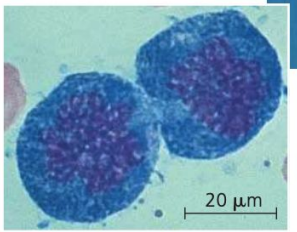
- Reproduction in prokaryotes and unicellular eukaryotes
- Formation of a multicellular eukaryote from an egg
- Renewal and repair in grown multicellular eukaryotes
    - Bone marrow makes new blood cells



◀ **(a) Asexual reproduction.** An amoeba, a single-celled eukaryote, is dividing into two cells. Each new cell will be an individual organism (LM).



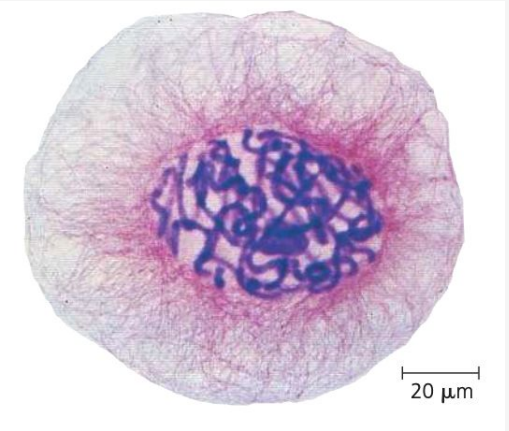
▶ **(b) Growth and development.** This micrograph shows a sand dollar embryo shortly after the fertilized egg divided, forming two cells (LM).



◀ **(c) Tissue renewal.** These dividing bone marrow cells will give rise to new blood cells (LM).

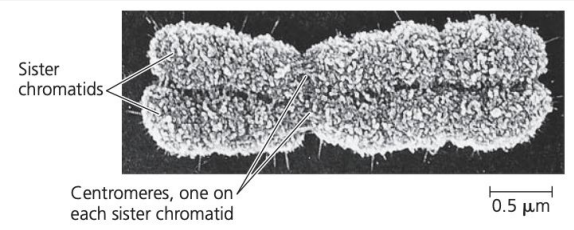
Genetic Material in the Cell

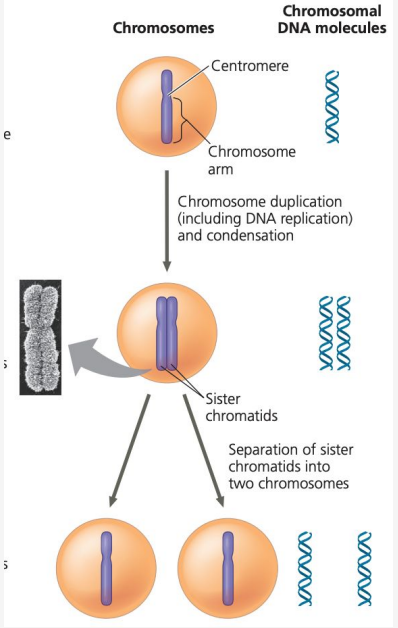
- Genome – DNA/genetic information – must be replicated before division
  - 2m of DNA in human cell
- Chromosome – how DNA is packaged
  - ~a few hundred-a few thousand genes
- Chromatin – DNA and proteins it's wrapped around; forms chromosomes
- Human somatic cells have 46 chromosomes, gametes have 23
  - Varies by species



Chromosomes During Cell Division

- Chromosomes condense from chromatin after DNA is replicated to prepare for cell division
- Duplicated chromosomes
  - 2x sister chromatids (copies)
  - Chromatids attached with cohesins (sister chromatid cohesion)
  - Centromere – region where chromatids are attached closest, has repeated sequences
  - Arms – below/above centromere
- Sister chromatids separate during cell division
- Mitosis = division of genetic material
- Cytokinesis = division of cytoplasm



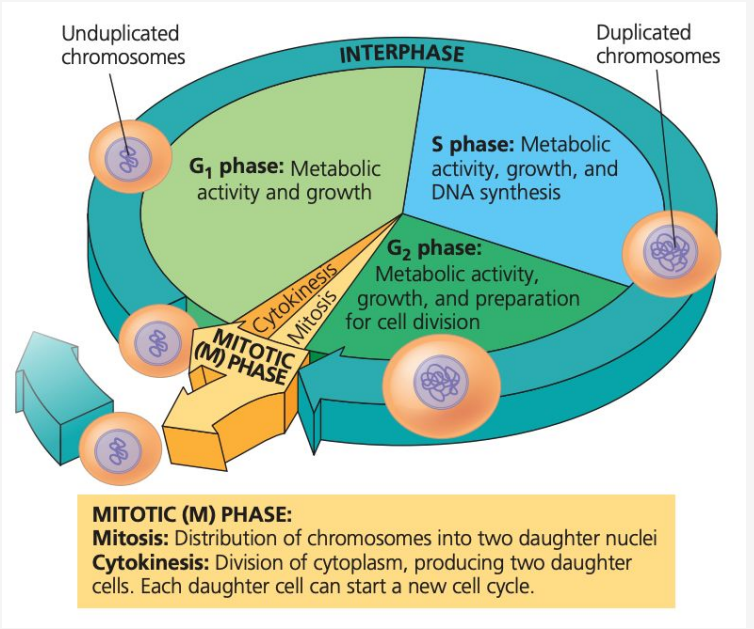


02

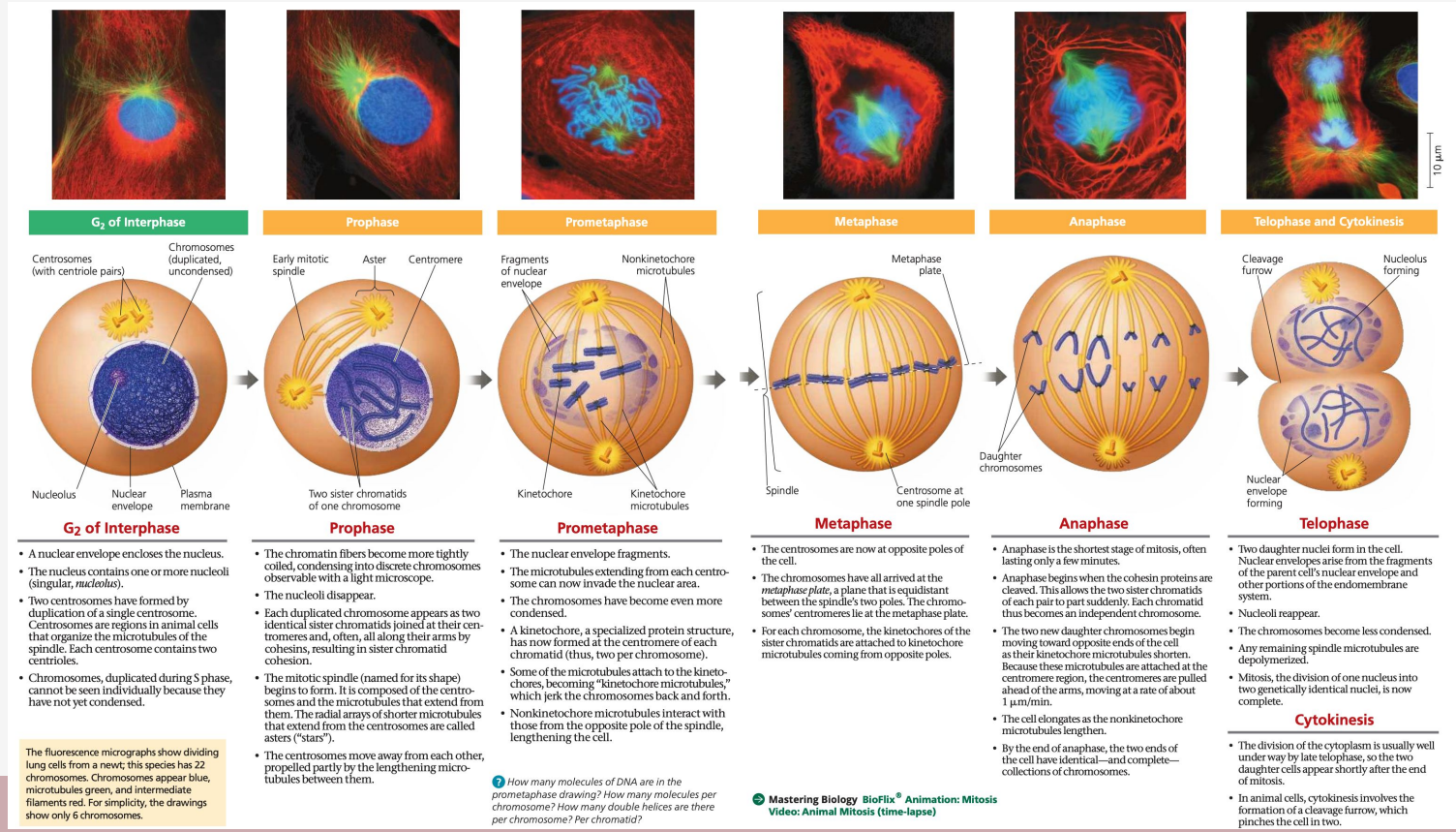
Cell Cycle

Cell Cycle Phases

- Interphase ~90% of cycle
  - G1 (first gap) – grows
  - G0 – no division
    - Secretory cells in pancreas
  - S phase (synthesis)
    - Duplication of chromosomes
  - G2 (second gap) – prepares to divide
- Mitotic (M) phase



Mitosis



G_2 of Interphase

- A nuclear envelope encloses the nucleus.
- The nucleus contains one or more nucleoli (singular, *nucleolus*).
- Two centrosomes have formed by duplication of a single centrosome. Centrosomes are regions in animal cells that organize the microtubules of the spindle. Each centrosome contains two centrioles.
- Chromosomes, duplicated during S phase, cannot be seen individually because they have not yet condensed.

The fluorescence micrographs show dividing lung cells from a newt; this species has 22 chromosomes. Chromosomes appear blue, microtubules green, and intermediate filaments red. For simplicity, the drawings show only 6 chromosomes.

Prophase

- The chromatin fibers become more tightly coiled, condensing into discrete chromosomes observable with a light microscope.
- The nucleoli disappear.
- Each duplicated chromosome appears as two identical sister chromatids joined at their centromeres and, often, all along their arms by cohesins, resulting in sister chromatid cohesion.
- The mitotic spindle (named for its shape) begins to form. It is composed of the centrosomes and the microtubules that extend from them. The radial arrays of shorter microtubules that extend from the centrosomes are called asters ("stars").
- The centrosomes move away from each other, propelled partly by the lengthening microtubules between them.

Prometaphase

- The nuclear envelope fragments.
- The microtubules extending from each centrosome can now invade the nuclear area.
- The chromosomes have become even more condensed.
- A kinetochore, a specialized protein structure, has now formed at the centromere of each chromatid (thus, two per chromosome).
- Some of the microtubules attach to the kinetochores, becoming "kinetochore microtubules," which jerk the chromosomes back and forth.
- Nonkinetochore microtubules interact with those from the opposite pole of the spindle, lengthening the cell.

? *How many molecules of DNA are in the prometaphase drawing? How many molecules per chromosome? How many double helices are there per chromosome? Per chromatid?*

Metaphase

- The centrosomes are now at opposite poles of the cell.
- The chromosomes have all arrived at the *metaphase plate*, a plane that is equidistant between the spindle's two poles. The chromosomes' centromeres lie at the metaphase plate.
- For each chromosome, the kinetochores of the sister chromatids are attached to kinetochore microtubules coming from opposite poles.

Anaphase

- Anaphase is the shortest stage of mitosis, often lasting only a few minutes.
- Anaphase begins when the cohesin proteins are cleaved. This allows the two sister chromatids of each pair to part suddenly. Each chromatid thus becomes an independent chromosome.
- The two new daughter chromosomes begin moving toward opposite ends of the cell as their kinetochore microtubules shorten. Because these microtubules are attached at the centromere region, the centromeres are pulled ahead of the arms, moving at a rate of about 1 µm/min.
- The cell elongates as the nonkinetochore microtubules lengthen.
- By the end of anaphase, the two ends of the cell have identical—and complete—collections of chromosomes.

Mastering Biology BioFlix® Animation: Mitosis
Video: Animal Mitosis (time-lapse)

Telophase

- Two daughter nuclei form in the cell. Nuclear envelopes arise from the fragments of the parent cell's nuclear envelope and other portions of the endomembrane system.
- Nucleoli reappear.
- The chromosomes become less condensed.
- Any remaining spindle microtubules are depolymerized.
- Mitosis, the division of one nucleus into two genetically identical nuclei, is now complete.

Cytokinesis

- The division of the cytoplasm is usually well under way by late telophase, so the two daughter cells appear shortly after the end of mitosis.
- In animal cells, cytokinesis involves the formation of a cleavage furrow, which pinches the cell in two.

Mitotic Spindle

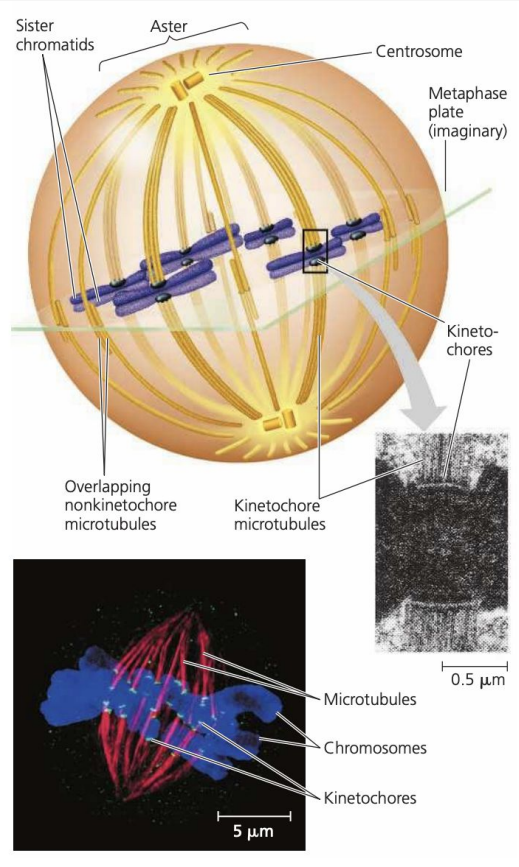
Microtubules + associated proteins, formed partially by the dissociation of other microtubules

- Grow from centrosome
- Asters – short microtubules
- Kinetochore – group of proteins assembled near centromere
    - Kinetochore microtubules
    - Nonkinetochore microtubules elongate cell, overlap

Metaphase plate

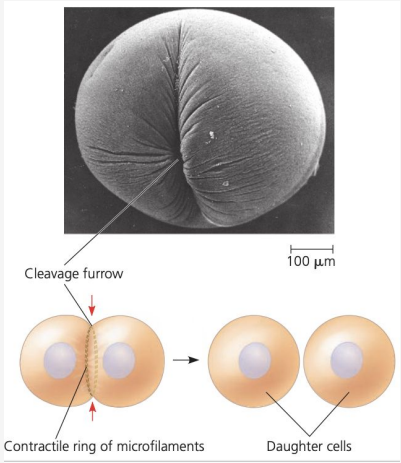
Separase cleaves sister chromatids during anaphase

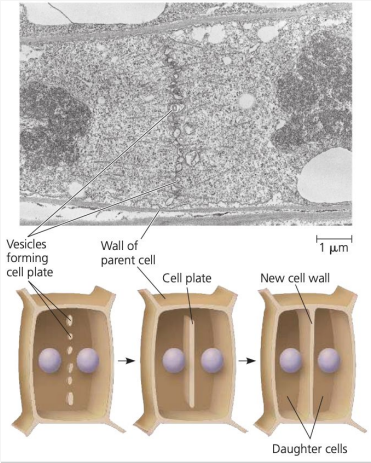
Pac-man vs reel



Cytokinesis

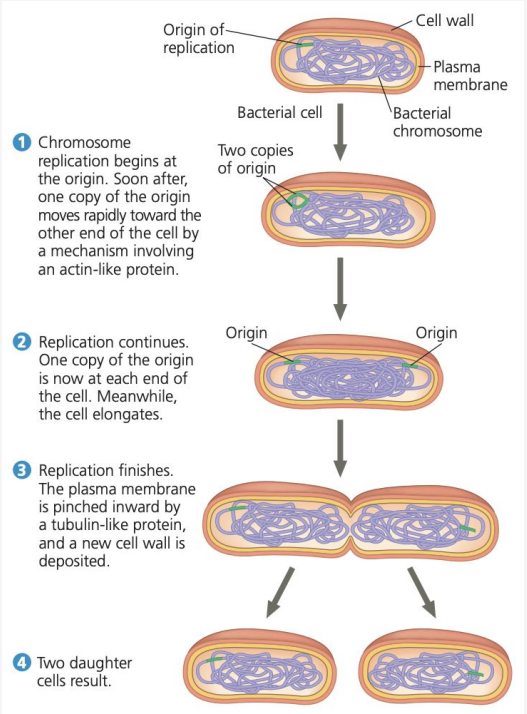
- Cleavage for animals
  - Cleavage furrow – actin microfilaments + myosin inside the cell
- Cell plate in plants
  - Formed from vesicles from golgi



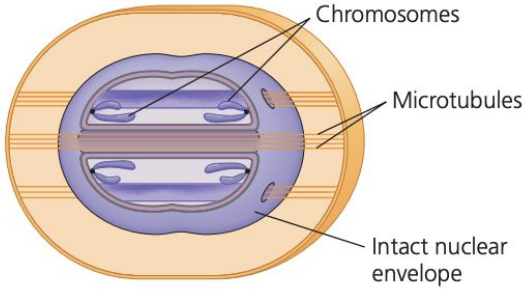


Binary Fission (Asexual Reproduction)

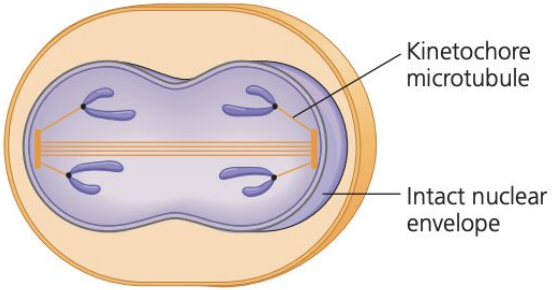
- Cell division begins at origin of replication → 2 origins
- Replication is paired with elongation of the cell
- Cell pinches in half



Other types of nuclear division



(b) Dinoflagellates. In unicellular eukaryotes called dinoflagellates, the chromosomes attach to the nuclear envelope, which remains intact during cell division. Microtubules pass through the nucleus inside cytoplasmic tunnels, reinforcing the spatial orientation of the nucleus, which then divides in a process reminiscent of bacterial binary fission.



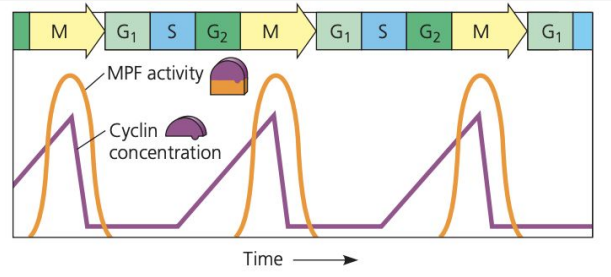
(c) Diatoms and some yeasts. In these two other groups of unicellular eukaryotes, the nuclear envelope also remains intact during cell division. In these organisms, the microtubules form a spindle *within* the nucleus. Microtubules separate the chromosomes, and the nucleus splits into two daughter nuclei.

03

Cell Cycle Control

Cell Cycle Control System

- Experiments reveal was controlled by molecules
  - Fuse S phase and G1 cell → G1 cell becomes S phase cell
  - Fuse M phase and G1 cell → G1 cell enters mitosis
- Regulation by checkpoints in G1, G2, and M phases
- Controlled by fluctuations in regulatory molecules, mainly protein kinases and cyclins (there are multiple types)
  - Cyclin – protein
  - Cyclin-dependent kinases (Cdks)
  - Combine to make MPF (maturation-promoting factor) – starts M phase
    - Phosphorylates proteins
    - Also acts on other kinases
  - MPF destroys its own cyclins during anaphase



Checkpoints

G1 checkpoint – most important

- May enter G0 phase

S phase checkpoint

- Checks for DNA damage

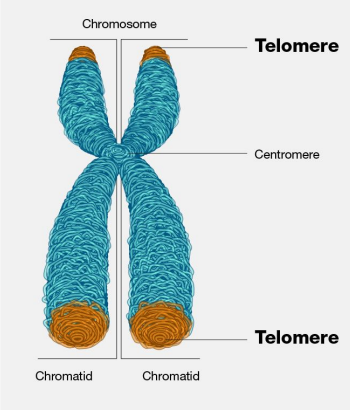
M checkpoint

- Checks for attachment of kinetochores to spindle microtubules before anaphase

Checkpoints are influenced by external factors

- Growth factor
  - Platelet-derived growth factor – binds to RTK's on fibroblasts to pass G1 checkpiint

Cancer Cells



- Do not exhibit density-dependent inhibition or anchorage dependence
- Don't need growth factors
- Divide indefinitely in culture
    - HeLa cells
    - Transformation – cells in culture acquire that ability
    - Telomerase – keeps replacing telomeres
        - Hayflick limit
- Evade triggers for apoptosis
- Benign tumor – abnormal cell doesn't move
- Malignant tumor – abnormal cells can spread to new tissues (sometimes called transformed cells)
    - Excessive proliferation
    - Unusual chromosome numbers
    - Changes on cell surface
    - Angiogenesis
    - Metastasis
- Sometimes treated with high-energy radiation or chemotherapy
    - Taxol – prevents microtubule depolymerization

04

Practice

Which of the following would NOT be important for a typical cell dividing by binary fission?

W) DNA is replicated

X) The nuclear envelope disintegrates

Y) Cytoplasm and its content is divided between daughter cells

Z) New cell wall is formed between the developing daughter cells

Which of the following phases is typically the longest in a normal cell's life cycle?

W) Interphase

X) Metaphase

Y) Prophase

Z) Anaphase

Which of the following is not true regarding mitosis?

W) Sister chromatids are held together by cohesin complexes

X) M-Cdk drives entry of the cell into mitosis

Y) The mitotic spindle is built from actin filaments

Z) The Golgi apparatus becomes less prominent during metaphase

Which of the following is not a behavior generally associated with cancerous cells?

W) They induce angiogenesis [an-gee-oh-gen-uh-sis]

X) They produce telomerase [tel-aw-mer-ayse]

Y) They cannot stop cell division

Z) They cannot proliferate when not adherent to substrate

The drug colchicine inhibits polymerization of tubulin in microtubule assembly. Which of the following cell processes would be most severely impacted by colchicine activity?

W) DNA replication

X) Mitosis

Y) Translation

Z) Cellular respiration

2018 Opens

2. You are working with Dr. Lee at University of Wisconsin-Madison to investigate cytokinesis in a newly discovered marine worm. You generated antibodies to conserved proteins involved in cell division in other organism to look for proteins that localize to important structures during cell division. What molecular motor protein should you look for in the contractile ring?

A. Actin.
B. Myosin.
C. Dynein.
D. Kinesin.
E. Cyclin.

2015 Opens

Affects DNA replication

4. Which phase of the cell cycle do cells treated with the drug specified in Question 3 become arrested?

A. G0 phase.
B. G1 Phase.
C. G2 phase.
D. M phase.
E. S phase.

2015 Opens

7. A replication inhibitor is added to stem cells in the middle of DNA replication. At what phase of the cell cycle would these cells remain?

A. Mitosis.
B. G0 phase.
C. G1 phase.
D. S phase.
E. G2 phase.

2014 Opens

18. When comparing mitosis in a plant cell to an animal cell, which one of the following summarizes the major differences?

A. Plant cells do not normally undergo anaphase.
B. Plant and animal mitosis stages share no differences.
C. Plant cells spend a longer time in metaphase and anaphase than animal cells.
D. Animal cells spend longer in metaphase and lack spindle fibers that are present in plant cells.
E. Plant cells differ in teleophase and do not use centrioles to form the spindle system.

2017 Semis

75. The maturation-promoting factor (MPF) is a cyclin-Cdk complex discovered to promote the onset of M-phase in the embryos of *Xenopus laevis*, the African clawed toad. Which of the following statements is MOST accurate?

A. The cyclin-dependent kinase component of MPF is degraded by the cyclin at the end of the M phase, when cyclin levels are at their maximum. The Cdk levels then gradually build up again.
B. MPF binds to and phosphorylates DNA, which initiates the transcription of genes responsible for mitosis.
C. MPF possesses kinase activity and, among other targets, phosphorylates proteins of the nuclear lamina, leading to the fragmentation of the nuclear envelope that is necessary for mitosis to proceed.
D. Yeast cells with a temperature-sensitive loss-of-function mutation in cdc2 kinase, the yeast homolog of the vertebrate Cdk, are unable to divide and become polyploid as a result of multiple rounds of DNA replication without cell division.
E. MPF kinase activity would be highest just before the G2 checkpoint, as the Cdk component degrades its cyclin partner to initiate mitosis.

2015 Semis

2. Which of the following is TRUE about Anaphase of Mitosis?

A. The chromosomes condense.
B. The nuclear membrane disintegrates.
C. Chromosomes line up at the metaphase plate.
D. Spindle microtubules attach to chromatids.
E. Sister chromatids separate and move towards the opposite poles.

2014 Semis

Questions 64 to 68. A new cancer drug is being developed to target a certain point in the cell cycle. The drug stops the cell cycle from proceeding and halts growth in the rapidly dividing cells. The drug could work by (Use "A" for TRUE and "B" for FALSE):

64. Mimicking a growth factor.

65. Causing premature degradation of cyclin proteins.

66. Promoting mitosis.

67. Enhancing the binding of cyclins to CDKs.
M
68. Blocking the signal to enter the G2 phase.

Thanks!

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