

# 1 Chromosomal Basis of Inheritance

Chapter 15

## 2 Timeline

- ✳ 1860's Mendel proposed discrete inherited factors segregate and assort independently during gamete formation
- ✳ 1875 cytologists work out mitosis
- ✳ 1890 cytologists work out meiosis
- ✳ 1900 Coffens, de Vries, and van Seysenegg independently rediscover segregation and independent assortment
- ✳ 1902 cytology and genetics converge w Sutton, Boveri who notice parallels between meiosis and Mendel's factors

## 3 Thomas Hunt Morgan

- ✳ Traced gene to a specific chromosome (early 1900s)
- ✳ Used *Drosophila melanogaster*
- ✳ Flies are easily cultured, breed prolifically, short generation time, only 4 pr of chromosomes visible w light microscope
- ✳ Identified X and Y chromosomes
- ✳ Discovered sex linked genes

## 4 Laboratory Research on Fruit Flies

- ✳ Bred flies and observed characters for a year before finding a single male fly with white eyes
- ✳ Wild type is normal or most frequently observed phenotype (red eyes brown body straight wings)
- ✳ Mutant phenotypes: alternatives to the wild types which are due to mutations of the wild type gene

## 5 Wild type fruit flies

female

male

## 6 Sex Linked Genes

- ✳ Deduced eye color linked to sex and gene for eye color is located only on the X chromosome
- ✳ If only on X, then females XX carry two copies of the gene and males have only one
- ✳ If recessive, females must be homozygous to show trait
- ✳ Sex-linked genes: located on sex chromosomes (X or Y)
- ✳ X is larger and has more genes on it; both genders may be affected

## 7 Fly Life Cycle

## 8 Red Eyes      White Eyes

## 9 Linked genes and independent assortment

- ✳ Linked genes are located on the same chromosome and tend to be inherited together unless there is a crossover
- ✳ Linked genes do not assort independently; move together through meiosis and fertilization
- ✳ Dihybrid cross will not result in new phenotypes (unless there is a crossover) or in phenotypic ratio of 9:3:3:1

## 10 Genetic Recombination

- ✳ Offspring with new combinations of traits different from those combinations found in the parents
- ✳ Results from events of meiosis (crossovers) and random fertilization
- ✳ When 50% of offspring are recombinants, indicates that the two genes assort randomly

## 11 Gray, wild wings crossed w black, vestigial wings

Recombination frequency

$391 \text{ recomb} / 2300 \text{ total offspring} \times 100 = 17\%$

## 12 Crossing over can unlink genes

- ✳ Morgan's results from this dihybrid testcross showed that the genes were neither unlinked nor totally linked
- ✳ If unlinked, 1:1:1:1 ratio of all possible phenotypic combinations
- ✳ If completely linked, then 1:1 of parent types only
- ✳ Morgan proposed mechanism to break linkage: crossing over

## 13 Mapping linear sequences on genes

- ✳ Some genes linked more tightly than others
- ✳ b and vg frequency is 17%
- ✳ b and cn (cinnabar eyes) is 9%
- ✳ Sturtevant: probability of crossing over is directly proportional to distance between them
- ✳ one map unit is 1% : one centimorgan
- ✳ If recombination frequency is 50%, they are not distinguishable from unlinked genes

## 14 Determination of gender

- ✳ 2 kinds of gametes determines sex of offspring: heterogametic sex
- ✳ XX – homogametic female all ova X
- ✳ XY – heterogametic male  $\frac{1}{2}$  sperm X;  $\frac{1}{2}$  Y
- ✳ Sry-sex determining region on Y is responsible for triggering events that lead to testicular development
- ✳ Sry (pleiotropic) codes for protein that regulates other genes

## 15 Sex linked Disorders in Humans

- ✳ Color blindness; male pattern baldness X
- ✳ Hairy ears Y

- ✦ Hemophilia X
- ✦ Duchenne muscular dystrophy X
- ✦ If X linked and male gets a mutant X, male expresses trait even if recessive-only one X: hemizygous-only one copy of gene present
- ✦ Father's can't pass on to sons; pass to all daughters

16  **Barr body**

- ✦ In females, most diploid cells have only one fully functional X chromosome
- ✦ Lyon hypothesis (Mary Lyon) each embryonic cell inactivates one X producing densely staining body: Barr body
- ✦ Barr bodies are highly methylated: XIST gene X Inactive Specific Transcript (RNA)
- ✦ Barr bodies are reactivated in gonadal cells that undergo meiosis to form gametes
- ✦ Females are mosaic- could be paternal or maternal X expressed (calico cats; sweat gland dev in humans)

17  **Calico Cat**

18  **Phenylketonuria**

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- ✦ Autosomal recessive
- ✦ Many have blue eyes and are lighter than other family members
- ✦ Inability to breakdown phenylalanine or its breakdown products (tyrosine)
- ✦ Mental retardation if not detected early
- ✦ Prominent cheek/jaw bones
- ✦ Microcephaly in untreated cases

19  **Alterations of chromosome number**

- ✦ Nondisjunction: meiotic or mitotic error during which certain homologous chromosomes or sister chromatids fail to separate
- ✦ Meiosis I: homologous pair does not separate
- ✦ Meiosis II: sister chromatids do not separate
- ✦ Results in one gamete receiving two of same type of chromosome and another gamete receiving no copy

20  **Aneuploidy**

- ✦ Aneuploid offspring may result if normal gamete unites w aberrant one produced as a result of nondisjunction
- ✦ Aneuploid cell has a chromosome in triplicate: trisomic
- ✦ Aneuploid with missing chromosome is monosomic
- ✦ When aneuploid zygote divides by mitosis, every cell has chromosomal anomaly

21  **Down's Syndrome Karyotype**

22  **Down's Syndrome**

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- ✦ Age 35 1/380
- ✦ Age 45 1/30
- ✦ Sm head/flat back
- ✦ Thick tongues
- ✦ Extra skin on neck
- ✦ Slant eye/ epicanthal folds
- ✦ Flat nose bridge

- ✦ Short fingers/ single crease
- ✦ Wide space btwn 1<sup>st</sup> and 2<sup>nd</sup> toe
- ✦ Vary degrees MR
- ✦ Heart malformed
- ✦ Digestive tract problems

23  “somy” vs “ploidy”

- ✦ “somy” a chromosome or gene or piece of a chromosome is altered in number
- ✦ “ploidy” an entire set of chromosomes is added or missing
- ✦ Triploidy: 3n; tetraploidy: 4n
- ✦ Triploid: fertilization of an abnormal diploid egg produced by total nondisjunction
- ✦ Tetraploid: diploid zygote mitosis w no cytokinesis
- ✦ Important in plant evolution; rare among animals (may occur in patches)

24  Sex chromosome aneuploidies

- ✦ Less severe than autosomal aneuploidies
- ✦ May be due to the Y carrying few genes and copies of the X becoming Barr bodies
- ✦ XO Turner’s girls; XXX superfemale or triple X syndrome
- ✦ XXY Klinefelter’s syndrome
- ✦ XYY Extra Y syndrome; normal male, taller than family

25  Turner’s Girls

2

- ✦ XO
- ✦ Short stature, short web neck
- ✦ No ovarian function
- ✦ Short fingers/toes
- ✦ Irregular rotation wrist and elbow joints
- ✦ Heart problems
- ✦ Kidney problems
- ✦ Osteoporosis
- ✦ Problems w social interactions
- ✦ Problems w nonverbal problem solving
- ✦ Problems spatial/visual-like driving

26  Klinefelter’s Syndrome

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- ✦ XXY
- ✦ Breast development/ sparse body hair
- ✦ Sm testes
- ✦ Taller than family
- ✦ Tend to be overweight
- ✦ Language dev problem

27  Alterations of chromosome structure

- ✦ Deletion: lose fragment lacking a centromere
- ✦ Fragment joins to homologous chromosome: duplication
- ✦ Joins to nonhomologous chromosome: translocation
- ✦ Reattach to original chromosome in reverse order: inversion
- ✦ Occurs in unequal or nonreciprocal crossovers (position effects alter phenotype)

28  Cri du Chat Karyotype

29  Cri du Chat

## Deletion #5 short arm

- 30  **William's Syndrome**  
2
  - ✦ Elphin features-wide mouth, slack lower lip, full cheeks, wide spaced teeth
  - ✦ Microdeletion of #7
  - ✦ Highly verbal
  - ✦ Obsession on some objects-wheels, cars, hoovers...
  - ✦ Hypersensitivity to noise
  - ✦ Low attention span
  - ✦ gregarious
- 31  **CML: Chronic Myelogenous Leukemia**
  - ✦ Philadelphia chromosome: translocation of a piece of chromosome 22 with a small fragment from chromosome 9
  - ✦ Chronic phase may last decades, few symptoms
  - ✦ Accelerated phase: enlarged spleen, fever, bone pain
  - ✦ Blast crisis: >>#immature white blood cells- leukemia
  - ✦ Risk from infection and treatment
- 32  **Genomic imprinting**
  - ✦ Expression of some traits depend on which parent contributes the alleles for those traits
- 33  **Angelman Syndrome**  
2
  - ✦ head flat/microcephaly
  - ✦ Tongue thrusting
  - ✦ Swallowing disorders
  - ✦ Wide mouth; wide spaced teeth
  - ✦ Light hair & eyes compared to family
  - ✦ Strabismus
  - ✦ Sleep disorders
  - ✦ Fascination w water
  - ✦ Seizures
  - ✦ Dev delay; functionally severe
  - ✦ Speech problems/ nonverbal
  - ✦ Motor problems
  - ✦ Gene on maternal #15 gene
- 34  **Prader-Willi Syndrome**  
2
  - ✦ Poor muscle tone
  - ✦ Chronic hunger
  - ✦ MR
  - ✦ Problem behaviors
  - ✦ Short stature
  - ✦ Light hair/eyes compared to family
  - ✦ Deletion #15 paternal
  - ✦ Or 2 copies #15 maternal
- 35  **Triplet repeats**
  - ✦ Sections of DNA where specific triplet of nucleotides is repeated many times
  - ✦ Occur normally in many places in human genome
  - ✦ Progressive addition of triplet repeats can lead to genetic disorders such as Fragile X

syndrome and Huntington's disease

36  **Fragile X**

- ✦ Occurs in males and females
- ✦ Most common genetic cause of mental retardation
- ✦ Triplet repeat, CGG, is repeated up to 50x on one tip of a normal X chromosome, but on a fragile X chromosome is repeated >200x
- ✦ Occurs incrementally over generations; repeats accrue from one generation to the next (prefragile X to fragile X)
- ✦ More likely to occur if X inherited from mother

37  **Huntington's disease**

- ✦ Locus is near tip of #4, has a CAG extended triplet repeat
- ✦ Triplet repeat at the locus is more likely to extend if allele is inherited from father rather than from mother

38  **Extranuclear Genes**

- ✦ Occur in cytoplasmic organelles such as plastids and mitochondria
- ✦ Are not inherited in Mendelian fashion
- ✦ In plants, maternal plastid genes control variegation of leaves
- ✦ Mitochondria are exclusively from maternal cytoplasm (some metabolic diseases transmitted this way)