Biology 1090 Midterm Study Sheet

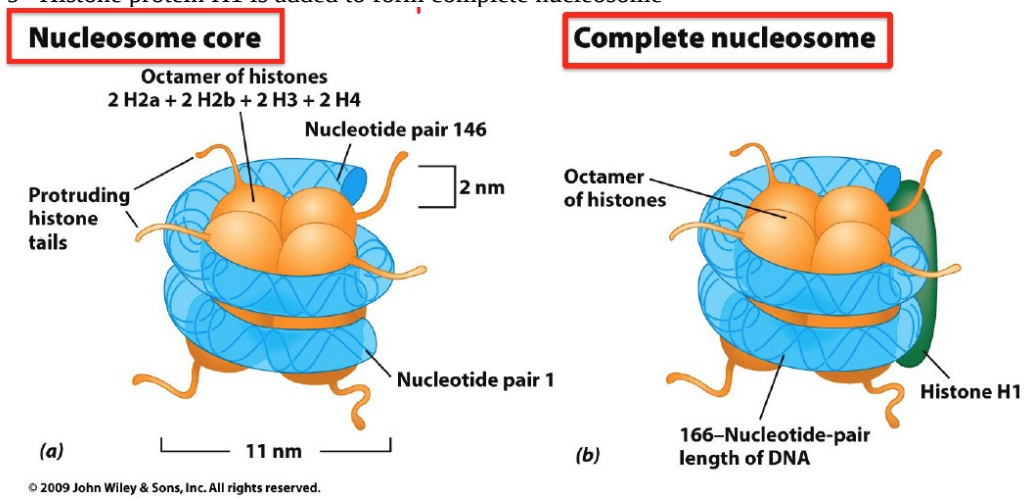
Structures of DNA and RNA

- Both DNA and RNA are polymers
- Each subunit consists of a phosphate group and a 5-carbon sugar(Pentose does not have hydroxyl group on 2nd carbon)
- Purines: Guanine and Adenine
- Pyrimidines: Cytosine and Thymine, Uracil (RNA only)
- Purines and Pyrimidines are connected by Phosphodiester bonds between the 5' and 3' Carbons
- DNA is double stranded and strands run antiparallel. Strands held together by H-Bonds
- One 360 degree turn has 10 base pairs = 3.4nm
- DNA strands are polar due to **Phosphate group on 5' end** and Free **Hydroxyl group on 3' end**
- Opposing strands are complimentary
- Most common DNA is **B-DNA** which contains **Major groove and Minor Groove** important for protein binding

DNA Condensation

First Level- Packaging DNA into Nucleosomes

>DNA packaged into supercoils of nucleotide pairs connected by linker regions (can be digested by **endonuclease**)
>Produces 11nm Fiber
>DNA is wrapped around 8 histone proteins to create nucleosome core
>9th Histone protein H1 is added to form complete nucleosome

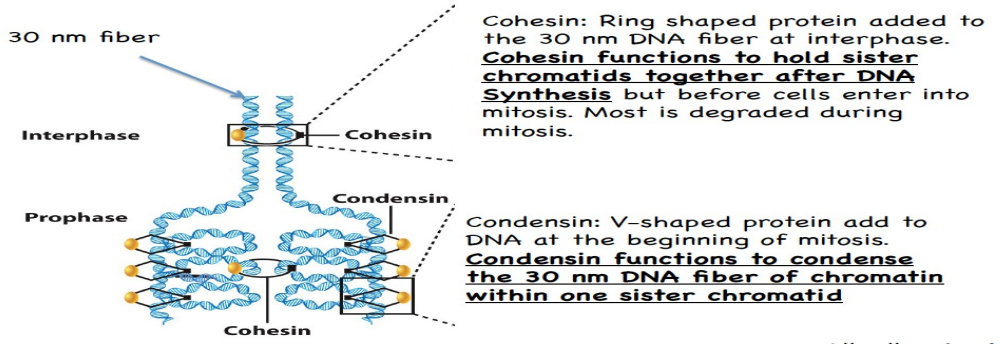


Second Level- Additional level of Supercoiling

>Additional level produces a 30nm fiber
>Histone H1 plays a large role in nucleosomal interaction
>30 nm fiber is basic structural unit of metaphase chromosome

Third Level-Attachment of 30nm fibre to no-histone protein scaffold

>**Cohesin:** holds sister chromatids together after DNA synthesis
>**Condensin:** condenses 30nm fibre into sister chromatids



Centromeres
>Provide the point of attachment of chromosomes to microtubules in the mitotic spindle
Telomeres (get shorter with age)
>Protect ends of Chromosomes
>Resist Degradation of DNases
>Prevent fusion of chromosomal ends
>Facilitate replication of the ends of the linear DNA

Cell Division and Mitosis

- Occurs within Stem Cells
- Each mitotic chromosome consists of a pair of identical **sister chromatids**
- Cellular organelles and contents are divided almost equally b/t daughter cells
- ER and Golgi complex are cut and later reformed
- Mitochondria and Chloroplasts are randomly divided b/t daughter cells

Cell Cycle *(30 mins to several years)*
***G Phase**:* Growth/ Cellular metabolism
***S Phase**:* DNA Replication
G_2 Phase: Preparation for Mitosis
M Phase: Chromosomal Separation and *Cytokinesis*
Interphase: The time between all other phases

- Cells not cycling go from G Phase to G_0 Phase and are called **quiescent**

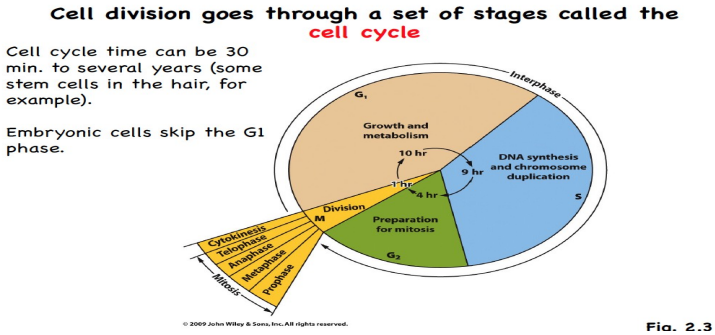


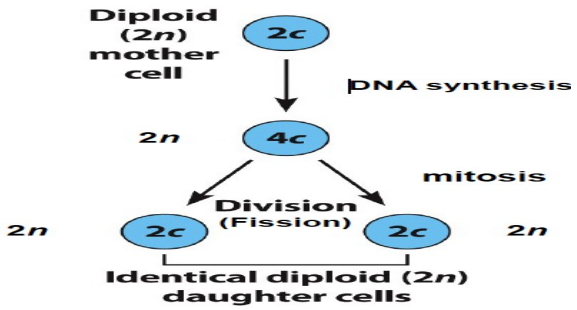
Fig. 2.3

- Centrosome Cycle (centrioles duplicate) progresses along with cell cycle
- In animal cells, **centrosomes are Microtubule organizing centers** (MTOC's). They help reorganize microtubules during mitosis
- When mitosis begins chromosomes are duplicated and condensed (condensin)

Diploid vs Haploid

Diploid Cell	Haploid Cell
Contains two sets of chromosomes	Only one complete set of chromosomes
Results of Mitosis (2 identical daughter cells)	Results of Meiosis

2n;2c values 1n; 1c values



Stages of Mitosis

Interphase

- Chromosomes duplicate to produce sister chromatids
- Chromatids joined and held together by cohesisn
- Centrosome is duplicated
- 2n;4c values

Prophase

- Duplicated Chromosomes condense
- Condensation of duplicated Chromosomes
- Membrane breaks done
- Spindle formation and spindle microtubules invade nuclear space

Prometaphase

- Chromosomal microtubules attach to the kinetochores
- Chromosomes move towards the equator of the spindle

Metaphase

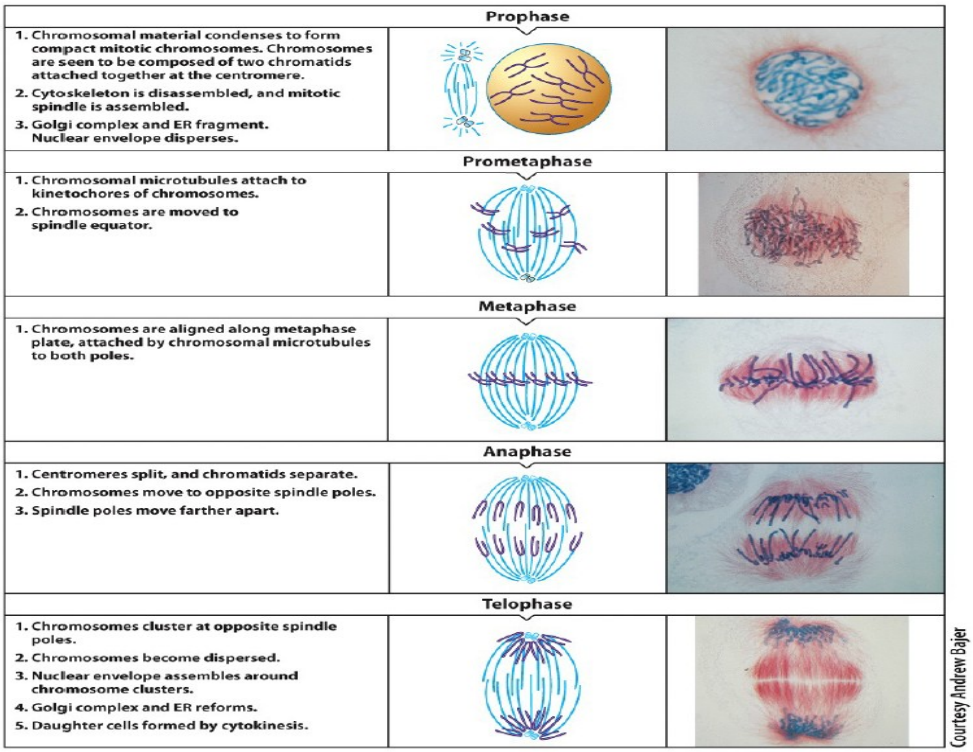
- Duplicated Chromosomes migrate to middle of spindle poles
- Equatorial plane is called metaphase plate
- Nuclear membrane broken down

Anaphase

- Cohesin breaks down, releasing sister chromatids
- Centromeres split and chromatids separate
- Chromosomes move to opposite spindle poles

Telophase

- Chromosomes cluster at opposite spindle poles
- Condensin degrades
- Daughter cells form by **cytokinesis**
- Nuclear envelope assembles around new chromosomes
- 2n; 2c values



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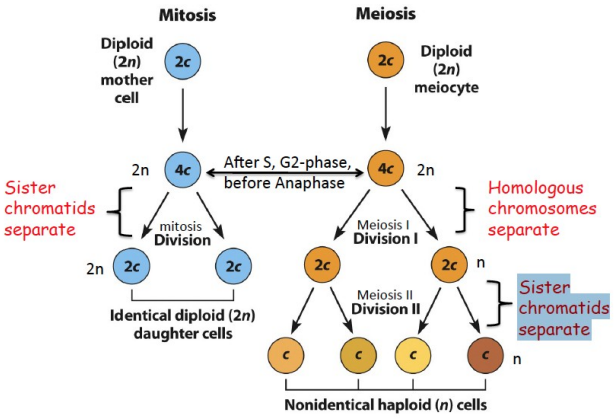
Meiosis

- Occurs in germ (sex cells)
- Produces 4 genetically distinct haploid cells
- G1, S and G2 are the same as mitosis but homologous chromosomes separate first, then sister chromatids separate



Stages

Meiosis 1 (Reduction Division):

- Produces two haploid daughter cells that are distinct… n;2c

Prophase 1: Leptonena

- Chromosomes (w/ sister chromatids) begin to condense

Prophase 1: Zygonema

- Homologous Chromosomes begin to pair

Prophase 1: Pachynema

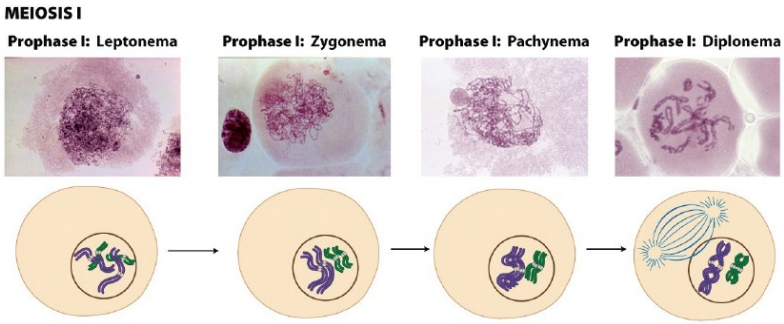
- Homologous chromosomes are fully paired
- Crossing over/recombination occurs
- Pairing of chromosomes is called synapsis and is facilitated by formation of synaptonemal complex

Prophase 1: Diplonema

- Homologous chromosomes separate, except at chromatids

Prophase 1: Diakinesis

- Paired chromosomes condense further and attach to spindle fibers



Metaphase 1:

- Paired Chromosomes align on equatorial plane

Anaphase 1:

- Homologous chromosomes disjoin and move to opposite poles

Telophase 1:

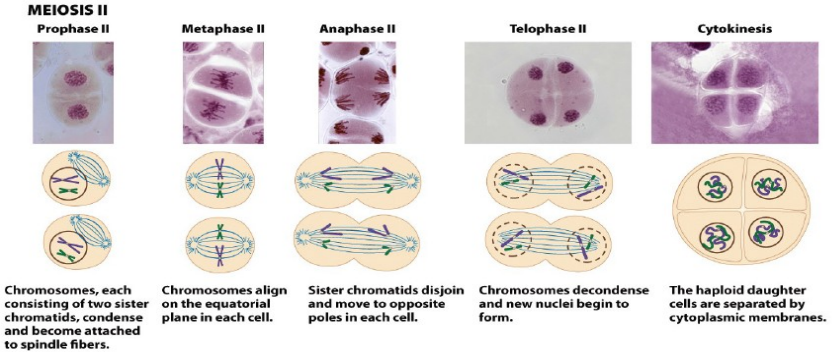
- Chromosomes are separated and new nuclei begins to form

Crossing Over

- Involves breakage of chromatids and the exchange of broken pieces b/t homologous pairs
- Homologous Chromosomes begin to pull apart but remain joined at crossing over junctions (**chiasmata**)

Meiosis II

- Mimic Mitotic division but products are haploid
- Kinetochore position changes b/t prophase 1 and II



Mendelian Inheritance

Chromosome Terminology

Locus*:* Specific region on chromosome. Could be gene our unique sequence
Allele: Alternate forms of a gene. Ex: "A or a" (Typically designated after recessive trait)
Dominant: Expressed factor
Recessive: Latent/Hidden Factor

Genotype: Allelic combination
Phenotype: Physical appearance
In-bred: Reproduction of same plant. Plant structure promoted self fertilization
Homozygous: Both alleles identical
Heterozygous: Both alleles are different
Monohybrid Cross: Single Trait. Results in 3:1 Ratio in F2 Generation
Dihybrid Cross: Two Traits. Results in 9:3:3:1 Ratio in F2 Generation

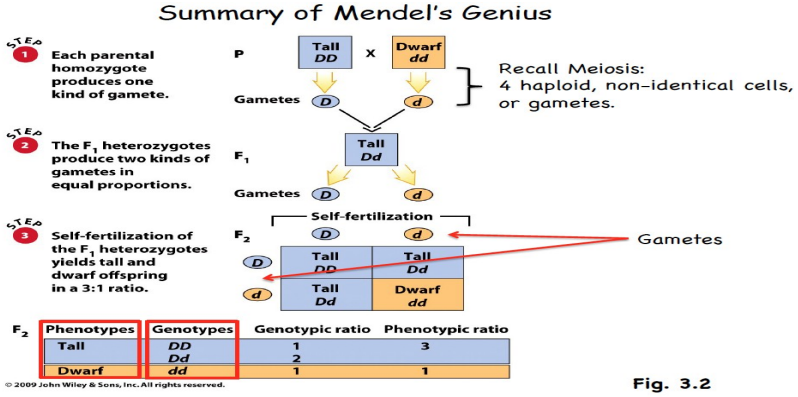


Fig. 3.2

Principle of Dominance

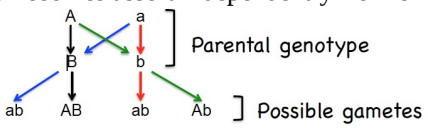
- One allele may conceal the presence of another

Principle of Segregation

- Two different alleles segregate from each other during the formation

Principle of Independent Assortment

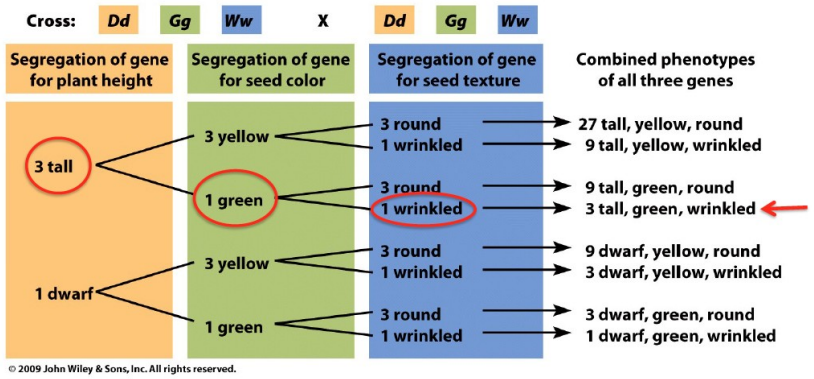
- Alleles on different pairs of chromosomes assort independently from one another (Anaphase 1)



Applications of Mendel's Principles

Fork-Lined Method

- Used for predicting the outcome of a cross involving three independently assorting genes



Probability Method

Multiplicative Rule

- Events A and B are independent, then the probability that they occur together is the product of their individual probabilities

Additive Rule

- If events A and B are independent and do not overlap, then the probability of <u>at least one of them occurring</u> is the sum of their individual probabilities

<u>Test Cross</u>

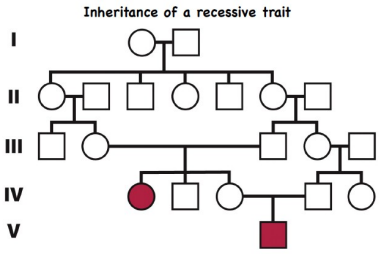
- Individual of unknown genotype crossed with homozygous recessive individual

Pedigrees and Sex Chromosomes

- Show the relationships b/t members of a family member (usually phenotypes are mapped)
- Assume individuals marrying in family are homozygous dominant

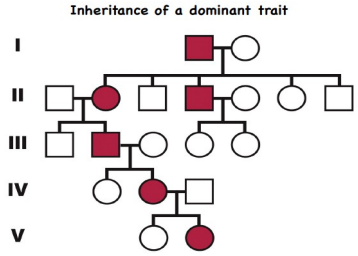
Recessive Inheritance is likely when:

- Trait suddenly appears
- Trait skips a generation



Dominant Inheritance is likely when:

- Every affected individual has at least one affected parent
- Trait manifested in at least one person in every generation

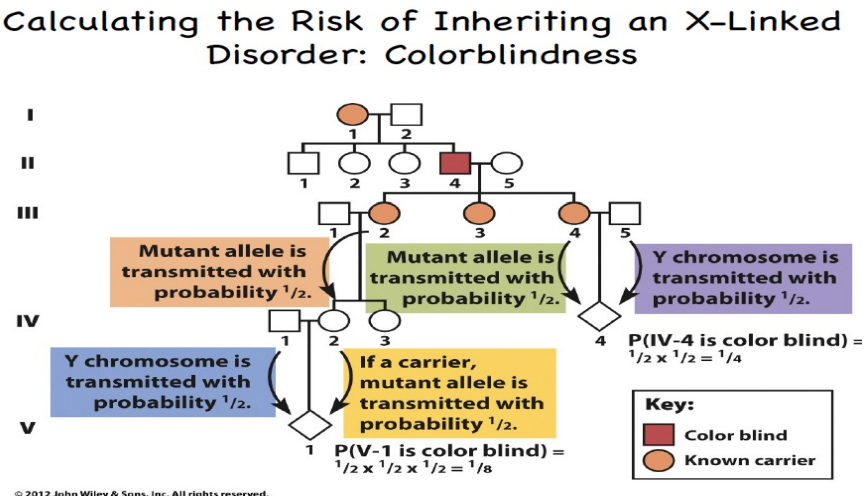


<u>Factorials</u>

- Used to calculate Binomial probability that exactly *x* progeny will fall into one class and y into the other class

<u>Sex Chromosomes</u>

- Non-autosomal Chromosomes
- Females are XX
- Males are XY
- During meiosis in males, the X and Y chromosomes pair
- There are roughly 397 genes on the Y chromosome but fewer than 100 are functional. Thus there are few Y-Linked Traits
- Y chromosome carries fewer genes than the X chromosome
- ***<u>Psedoatosomal</u>** <u>Genes</u>* are present on terminal regions of both X and Y chromosomes and do not follow X or Y-Linked patterns of Inheritance
- Lots of genes on X chromosome don't have a homologue on the Y chromosome therefore are hemizygous
- **<u>Hemizygous:</u>** Recessive allele would manifest itself. Mutation is X-Linked
- X-Linked mutations are more common in males



X-Chromosome Inactivation

- In mammals, one of the female X chromosomes are inactivated
- In cats and mice, one of the female X-chromosomes become inactivated. Resulting in change of coat color (mosaic)
- Inactive X-chromosome condenses into matter called Barr Body. Chromosome remains in this state through all somatic tissues
- In drosophila the dosage compensation for X-linked genes is achieved through hyper activating the single X chromosome in males
- In mammals, dosage compensation for X-linked genes is achieved by inactivating one of the two X Chromosomes in females

Mutations and Allelic Variations

The effects of Random Mutations

- Mutations can arise spontaneously as a result of an error during DNA synthesis
- Base pairs undergo altered pairing properties
- ***Tautomers:*** two isoforms of DNA
- Rare Isoforms have altered base pairing properties and incorporation of the rare isoform during replication leads to altered DNA sequences
- Mutations of DNA in germ line will be inherited
- Mutations can also be induced by exposure to chemical mutagens

What induces mutations

Chemical Mutagens:

Type 1: Mutagenic only to replicating DNA

Type 2: Mutagenic to replicating and non replicating DNA

Radiation:

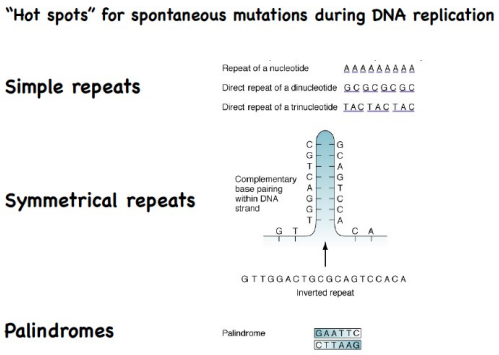
- Absorption of UV energy by pyrimidines results in dimerization

DNA:

- Induced by DNA itself due to transposable elements from viruses

Hotspots for mutations

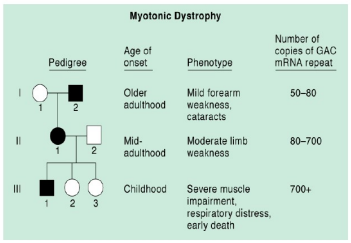
- Simple repeats
- Symmetrical Repeats
- Palindromes



Single Base Mutations
Silent Mutation: No effect
Nonsense: Codes for early stop codon
Missense: Results in change of amino acid

- Up to 40 copies of triplet repeat are stably inherited, but larger number of copies are unstable

The expanding triplet/trinucleotide repeat diseases can show increased severity and/or earlier onset from one generation to the next



Mutations affect the coding region by:
Changing protein to non-functional form:

- Premature Truncation
- Changes to protein folding (targeted for degradation, compromised activity, prevents protein localization
- Changes in post-translational modifications (prevents protein localization)

Mutations can affect the coding region by:

- Prevent or reduce transcription
- Prevent or reduce translation (mRNA is unstable, ribosomes can't bind, mutation of start codon)

Allelic Variation and Gene Function

- A single gene may control several traits
- Multiple genes may control a single trait

Wild Type: Most common allele (+ sign superscript is used)

- All other alleles are considered mutants
- Any allele found to bet at frequencies of 1% is considered to be **polymorphic**

What makes allele Dominant/Recessive
Recessive mutations almost always involve loss of gene function

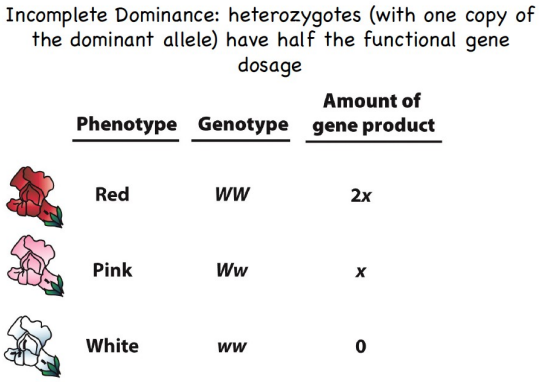
- Complete loss of function = **null allele**
- Partial Loss of function = **hypomorphic allele**
- Loss of function mutations are usually recessive

Dominant mutations can involve a loss of protein function of gain of protein function

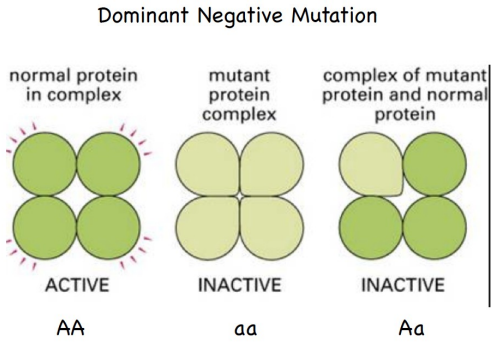
Loss of Protein Function:

Incomplete Dominance: Mutant phenotype is between Aa and AA (heterozygous and homozygous)

- One allele is partially or incompletely dominant over the other



- *Dominant Negative:* Can interfere with function of the wild type protein



Gain of Protein function:

- Enhances the function of wild type protein
- New function is created

Codominance

- Heterozygote expresses the phenotypes pf both homozygotes
- Neither allele is dominant

Allelic Series: Describes the dominance hierarchy of multiple alleles

Multiple Genes may contribute to same phenotype

Complementation Test: used when we need to discover if there lies a new mutation in a novel gene or if its just another allele of an already known mutation (cross two mutants together)

Gene Action

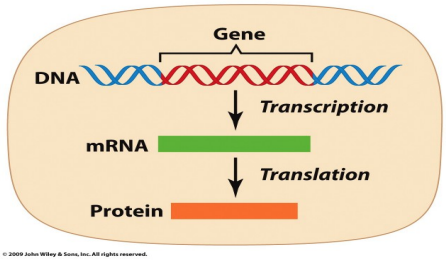
Conditional Mutations: Phenotypes are influenced by both genetic and environmental (internal or external) factors

Incomplete Penetrance: Individuals do not express a trait even though they have the genotype for it

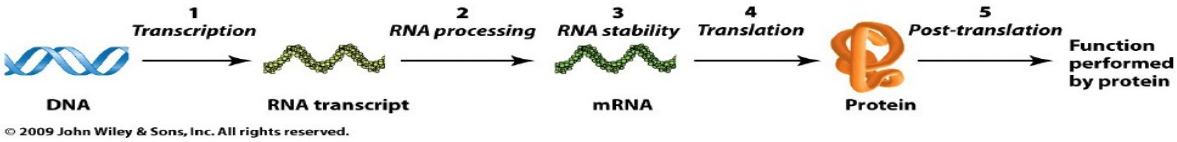
Variable Expressivity: A trait is not manifested uniformly among individuals that show it

Prokaryotic and Eukaryotic Transcription

Central Dogma: Transfer of information from DNA to protein is a two step process in all organisms

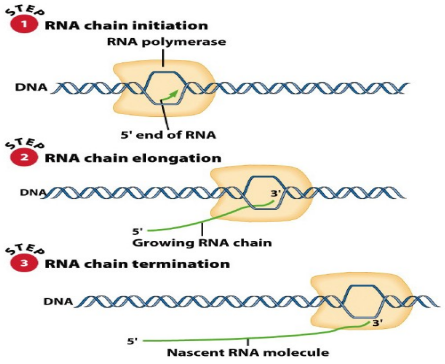


The central dogma of molecular biology



General features of RNA synthesis from DNA template include:

- Template strand (3' to 5')
- Non Template strand (5' to 3')
- mRNA strand
- RNA polymerase moves across DNA strands and unwinding DNA double helix



There are significant differences between prokaryotes and eukaryotes in the initiation and termination of transcription.

- 5 Kinds of RNA (tRNA, mRNA, rRNA, snRNA, pre-mRNA)

Steps of RNA transcription(Prokaryotes)

Initiation

- RNA polymerase binds to promoter region(occurs at -10 and -35 base sequences)

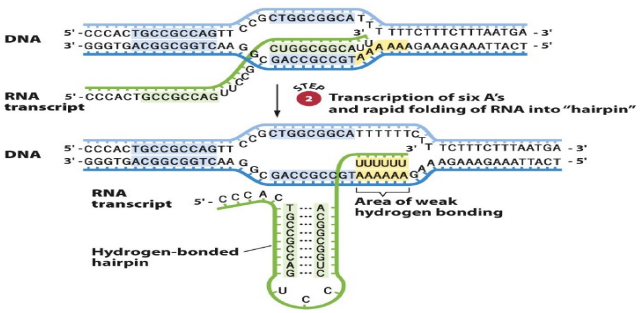
Elongation

- In prokaryotes genes are closely spaced and several can be encoded on a single RNA molecule

Termination

- Occurs at transcription terminator sequence

Step 3: Termination. A transcription terminator sequence in *E. coli* (prokaryote)



Steps of RNA transcription(Eukaryotes)

- Primary transcript is processed and exported to the cytoplasm for translation
- Promoter of a typical eukaryote is usually a CAAT box or TATA box
- Eukaryotic promoters also position RNA polymerase for accurate initiation of transcription
- Transcription factors are recruited first to DNA then polymerase binds to transcription factor and DNA

Introns and Splicing

Introns:

- noncoding sequences located b/t coding sequences
- Introns are removed from the pre-mRNA and are not present in mature mRNA

Exons:

- Both coding and non-coding sequences
- Remain in mRNA after splicing

Differences in the initiation, elongation, termination and processing of transcripts between Prokaryotes and Eukaryotes.

Prokaryotes	Eukaryotes
1. -10 and -35bp regions upstream of start site	1. TATA box and CAAT box ~-20 and -80 bp upstream of mRNA start site
2. Polymerase binds DNA	2. Transcription factors bind DNA, which then recruits the polymerase
3. Several genes can be transcribed on one mRNA transcript	3. Typically one gene per mRNA transcript
4. Transcription and translation can occur simultaneously	4. Transcription occurs in the nucleus, translation occurs in the cytoplasm
5. mRNA does not undergo further processing	5. mRNA is further processed (5' cap, 3' poly A tail added, introns removed)
6. Termination requires a hairpin sequence followed by 6 A's, polymerase falls off	6. Polymerase recognizes termination sequence AAUAAA, and the mRNA is cleaved at downstream GU site