BIOL 230: Cell & Molecular Biology

Fall 2019 17-205 W, Nov. 13

http://accounts.smccd.edu/staplesn/biol230/

1. Pre-Lab writeups due each Mon. (for both M&W!!) ***WRITTEN!!!***: *briefly*, **What**? **Why**? **How**? for each expt. Question & **Hypothesis**?!
2. **GENETICS PRIMER: http://anthro.palomar.edu/mendel/mendel_1.htm**
3. **Prelab: do Mendelian Genetics exercises (A-C for Mon., 11/25) – & Ch. 12 Homework Problems:**
   a) **http://sonic.net/~nbs/projects/anthro201/;** *** **http://sonic.net/~nbs/projects/anthro201/exper/**
   b) **http://www.biology.arizona.edu/mendelian_genetics/mendelian_genetics.html** ***
   c) **https://www.ndsu.edu/pubweb/~mcclean/plsc431/mendel/mendel1.htm** (see left side INDEX!)
      - **https://www.ndsu.edu/pubweb/~mcclean/plsc431/mendel/mendel9.htm (see left side INDEX!)**
   d) **https://concord.org/teaching-genetics/dragons/ DRAGONS!!! – see Geniverse & Genigames**
   e) **http://www.dnaftb.org/ → Classical Genetics, and Genetic Organization.**
   f) **TURN IN your calculations of your D1S80 Genotype!! Also: ARE you an Alien Clone????**
4. **LAB THIS week: pGLO plates, Biotech, & Exam 3 Review!**
5. **Find Anastasia & Alien GEL DATA under *ADDITIONAL MATERIALS*.**
6. **Extra Credit: STEM SPEAKER SERIES,** ALL DUE by Next Wednesday!!!
7. ******NOTEBOOK/Lab MANUAL is due today!!**
8. **TODAY.: QUIZ #6 first attempt due!!!**
9. **RESEARCH Outlines will be reviewed by early next week!! FINAL REPORT due week of Dec. 4th. NO EXCEPTIONS!!!**

1

REVIEW

1. Compare the Lytic & lysogenic **bacteriophage** reproductive cycles, & describe how they are controlled by the ***late*** and ***early*** genes.
2. Diagram the structure of an **operon**, including 3 DNA components and 3 other molecules involved in its regulation.
3. ** Compare the utility and regulation of an **inducible** system for catabolic genes, and a **repressible** system for anabolic genes.
4. Compare & contrast the 3 different mechanisms of **Horizontal Gene Transfer** in bacteria: ***Transformation***, ***Conjugation***, ***Transduction***. Define and explain the mechanism of *Transposition*.
5. **Ch. 16B:** Describe 4 factors that **differentiate eukaryotic chromosomes/genome** from a **prokaryotic** chromosome/genome…..
6. Compare/contrast **4** differences between **Eukaryotic and Prokaryotic *GENE* structure** (including regulatory sequences)…..
7. Describe and explain the function of **3 modifications that occur to a eukaryotic transcript** before it is translated.
8. Diagram/define and **explain the utility** of **2** examples ***EACH*** of eukaryotic Transcriptional, Posttranscriptional, Translational & Posttranslational regulation.

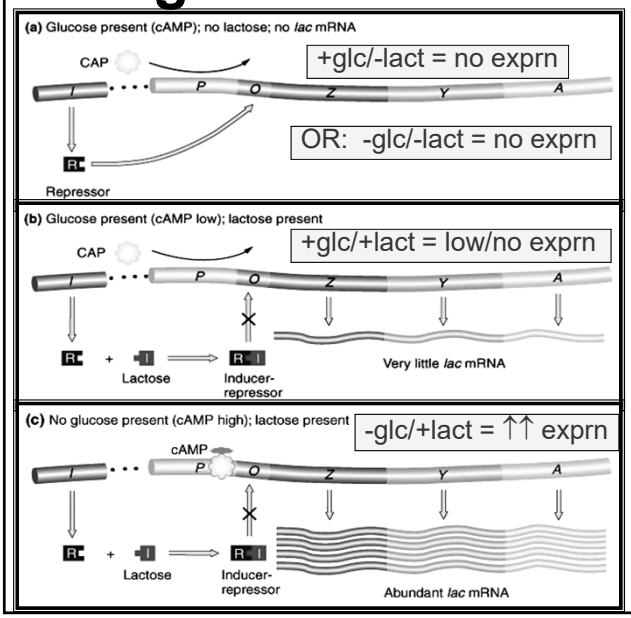
TODAY's Objectives: Students should be able to....

1. **Ch. 11:** Describe and Diagram the **4 phases of the cell cycle**, and how they are regulated by **Cyclin/CDK complexes**.
2. Diagram and compare the 4 main phases of Mitosis, Meiosis I & Meiosis II.
   - Chromosome, Chromatid, Centromere, Centriole, Spindle, Cortical MT's, Spindle fibers/ MT's, Sister Chromatid, Homologous Chromosome, Nuclear Envelope, Cytokinesis (plants/animals).
3. Describe and diagram how **meiosis** generates **diversity** in gametes.
4. Define and explain the function of **Apoptosis**.

❖ ***Objectives and Study Guide Questions are your HOMEWORK between classes!!! DUE WED. at the end of Lecture!!***

2

SUMMARY: Transcriptional Regulation of the *lac* Operon



a) Glucose present (cAMP low): <u>no lactose</u>:
- **no lac mRNA**

b) Glucose present (cAMP low): lactose present:
- **very little lac mRNA**

c) <u>No glucose</u> (cAMP high): lactose present:
- **abundant lac mRNA**

3

Summary of LAC Operon Regulation

TABLE 16.1

Positive and Negative Regulation in the *lac* Operon[a]

GLUCOSE	cAMP LEVELS	RNA POLYMERASE BINDING TO PROMOTER	LACTOSE	LAC REPRESSOR	TRANSCRIPTION OF *lac* GENES?	LACTOSE USED BY CELLS?
Present	Low	Absent	Absent	Active and bound to operator	No	No
Present	Low	Present, not efficient	Present	Inactive and not bound to operator	Low level	No
Absent	High	Present, very efficient	Present	Inactive and not bound to operator	High level	Yes
Absent	High	Absent	Absent	Active and bound to operator	No	No

Negative regulators are in red type.

http://highered.mheducation.com/sites/0072995246/student_view0/chapter7/combination_of_switches__the_lac_operon.html

https://www.sophia.org/tutorials/lac-and-trp-operons-gene-regulation?playlist=biology--11

LIFE 9e, Table 16.1

https://highered.mheducation.com/sites/9834092339/student_view0/chapter15/the_lac_operon.html

http://life9e.sinauer.com/life9e/pages/16/162001.html

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Operon Regulation: Summary

OPERON TYPE	ACTIVITY of	"Ligand" Molecule Absent	"Ligand" Molecule Present
Inducible*, ~*lac (**Catabolic**)	Repressor Protein	**ON**	**OFF** (lactose "inducer")
	CAP Protein	**OFF**	**ON** *(if ↑cAMP; NO glucose!)*
	Operon (transcription)	**OFF**	**ON**
Repressible*, ~*trp (**Anabolic**)	Repressor Protein	**OFF**	**ON** (tryptophan "corepressor")
	Operon (transcription)	**ON**	**OFF**

[Reminder: both signal molecules/ Ligands bind to the Repressor protein, **allosterically** changing its activity. Inducer, or Corepressor? **]**

- **Positive Control:** Regulatory Protein **ACTIVATES** genes.
- **Negative Control:** Regulatory protein **REPRESSES** genes.

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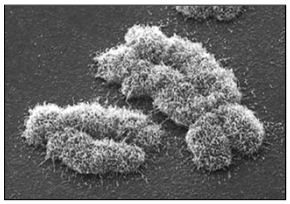
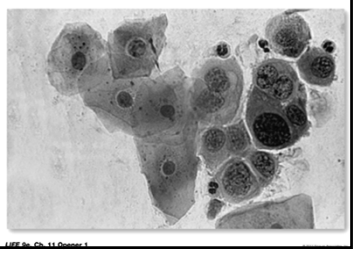
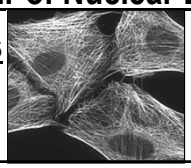
Chapter 11: Chromosomes, the Cell Cycle, & Cell Division

1. Systems of Cell Reproduction
2. Interphase and the Control of Cell Division
3. Eukaryotic Chromosomes
4. Mitosis: Distributing Exact Copies of Genetic Information
5. Cytokinesis: The Division of the Cytoplasm
6. Reproduction: Sexual and Asexual
7. Meiosis: A Pair of Nuclear Divisions
8. Meiotic Errors
9. Cell Death







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11.1) Systems of Cell Reproduction

- Cell division is necessary for ***reproduction, growth, and repair*** of an organism.
- Cell division must be initiated by a **reproductive signal**, consisting of three steps:
  1) replication of the genetic material (DNA)
  2) separation of the two DNA molecules in the cell
  3) division of the cytoplasm

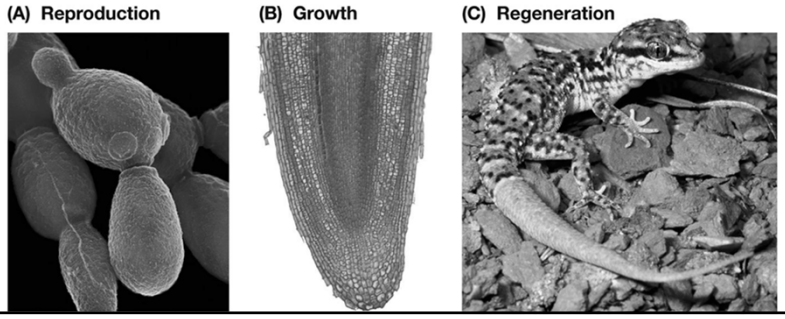

Fig. 11.1

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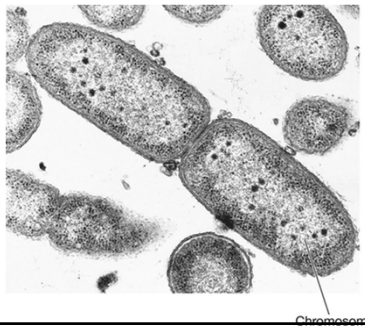
Prok. vs. Euk. Reproduction

- In **prokaryotes**, cellular DNA is a single molecule, or chromosome
  - Circular!
  - reproduce by ***Binary Fission.***
- In **eukaryotes**, nuclei divide by either *Mitosis* or *Meiosis.*



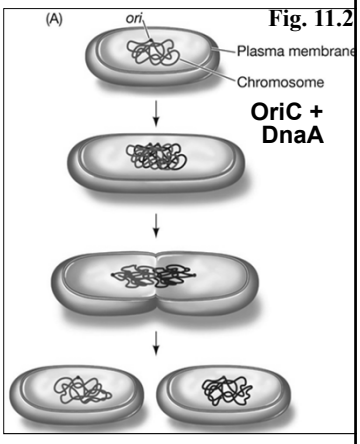
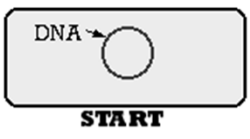


Fig. 11.2



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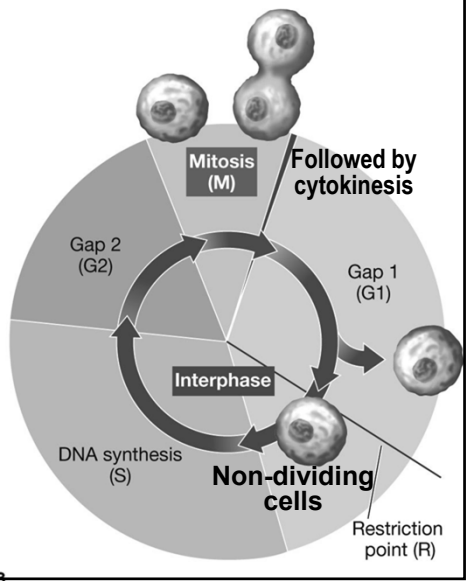
11.2) Interphase and the Control of Cell Division

- The mitotic cell cycle has two main phases: **Interphase** and **Mitosis**.
- During most of the cell cycle, the cell is in ***INTERPHASE***: (3 subphases)
  - **S**, **G1**, and **G2**.
  - DNA is replicated during **S phase**.
    - (***SYNTHESIS***)



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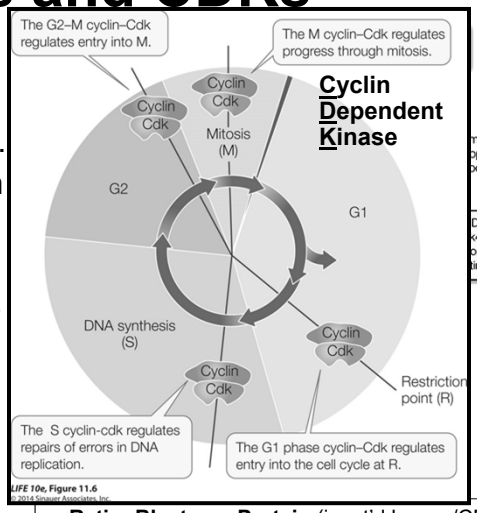
Cell Cycle Regulation: Cyclins and CDKs

Cyclin-Cdk complexes:

- regulate the passage of cells from **G1 → S,** and **G2 → M**.
- Cyclin activates CDK, then cyclin is rapidly degraded
  - *Specific CYCLIN-CDK interactions regulate phase-transitions!!*
  - *Expressed briefly; degraded quickly!!*
- ***CDK*** phosphorylates cellular proteins (w/ ATP)
  - Change activities to move into S, etc…..
  - Always present; active site hidden without specific Cyclin.
- *both* = ***Allosteric control!***



- **RetinoBlastoma Protein** (inact'd by cyc/CDK)
- **p21 tumor suppressor can block Cyclin D/E**
- **Cancers: lose Cyclin-CDK "Checkpoint" Controls (eg: p53→p21⊠block Cyclins)**

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Control of Cell Division

- Internal controls: **Cyclin-CDK Complexes**
- External controls (outside cell):
  - growth factors ***("mitogens")*** and hormones – can also stimulate a division cycle
    - **Platelet-derived growth factor (PDGF)** – skin wounds.
    - **Interleukins (ILs)** – **WBCs** (white blood cells).
    - **Erythropoietin** – **RBCs** (red " ").

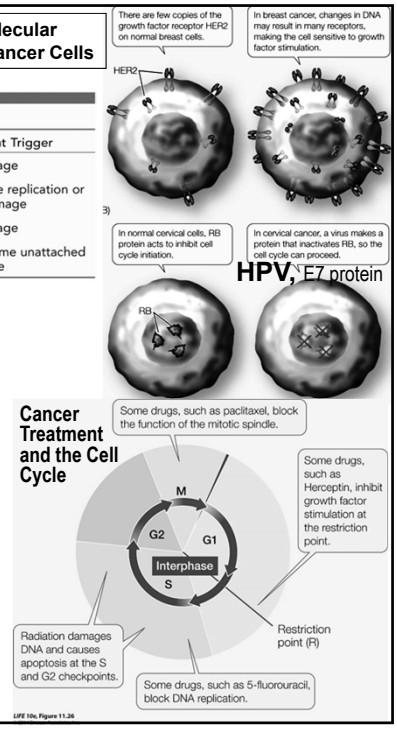
http://www.cellsalive.com/cell_cycle.htm

GAME:http://nobelprize.org/educational_games/medicine/2001/cellcycle.html

Fig. 11.24 Molecular Changes in Cancer Cells

TABLE 11.1 Cell Cycle Checkpoints

Cell Cycle Phase	Checkpoint Trigger
G1	DNA damage
S	Incomplete replication or DNA damage
G2	DNA damage
M	Chromosome unattached to spindle



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11.3) Eukaryotic Chromosomes

1. **Chromosomes = DNA and proteins.**
   - At mitosis, chromosomes initially appear double:
     - two ***sister chromatids*** ***(only AFTER S-Phase!!)***
     - held together at the ***centromere*** (= compressed region)
   - Each sister chromatid = one double-stranded DNA molecule complexed with proteins
     - Called ***CHROMATIN!*** (~50% prot/ 50% DNA)
2. During interphase, DNA in chromatin is wound around **histone** cores to form **nucleosomes**.
   - Histones = basic (+) proteins (rich in Lys & Arg)
3. DNA folds repeatedly, packing within the nucleus.
4. At Mitosis, DNA folds even more!!

http://www.biochem3d.com/animations/UofM/UofM.mpg

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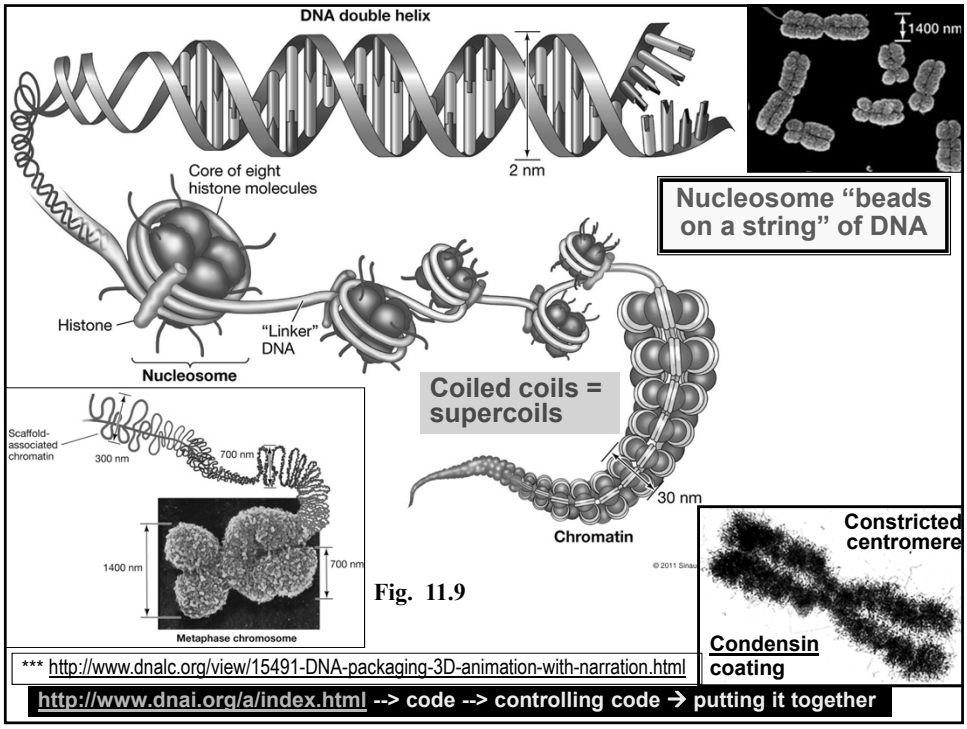

Fig. 11.9

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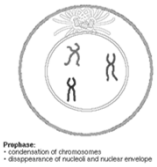
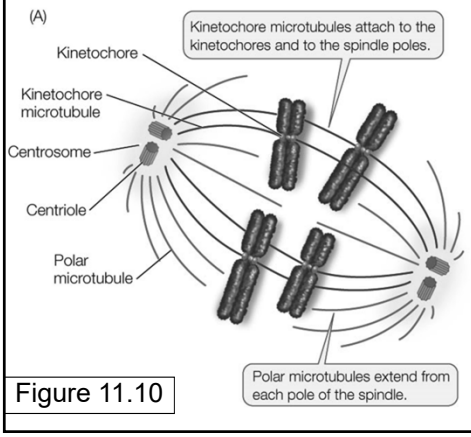
11.4) *Mitosis*: Distributing Exact Copies of Genetic Information

- After S-phase, first sign of mitosis = **separation of centrosomes** (~basal body)
  - → ***initiate microtubule formation for the spindle.***





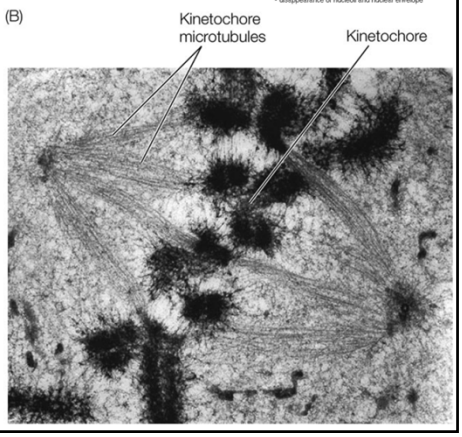


Figure 11.10

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Mitosis: Distributing Exact Copies of Genetic Information

- Mitosis can be divided into 4 main phases:

1. Prophase

– ***Prometaphase***

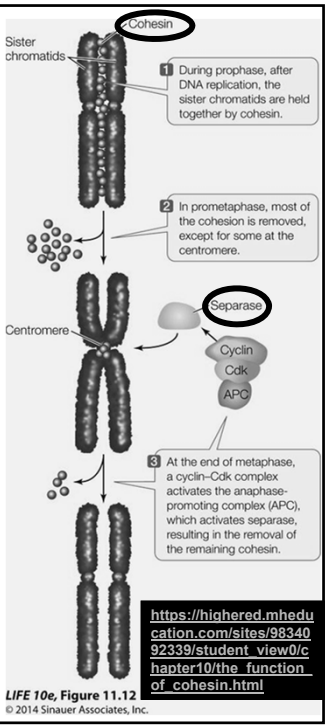
2. Metaphase

3. Anaphase

4. Telophase

http://www.cellsalive.com/mitosis.htm

Once spindle finds kinetochores, ***Separase*** **(protease)** released from ***Securin*** **(inhibitory subunit) → Hydrolyzes** ***Cohesin***



https://highered.mheducation.com/sites/9834092339/student_view0/chapter10/the_function_of_cohesin.html

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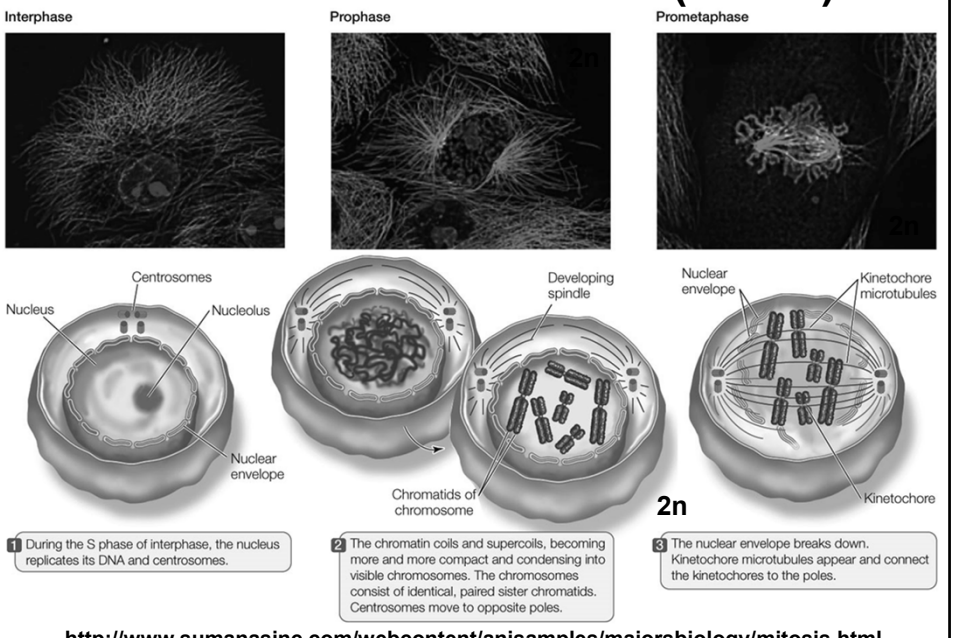
11.11 Phases of Mitosis (Part 1)



http://www.sumanasinc.com/webcontent/anisamples/majorsbiology/mitosis.html

LIFE 9e, **Figure 11.11 (1)**

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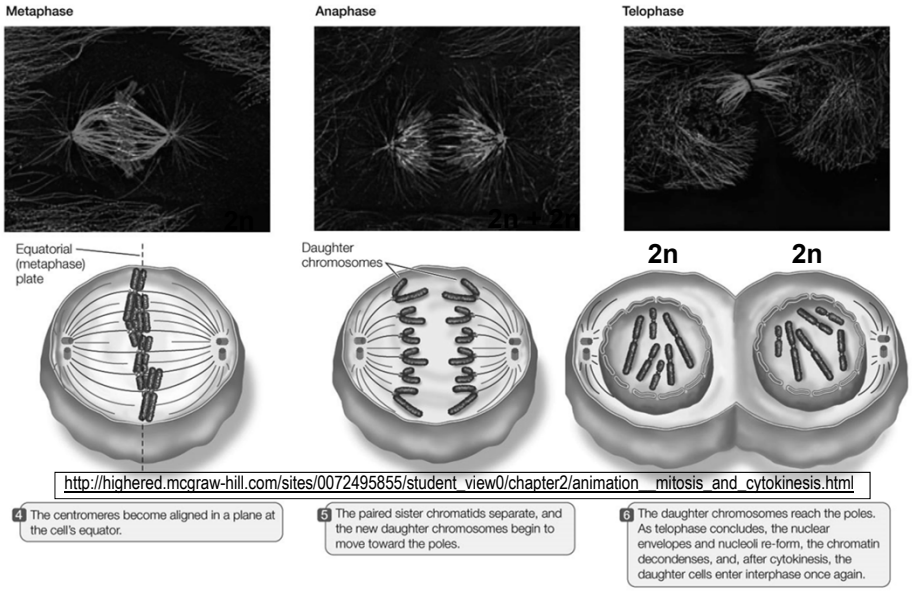
11.11 Phases of Mitosis (Part 2)



http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter2/animation__mitosis_and_cytokinesis.html

http://www.biology.arizona.edu/Cell_bio/tutorials/cell_cycle/MitosisFlash.html

***LIFE 9e*, Figure 11.11 (2)**

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Mitosis: Summary of Phases

1. **PROPHASE**:
   - the chromosomes condense into paired chromatids (***Cohesin; Condensin***);
   - polar MTs form (from ***centrosomes*** = 2 centrioles).
   - ➢ **PROMETAPHASE: (late prophase)**
     a) **nuclear envelope disintegrates;**
     b) **MTs attach to *kinetochores* on each chromatid.**
2. **METAPHASE**: chromosome centromeres align at equatorial plate.
3. **ANAPHASE**: two daughter chromatids separate to spindle poles (MTs shorten, ***minus-end-directed motors/dynein***). ***Separase.***
4. **TELOPHASE**: spindle disintegrates; chomosomes de-condense; nuc env and nucleoli reform.

3-D!!: http://www.hybridmedicalanimation.com/anim_mitosis.html

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11.5) *Cytokinesis*: The Division of the Cytoplasm

- Cytokinesis usually follows nuclear division.
  1. **Animal cell cytoplasm – divides by plasma membrane furrowing ("Cleavage Furrow")**
     - contraction of cytoplasmic microfilaments
     - Actin/Myosin = "***Contractile Ring***"!!

     Cytokinesis Movie: http://bement.molbio.wisc.edu/node/13

  2. **Plant Cell cytokinesis – by formation of a Cell Plate**
     - vesicle fusion
     - synthesis of new cell wall material.

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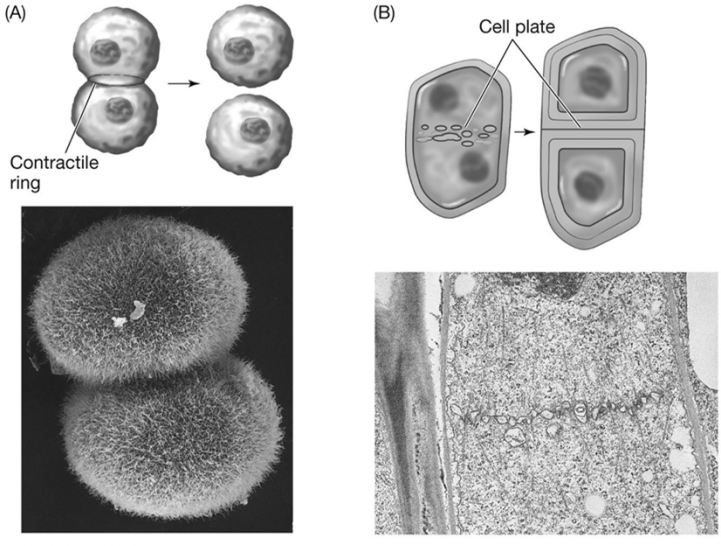
Cytokinesis

Animal – Cleavage Furrow **Plant – cell plate**



LIFE 9e, Figure 11.13 © 2011 Sinauer Associates, Inc.

http://highered.mcgraw-hill.com/sites/9834092339/student_view0/chapter10/animation_-_cytokinesis.html

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11.6) Reproduction: Sexual & Asexual

- The cell cycle can repeat itself many times, forming a clone of genetically identical cells.
- ***Asexual*** reproduction produces an organism genetically identical to the parent.
  - Any genetic variety is the result of mutations.
- In ***Sexual*** reproduction,
  - two haploid gametes (***n* # chromosomes**)
  - (one from each parent)
  - unite in fertilization to form a genetically unique, diploid zygote (***2n* # chromosomes**)

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Reproduction: Sexual and Asexual

- In sexually reproducing organisms, certain cells in the adult undergo ***MEIOSIS***:
  - ***a diploid cell produces haploid gametes.***
    - Each gamete contains a random mix of one of each pair of homologous chromosomes from the parent.
  - In: ***Gonads***
    - animals – testes, ovaries;
    - plant Flowers (anther, ovary)

http://www.cellsalive.com/meiosis.htm

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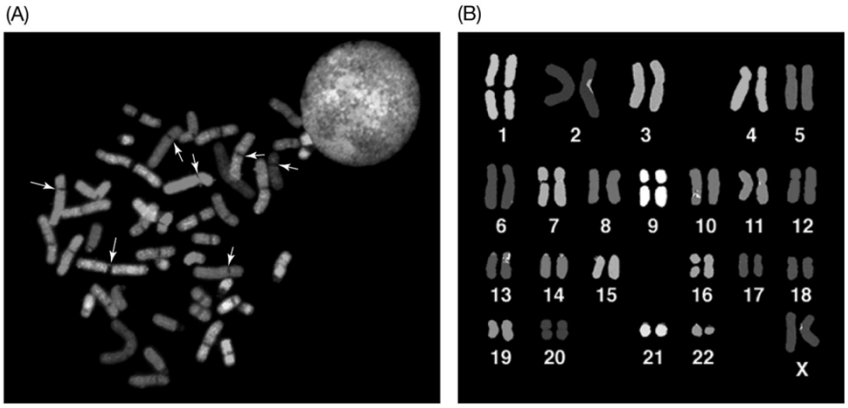
Reproduction: Sexual and Asexual

- ***Karyotype*** = the number, shapes, and sizes of the chromosomes of an organism.



The Human Karyotype

Chromosomes aligned in order, largest to smallest, except Sex chromosomes = always last.

LIFE 9e, Figure 11.16

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11.7) Meiosis: A Pair of Nuclear Divisions

1. Reduces the chromosome number from diploid to haploid *(**Reduction Division**!)*

2. Ensures that each haploid cell contains one member of each chromosome pair
   - Preparation for sexual reproduction/fertilization
   - ***(n-mom + n-dad → 2n)***

3. Consists of 2 nuclear divisions!

http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter12/animations.html# → Stages, etc.

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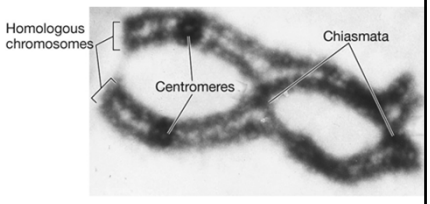
A. Meiosis I

1. **Prophase I**: homologous chromosomes pair.
   - ***material may be exchanged by crossing over between nonsister chromatids of two adjacent homologs***



2. **Metaphase I**: the paired homologs gather at the equatorial plate.
   - **Each chromosome: has one kinetochore & binds polar microtubules for one pole**

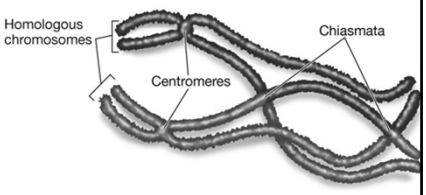


Figure 11.18

3. **Anaphase I**: entire chromosomes, each with two chromatids, migrate to the poles.
   - **At end of meiosis I: 2 nuclei, each with the ***haploid*** number of chromosomes with 2 sister chromatids

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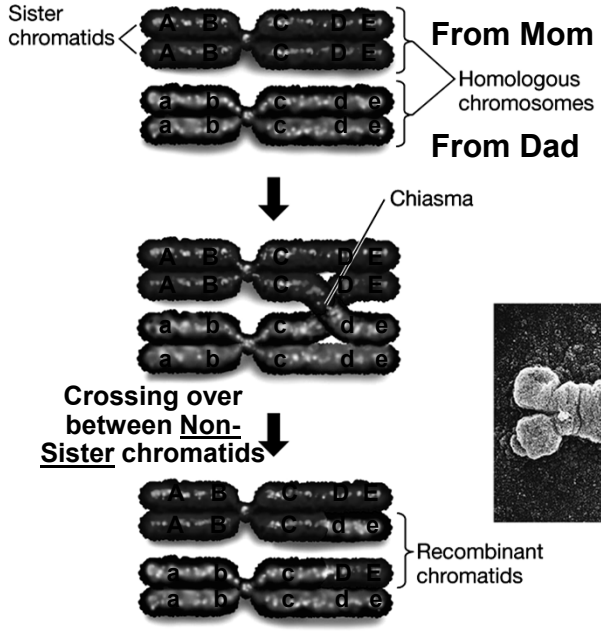
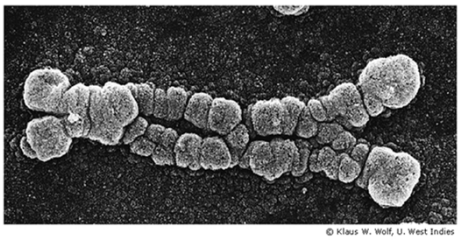
Chiasmata: Evidence of Exchange between Chromatids



PROPHASE I:
1. Synapsis (pairing)
2. Crossing over
3. Chiasmata form



11.19

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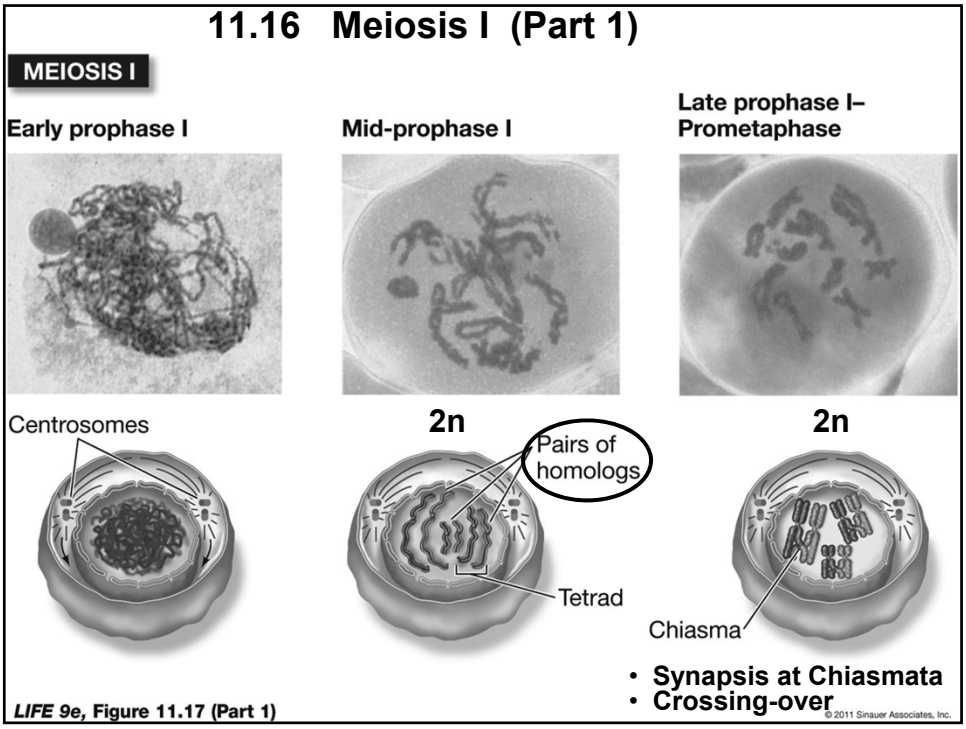
11.16 Meiosis I (Part 1)



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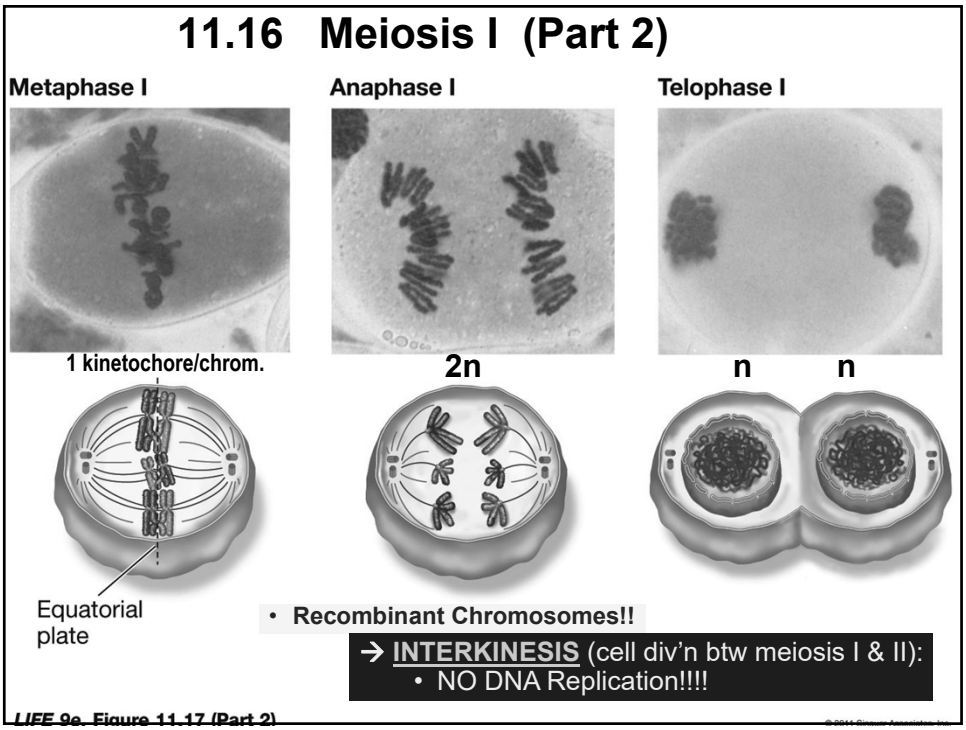
11.16 Meiosis I (Part 2)



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B. Meiosis II

1. No DNA replication precedes this division
   a) *(no S phase!)*
   b) ***Begins with haploid # of chromosomes***
   c) ***Otherwise similar to mitosis***

2. Sister chromatids separate

3. ***<u>MEIOTIC PRODUCTS = 4 haploid cells!</u>***

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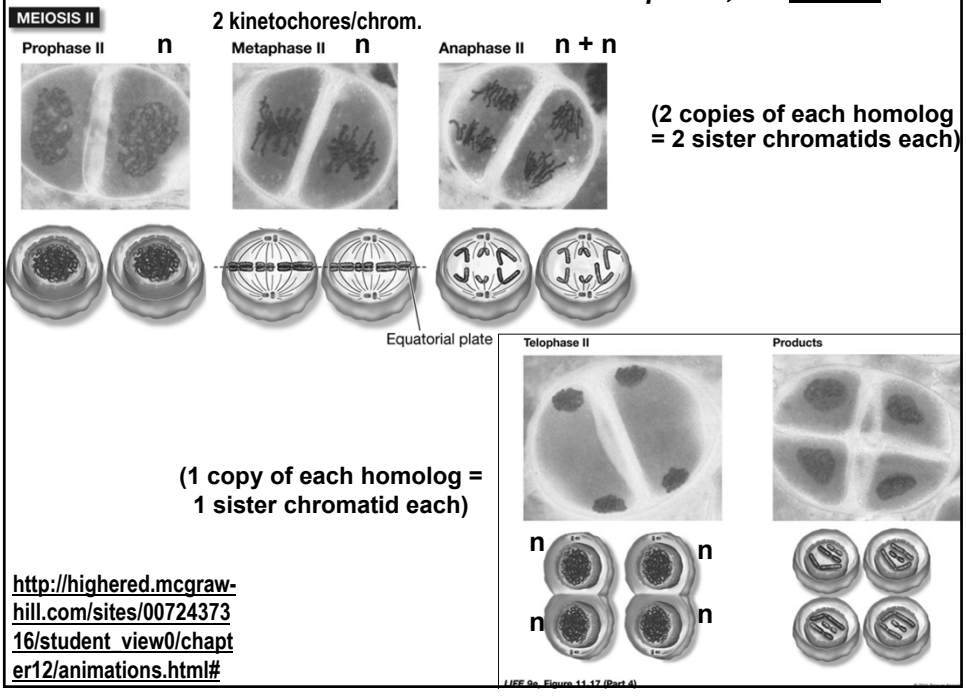
****** Similar to Mitosis!!: Sister chromatids separate, but <u>n → n!!</u>***



http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter12/animations.html#

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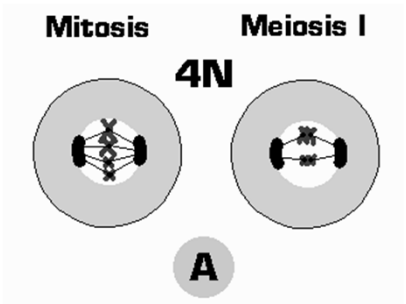
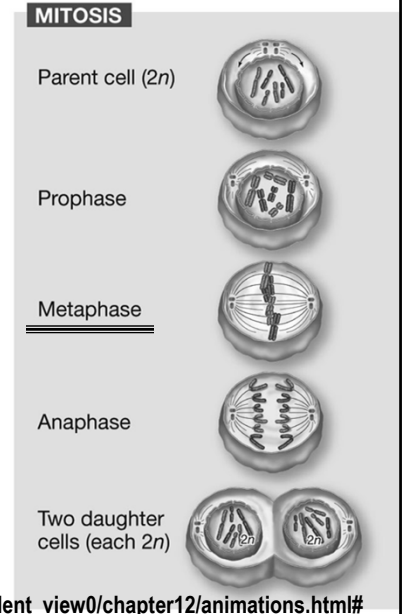
C. Mitosis vs. Meiosis

Mitosis is a mechanism for *constancy*: The parent nucleus produces two daughter nuclei, *identical* to the parent and to each other.





http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter12/animations.html#

LIFE 9e, Figure 11.20 (Part 1)

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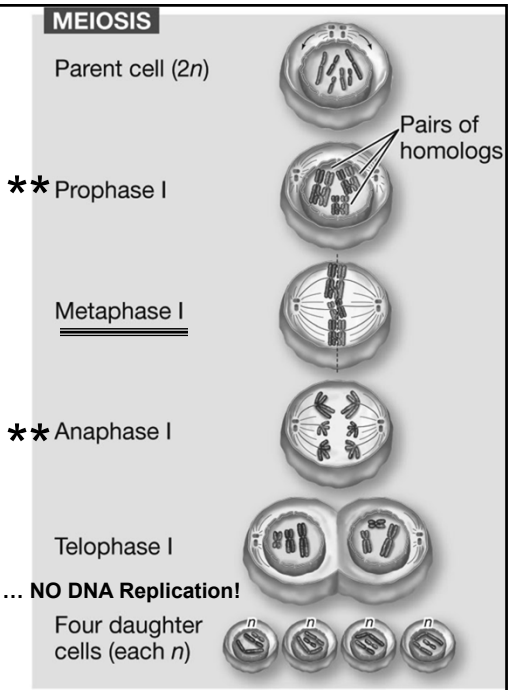
Meiosis is a mechanism for *diversity*: The parent nucleus produces four haploid daughter nuclei, each *different* from the parent and from its sisters.



LIFE 9e, Figure 11.20 (Part 2)

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D. Meiosis: Factors Promoting Genetic Diversity

1. Crossing over during Prophase I ***(IntRAchrom'l recomb.)***
   - During Synapsis & formation of Chiasmata
2. Random selection of which homolog of a pair *(from mom or from dad?)* migrates to which pole during Anaphase I ***(IntERchromosomal recombination)***
   - → genetic composition of each haploid gamete is different from that of the parent and sisters
   - The more chromosome pairs in a diploid cell, the greater the diversity of chrom. comb'ns generated by meiosis
     - (***2^n possibilities! n= # pairs***).

- ***[#3.) – & Sex/Fertilization: random combinations of 2 diverse gametes!!!! … #4.) and choice of partners!?]***

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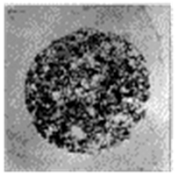
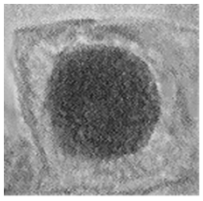
E. Meiotic Errors



- **Nondisjunction**:
  - one member of a homologous pair fails to separate from the other
  - both go to the same pole
    - → one gamete with an extra chromosome
    - → another other lacking that chromosome



- Fertilization with a normal haploid gamete:
  - results in ***aneuploidy*** (2n +/- 1, etc.)
  - and harmful genetic abnormalities
    - Eg: *Down Syndrome* = Trisomy of Chromosome 21.

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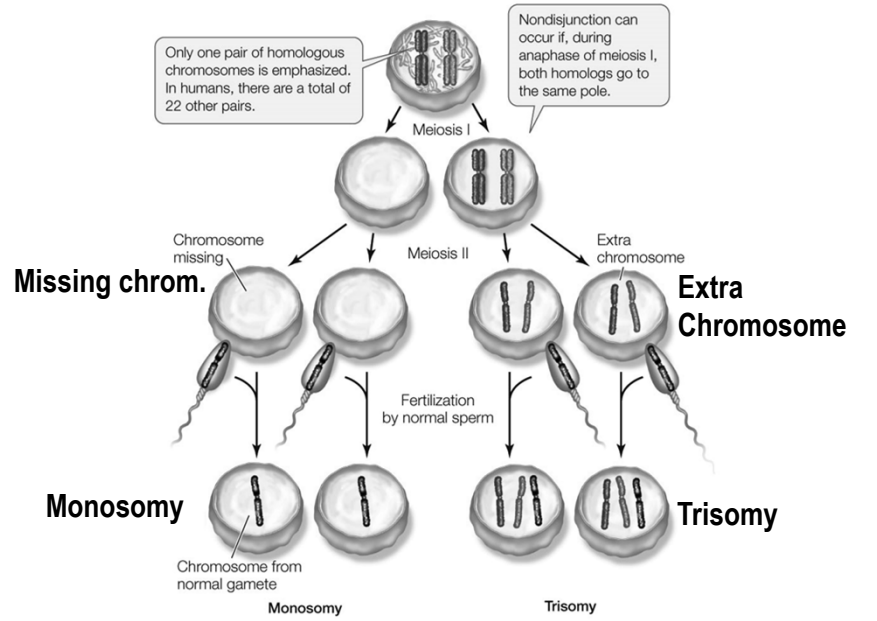
Nondisjunction leads to ***ANEUPLOIDY***:



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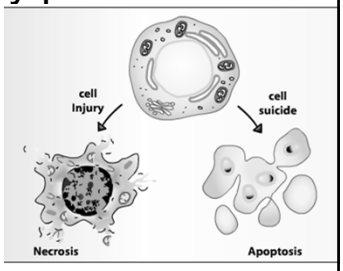
11.8) Cell Death

1. **NECROSIS:** cells damaged by poisons or starved of essential nutrients.
   - Swell up and burst.



2. **APOPTOSIS:** a genetically programmed series of events.
   - detachment of the cell from its neighbors.
   - fragmentation of its nuclear DNA.
     - Development: webbed fingers, nervous system, immune cells
     - Damaged or old cells (risk of DNA mutation, cancer)

http://www.whfreeman.com/kuby/content/anm/kb04an01.htm

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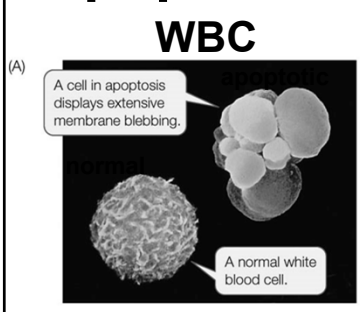
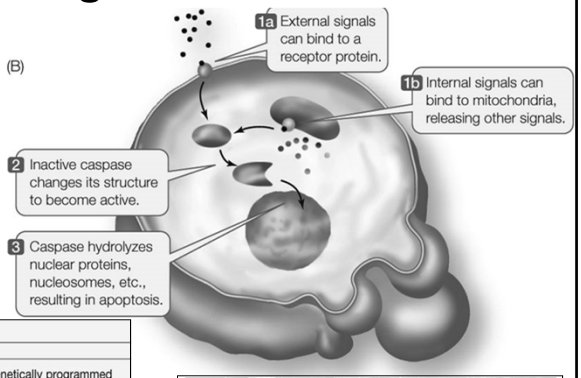
Apoptosis: Programmed Cell Death





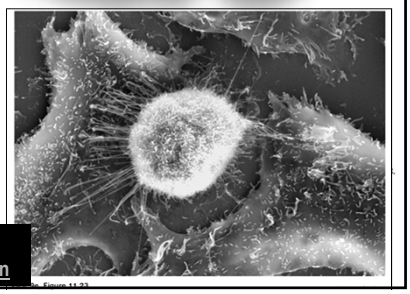
Two Different Ways for Cells to Die

	NECROSIS	APOPTOSIS
Stimuli	Low O_2, toxins, ATP depletion, damage	Specific, genetically programmed physiological signals
ATP required	No	Yes
Cellular pattern	Swelling, organelle disruption, tissue death	Chromatin condensation, membrane blebbing, single-cell death
DNA breakdown	Random fragments	Nucleosome-sized fragments
Plasma membrane	Bursts	Blebbed (see Figure 9.21A)
Fate of dead cells	Ingested by white blood cells	Ingested by neighboring cells
Reaction in tissue	Inflammation	No inflammation

***LIFE 9e*, Figure 11.22**

http://www.whfreeman.com/kuby/content/anm/kb04an01.htm

http://www.whfreeman.com/lodish4e/content/ld01/ld01vs01a.htm



http://sites.sinauer.com/cooper6e/animation1702.html

http://www.wehi.edu.au/wehi-tv/apoptosis-and-signal-transduction

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Review – Major Themes So Far!!

1. Molecular shape/**structure** → Molec./Biol. **Function**
   - Lipids, Polysacch., Proteins!…., RNA, DNA
2. In Biological systems: **Endergonic** processes are COUPLED to **Exergonic** processes so that they will proceed efficiently.
   - ETC/ATP, Active transport, etc.
3. Biological reactions in eukaryotes are **compartmentalized**.
   - glyc, TCA, ETC, lysosome, RER, SER
4. Eukaryotic Gene regulation has MANY levels of **complexity.**
   - ***Many steps for each phase of gene expression!***
   - ***Each one can be halted in several ways!!***
5. **Mitosis** → generate nuclei identical to each other & original
6. **Meiosis** → generate Haploid nuclei genetically different from each other or from either parent!

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