Exam I Study Guide

Table of Contents

Genetics & Genomics

- Genetics
  - Study of inherited traits and their variation and transmission
  - Levels: DNA → gene → chrom → genome → indiv → fam → pop
- Definitions
  - Exons: how DNA encodes proteins
  - Genes: units of inheritance
  - Chrom: long DNA molecule with part/ all of gen mat
  - Genome: complete gen instruc for organism
  - Euchromatin = light part of chrom, swappable dna
  - Heterochromatin = dark part of chrom filled with tandem repeats, telomeres/ centromere
  - Somatic cells: 23 chrom pairs (22 auto, 1 gamete cell)
  - Exome = entire exon genome (1.5% of genome, 21k genes); great for revealing rare mut since its more sensitive than GWAS
- Important Info
  - ~50% of genes are tandem repeats
  - Mutations cause disease via loss/ gain of fx, creating lethal, suppressive, blocked, or non-active genes
- Biotechnology
  - DNA info can be considered with other info types to learn about health/ diseases

- Precision medicine is a medical approach that consults DNA info to select drugs that are most likely to work/ have least side effects in an indiv
- Genome editing: remove, replace, and or add specific genes; practical apps include food biotech, agric, cell therapy, disease models

Mitosis

- Cell Cycle
  - Cells must divide in order for organism to grow
  - Monitored using cyclins which signal cell to divide
- Phases
  1. Interphase
  - G1: grow/ multiply org (goes to G0 or S from here)
  - S: dna rep, create mitotic spindles
  - G2: grow, MT assemble, 2 centrosomes/centrioles form
  2. Prophase: DNA coiling, MT organize into spindles, nuc mem breakdown
  3. Metaphase
  4. Anaphase
  5. Telophase: spindle breakdown, reformation of nuc
  6. Cytokinesis
- Definitions
  - Centromere: joint part of chromatids
  - Kinetochore: prot piece at site of centromere
  - Mitotic spindle: MT that connect to kinetochore
  - Centriole: org formed from MT
  - Centrosome: centriole + MTOC (MT organizing center)
- Ploidy

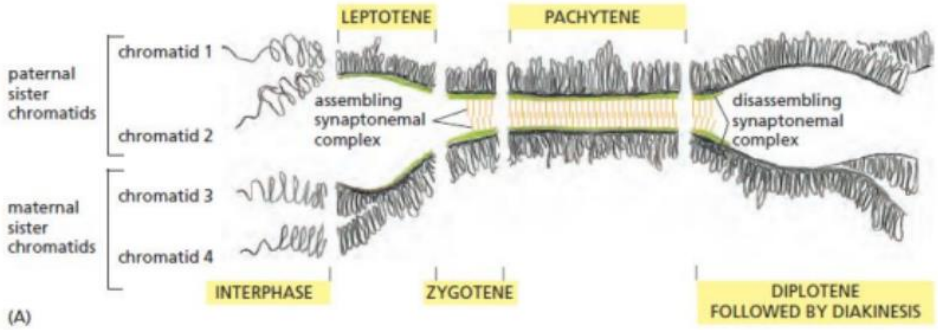
Phase (Mitosis)		# Chromosomes	# Chromatids
Prophase	2n	46	92
Metaphase	2n	46	92
Anaphase	4n	92	92
Telophase	4n	92	92
End of Mitosis (separated cells)	2n	46	46

- Endoreduplication: incr cell size/ DNA content by repeating interphase (skipping mitosis)

Meiosis

- Purpose of Meiosis: genetic diversity; enable survival from enviro challenges
- Homologs: same genes, *not same alleles* (unidentical)
- Meiosis I
  1. Prophase I: (Stages of **Crossing Over**)
  - Leptotene (S1): “thin ribbon”, sis chromatids coalesce
  - Zygotene (S2): “ fused”, synaptonemal complex formed by bridging chrom 2gthr
  - Pachytene (S3): “thick”, bivalent formeg (actual cross over bridge)

- Diplotene (S4): “two”, synaptonemal complex disassembles leaving a chiasma
- Diakinesis (stage 5): nuc disappears, DNA coil, centrosomes reach pole



2. Metaphase I
- Homo pairs on equator **(indep assort)**
- Possibilities: 2^n (n = #chrom); 2^23 = 8mil possible indep assort
3. Anaphase I
4. Telophase I: partial formation of nuc, spindles disappear

Phase (Meiosis I)	# Chromosomes	# Chromatids
Prophase I	46	92
Metaphase I	46	92
Anaphase I	46	92
Telophase I	46	92
End of Meiosis I (separated cells)	23	46

2n

n

- Meiosis II
  1. Prophase II: disassembly of nuc
  2. Metaphase II
  3. Anaphase II: sep by centromere; 2n after this
  4. Telophase II

Phase (Meiosis II)	# Chromosomes	# Chromatids
Prophase II	23	46
Metaphase II	23	46
Anaphase II	46	46
Telophase II	46	46
End of Meiosis II (separated cells)	23	23

n

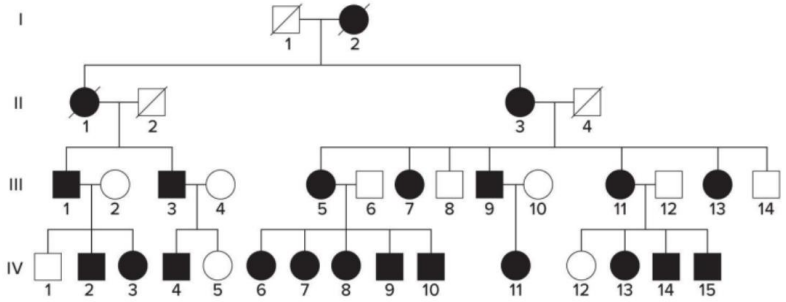
2n

- Comparison between mitosis and meiosis
  - Mitosis: sis chromatids sep
  - Meiosis I: homo chrom sep
  - Meiosis (overall): 27 crossovers in spermatogenesis; 42 in oogenesis
- XY Recombination
  - Purpose: remove possible mutations/ maintain genetic integrity
  - No need for X recombo bc of x inactiv

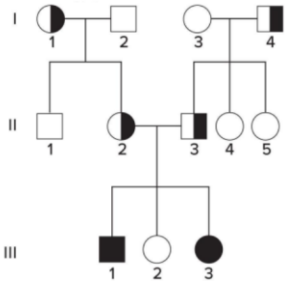
- Y recombo: hairpin that replaces alleles using identical palindromic set on other side of pin

Mendelian Inheritance

- Monogenics: single gene inheritance (rare) allows for disease prediction/ rx
- Work of Gregor Mendel
  - Observations: plant traits (plant color/ shape, stem location/ length, seed/ coat color)
  - Findings: certain traits appeared more freq (dom) and others less (rec)
  - Significance: genes (elementens) are hereditary/ inheritable
- Mendelian Laws
  1. Segregation: each allele inherited from parent is separated during meiosis (each daughter cell has one copy of allele which further leads to gen diversity)
  2. Independent Assortment: genes of diff traits on diff chrom (or far apart on same chrom) don't influence the chance of inheriting the other
  3. Dominance: dom alleles will display gene expression and mask rec allele
- Gain/ Loss of Function
  - Gain: dom trait; usually forms toxic prot
  - Loss: rec trait; no prot made which is usually why rec prod more severe diseases
- Genetic Problem Sets
  - Probability for dihybrid: RRrr x YYyy → do each as monohybrid → get ratios → multiply ratios together
  - Autosomal Dom: no generational skips



  - Autosomal Rec: generational skips; ex: albinism



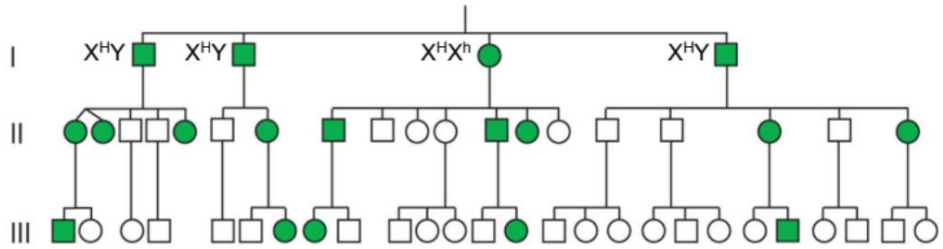
Non/ Mendelian Inheritance

- Factors that alter single-gene phenotypic ratios

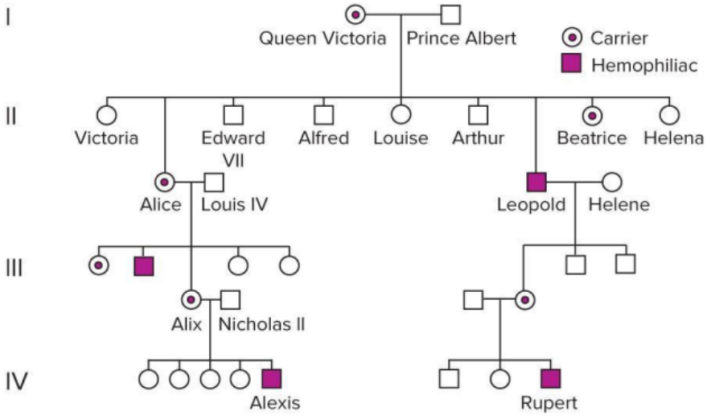
Factor	Effect	Example
Lethal alleles	Allele kills organism (homo dom)	Achondroplasia
Multiple alleles	Two germline gene mut (compound hetero) causing disease (auto rec) R*r* x R*r* → *rr*	Cystic Fibrosis
Incomplete dominance	Hetero pheno is in between (pink flowers from red/ white ones)	Familial hypercholesterolemia (lacks half of needed choles receptors)
Codominance	Hetero pheno is indistinct (polka dotted flowers from red/ white ones)	ABO blood type (A/B codom to each other and dom to O)
Epistasis	One gene masks another phenotypically	Bombay pheno (hh causes O no matter parents type)
Penetrance	Indiv with geno doesn't express assoc pheno; all or none expression (auto dom) $Pen. = \frac{\#\ showing\ pheno}{\#\ total\ with\ geno}\ x\ 100\%$	Polydactyly
Expressivity	Gen assoc with pheno of var intensity	Repeat expansion diseases
Pleiotropy	Pheno has many sx; one gen has many fx ('pleio' = many; 'tropy' = change)	Marfan syndrome Freidreich's ataxia
Phenocopy	Trait appears to be inherited but is from enviro	Infection (i.e. HIV)
Genetic heterogeneity	Diff geno cause same pheno	Osteogenesis imperfecta

- Y Chromosomes
    - Encodes 70-200 genes; many palindromes which destabilize DNA rep
    - 95% male specific region (MSY) with palindromes, SRY, and AZF
    - 5% pseudoautosomal regions (PAR1 and PAR2) where crossover occurs
    - SRY: sex-determining region Y located at Yp11.3 and encodes transcr factor
    - Y-linked traits rare bc few coding regions on Y
- X Chromosomes

    - Encodes 900-1,400 genes
    - mtDNA prone to free radical exposure leading to more mut (also no DNA repair or crossing over)
    - X-Linked Dom:
- Expressed in females in one copy
- More severe in males
- Passed from fathers to daughters (no sons)



    - X-Linked Rec:
- Expressed in males (always), Xh Xh female, and rarely in XH Xh female
- Passed from mothers to sons or from fathers and Xh Hh or XH Xh mothers to daughters
- Usually skips generation

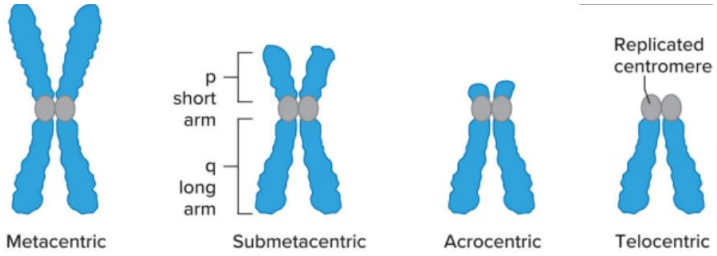


- Sex-Limited/ Influenced Traits
    - Limited: only seen in one sex (ex. preeclampsia)
    - Influenced: dominant in one sex and recessive in other (ex. baldness)
- X-inactivation
    - Needed to balance inequality of gene expression (aka dosage compensation)
    - Lyon hypothesis: either X chrom randomly selected/ activated in each cell creating a genetic mosaic in females
    - Is an ex of epigenetic change where gen is same but pheno diff
    - XIST (x inactiv specific transcript) transcribed at XIC (x inactiv center) to prod non coding RNA to silence x chrom
    - XA expressed in one cell Xa in other creating a **manifesting heterozygote**

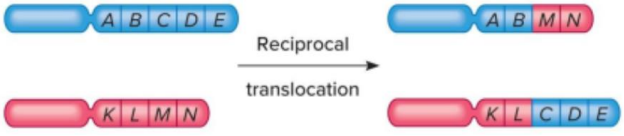
- Genomic imprinting (parent-of-origin effects)
    - Gene expression dep on parent who transmits gene
    - Silence specific genes in allele-dep manner **(can silence dom allele)**
    - Epigenetic phenomenon that occurs via cytosine methylation
    - Maintained in mitosis but disrupted in meiosis (so it becomes dep on indiv, not indiv's parent)

Aneuploidy & Chromosomal Rearrangements (Ch.12,13)

- Chromosome features: replication origins, centromeres, and telomeres (TTAGGG)
- Centromere position:

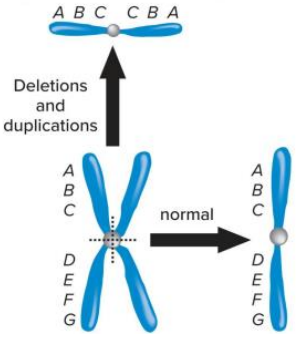


- Chromosome Visualization
    - Obtained: fetal (amniocentesis) and adult tissue (WBC or cheek swab)
    - Prepped: metaphase spread, then staining
    - Viewed:
    - Banding (dye applied to highlight diff b/w chrom)
    - Ideogram (shows cytogenetic bands using B/W diagrams)
    - FISH (fluoro in situ hybrid that labels cDNA to identify indiv genes & differentiate chrom)
    - Karyotype (displays by length and shows chrom # per set)
- Ploidy
    - Polyploidy: multiple fertiliz or diploid gametes leading to extra chrom sets
    - Aneuploidy
    - Extra or missing ***indiv*** chrom from **nondisjunction**
    - Usually lethal; trisomy 21, turner (XO), jacobs (XYY), and klinefelter (XXY) are ex
- Structural Abnormality Causes
    - Chrom breakage (deletion, inversion, duplication, translocation)
    - Illegitimate crossing-over
- Translocation Types
    - Reciprocal: two nonhomo change parts (ex: ABCD WXYZ → ACYZ WXCD)
    - Robertsonian: two nonhomo acrocentric chrom break at centromere and fuse long (p) arms 2gthr (*break a leg Robert*)

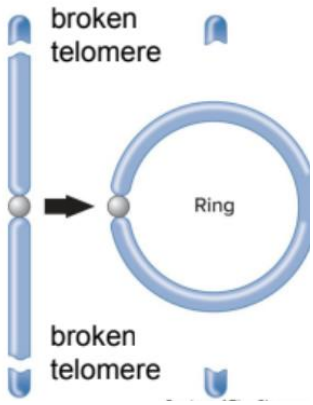


- Inversion Types
    - Pericentric: inverted region with centromere (peri = around, centric = center)

    - Paracentric: inverted region without centromere (para = beside)
- Alternate Chromosome Types
    - Isochromosomes: “iso” = equal; duplicated chrom from mitotic or meiotic error



    - Ring chromosomes: telomeres lost (from radiation), so sticky ends of chrom fuse to form ring; can be inherited or sporadic, but neither affects health



Genetic Diseases (Ch.12,22)

- Chrom # Aberrations
    - Down Syn (trisomy 21)
    - Edwards Syn (trisomy 18)
    - Patuau Syn (trisomy 13)
    - Sex Chrom: XXX (triple x), XO, (turner), XXY(klinefelter), XYY (jacobs), XXYY syn
- Subchrom Aberrations
    - Cri du Chat: short arm deletion in chrom 5
- Gene Aberrations
    - Copy Num Var: num of copies (duplic or del) varies b/w indiv
    - Ex: Charchot marie tooth
    - CGH (comparative genomic hybridization) array used for testing how many copies you have
- Identify and understand types of mutations and processes responsible for mutations.
- Know the definitions and classification of genetic diseases with examples presented during lecture and in the textbook.
- Understand the importance of genetic testing with appropriate, discussed examples.

- Know examples of modern approaches towards treatment of genetic diseases.
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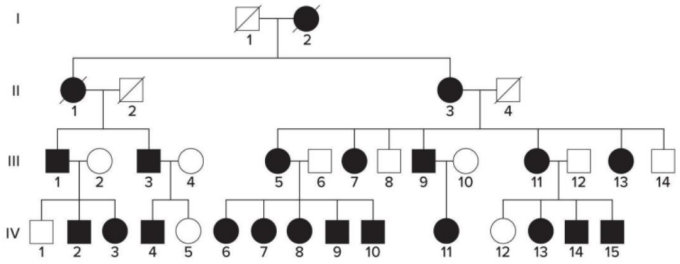
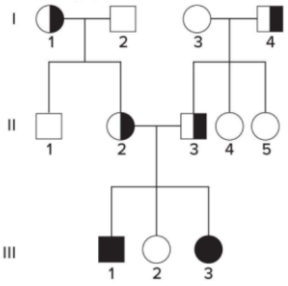
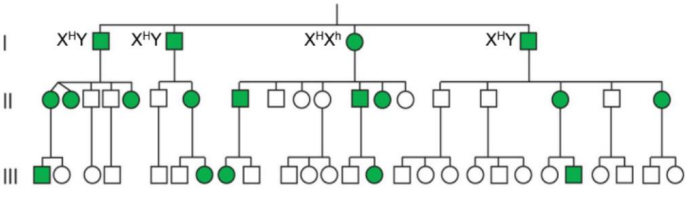
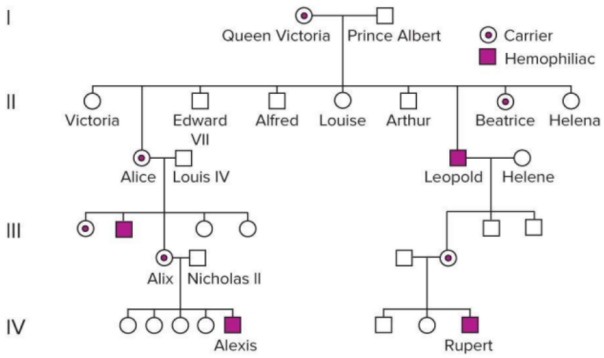
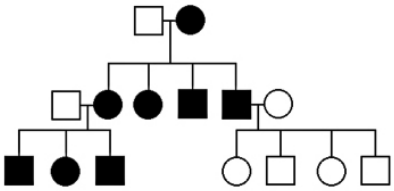
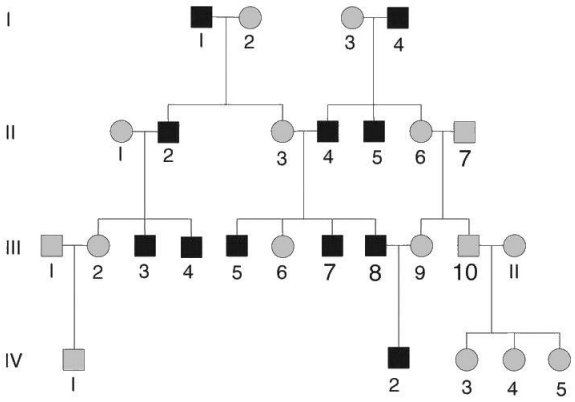
Mitochondrial Genetics (Pg.753-63,800-11)

- Learn about mitochondria structure.
- Roles of mitochondria in the cell.
- Mitochondria as energy factories – learn basic steps in energy production from different substrates.
- Electron chain and oxidative phosphorylation.
- ATP as a “power currency.”
- Mitochondria origin and dynamics.
- Mitochondrial inheritance and heteroplasmy.
- Disorders caused by mitochondrial DNA mutations.
    - MERRF → caused by heteroplasmy (diff mtDNA types in cell)

Pedigree Shortcuts

Condition	Diagram	Notes
Autosomal Dominant		Auto bc seen in both fe/males Dom bc no generation skips
Autosomal Recessive		Auto bc seen in both fe/males Rec bc not expressed in every generation
X-Linked Dominant		X bc fathers always pass to daughters/ mothers to sons Dom bc no

		generation skips
X-Linked Recessive		X bc always seen in males with affected mothers Rec bc skips generation
Mitochondrial		Mothers always pass to children
Y-Linked		Fathers always pass to sons only

Abbreviation Glossary

Auto: autosomal
Div: division
Det: determine
Dom: dominant
Eu: eukaryote
Enviro: environment
Fx: function
Freq: frequent(ly)
Gen: genetic
Geno: genotype
Homo: homozygous

Hetero: heterozygous
Indep: independent
Incr: increases
Mem: membrane
Multinuc: multinucleated
Molec: molecule
MT: microtubules
Nuc: nucleus
Org: organelle
Pro: prokaryote
Prot: protein
Prod: produce
RBC: red blood cell
Rec: recessive
Ribo: ribosomes
Rxn: reaction
Rx: treatment
Sx: symptoms
Sig: signal
Seq: sequence
Sim: simultaneously
Stim: stimulus
Syn: synthesis
Transc: transcribe
Transl: translate
Trans: transport
Var: variable/ varying